Abstract Book

Society of Surgical Oncology
70th Annual Cancer Symposium

Seattle, Washington
March 15-18, 2017

Electronic supplement to
Annals of Surgical Oncology
An Oncology Journal for Surgeons

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SYMPOSIUM

Society of Surgical Oncology

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Presentations Withdrawn

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ABSTRACTS

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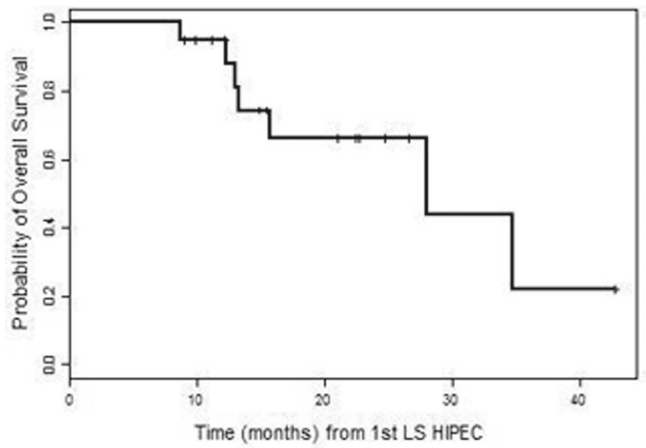
1

A Phase II Study of Laparoscopic Hyperthermic Intraperitoneal Chemoperfusion (HIPEC) for Gastric Carcinomatosis or Positive Cytology B. Badgwell,* M. Blum, P. Das, J. Estrella, X. Wang, L. Ho, K. Fournier, R. Royal, P. Mansfield, J. Ajani. *MD Anderson Cancer Center, Houston, TX.*

Background: Hyperthermic intraperitoneal chemoperfusion (HIPEC) has been reported as efficacious for patients with carcinomatosis of colonic, appendiceal, and (recently) gastric origins. The purpose of this clinical trial was to perform HIPEC in a neoadjuvant fashion via a minimally invasive approach without cytoreduction for patients with gastric cancer and positive cytology or low-volume carcinomatosis. Patients who were then found to have resolution of all extragastric disease were candidates for gastrectomy. Methods: Patients with gastric or gastroesophageal adenocarcinoma and positive peritoneal cytology or radiologically occult carcinomatosis who had completed systemic chemotherapy received laparoscopic HIPEC with 30-mg mitomycin C and 200-mg cisplatin. Patients whose peritoneal disease resolved were offered gastrectomy. The primary end point was overall survival (OS), with secondary end points of postoperative complications and gastrectomy rate. Results: We enrolled 19 patients and treated them with 37 laparoscopic HIPEC procedures. Median age was 51 years (range, 29-69 years). Six patients had positive cytology only, and 13 had carcinomatosis. All patients were treated with a median of 8 cycles (range, 3-12 cycles) of systemic chemotherapy before enrollment. Fourteen patients were also treated with chemoradiation therapy. After HIPEC, the major morbidity and mortality rates were 3% and 0%, respectively. Median length of hospital stay was 3 days (range, 3-6 days). Five patients went on to gastrectomy. Median follow-up was 18.9 months (calculated among survivors starting from the date of diagnosis of metastatic disease). Median OS from the date of diagnosis of metastatic disease was 34.7 months. Median OS from the first laparoscopic HIPEC (Figure) was 28.1 months. Conclusions: Laparoscopic preoperative HIPEC was well tolerated with an encouraging number of patients demonstrating an absence of peritoneal disease and undergoing gastrectomy. Comparative studies will be required to clarify survival outcomes. [NCT02092298]



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Immunotherapy with Anti-CD47 Antibody Inhibits Metastatic Outgrowth from Pancreatic Cancer in a Patient-Derived Xenograft Model A.D. Michaels,* S.J. Adair, S. Morioka, T.E. Newhook, M.G. Mullen, J.B. Persily, N. Jha, K.S. Ravichandran, J.T. Parsons, T.W. Bauer. *Surgery, University of Virginia, Charlottesville, VA.*

Background: Resident liver macrophages have been shown to suppress progression of hepatic micrometastases from pancreatic ductal adenocarcinoma (PDAC). We hypothesized that blockade of CD47, a tumor cell "don't eat me" signal, would inhibit outgrowth of micrometastases from PDAC in a murine model. Methods: CD47 was quantified by flow cytometry for three patient-derived PDAC (PDX) cell lines. In vitro assays were performed to evaluate the efficacy of murine macrophages to phagocytose tumor cells in the presence of an inhibitory mouse anti-CD47 monoclonal antibody (αCD47) or control mouse polyclonal IgG antibody (IgG). To assess the in vivo effects of CD47 blockade, we utilized a mouse model of occult liver metastasis from splenic injection of PDX cells. Mice were randomized to receive no treatment, control IgG (200 ug IP daily), or αCD47 (200 ug IP daily) for 50 days. Hepatic tumor growth was measured with bioluminescent imaging and progression-free survival (PFS) was determined. Results: Surface expression of CD47 of the PDAC cell lines was 41% in PDX 366, 75% in PDX449, and 95% in PDX608. αCD47 led to a 95% increase in engulfment of PDX608 cells by macrophages in vitro (7.4% vs 3.8% with IgG, $p<0.001$), while αCD47 had no significant effect on the engulfment of PDX449 cells. αCD47 significantly decreased hepatic metastases from PDX608 vs both IgG and no treatment at days 4, 7, 10, and 14 (all, $p<0.05$). Hepatic tumor burden at day 55 is displayed in Fig 1A. By 55 days, both αCD47 and IgG have led to an improvement in PFS vs no treatment (both, $p<0.05$), and αCD47 is approaching significance vs IgG ($p=0.059$) (Fig 1B). Through 21 days of treatment, αCD47 had no significant effect on hepatic tumor burden of PDX366. Both in vivo experiments are currently ongoing. Conclusions: Expression of CD47 varies among PDAC lines and correlates with efficacy of in vitro and in vivo CD47 blockade. In a preclinical study evaluating hepatic micrometastatic outgrowth from PDX cells, αCD47 inhibited micrometastatic outgrowth in the liver and increased PFS. Immunotherapy with anti-CD47 antibody is a promising strategy that warrants further investigation in PDAC.

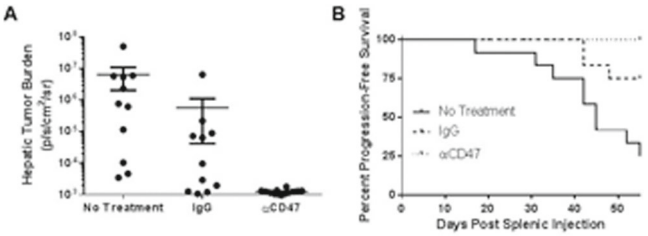

Figure 1. A) Hepatic tumor burden of mice bearing PDX608 under each treatment condition at day 55, as measured by hepatic average radiance. B) Progression-free survival of mice bearing PDX608 under each treatment condition through day 55.

3

Inhibition of Autophagy Improves Pathologic and Biomarker Response to Preoperative Gemcitabine/Nab-Paclitaxel in Potentially Resectable Pancreatic Cancer: A Phase II Randomized Controlled Trial J.L. Miller-Ocuin,* N.S. Bahary, A.D. Singhi, D.P. Normolle, B. Lembersky, r. Stoller, W. Sun, S. Ahrendt, M. Hogg, K. Lee, D. Bartlett, J. Marsh, A. Tsung, A.H. Zureikat, B.A. Boone, M.T. Lotze, H.J. Zeh. *University of Pittsburgh, Pittsburgh, PA.*

Background: Pancreatic ductal adenocarcinoma (PDA) is critically dependent on the cell survival pathway of autophagy. We previously reported the safety and feasibility of pre-operative gemcitabine in combination with the autophagy inhibitor hydroxychloroquine (HCQ) for potentially resectable PDA. Gemcitabine/nab-paclitaxel is more effective than gemcitabine alone in metastatic PDA. We sought to examine if autophagy inhibition improves efficacy of this regimen in the pre-operative setting. Methods: This is a phase II randomized, controlled trial for patients with resectable or borderline resectable PDA by NCCN guidelines. Patients were randomly assigned to 2 months of pre-operative PGH: [gemcitabine (1000mg/m2) plus nab-paclitaxel (125mg/m2) and oral hydroxychloroquine (1200mg/day)] or PG [gemcitabine (1000mg/m2) plus nab-paclitaxel (125mg/m2)]. Interim analysis was performed at 95% of accrual. Results: 54 patients (27 PGH and 27 PG) were analyzed. Primary endpoint was improvement in Evans pathologic response grade as scored by a blinded pathologist Evans grade histopathologic response was improved in PGH vs. PG (I: 11.5% vs. 37%, IIA: 34.6%, vs. 51.9% IIB: 34.6% vs. 11.1%, III: 19.2% vs. 0%; $p=0.004$). Evans grade IIB (>50% tumor destruction) or greater pathologic response was improved in PGH arm (53.9% vs. 11.1%; $p=0.001$). Secondary endpoints included improvement in serum CA 19-9 response, lymph node ratio (positive/total), and margin-negative (R0) resection rate. Percent change in CA 19-9 was greater in the PGH over PG (65.2% vs. 52.9%; $p=0.014$). PGH had decreased lymph node ratio (0.03 vs. 0.05; $p=0.002$). There was no statistical difference in R0 resection rate between groups (81.5% vs. 66.7%, $p=0.13$). Conclusions: This trial provides proof of principle for autophagy inhibition in PDA and establishes framework for future trials to evaluate novel regimens in the pre-operative setting. Ongoing corollary studies of resected tumors will help identify biomarkers of response.

4

Novel Neoadjuvant Targeted Therapy Trial with Dabrafenib + Trametinib Yields High Response Rates and Improved Relapse-Free Survival Over Standard of Care (SOC) Therapy in Patients with High-risk Resectable BRAF-Mutant Melanoma P.A. Prieto,[1]* R. Amaria,[2] A. Reuben,[1] V. Gopalakrishnan,[1] C. Spencer,[1] H. Jiang,[1] J. Zhang,[3] M. Tetzlaff,[4] A. Lazar,[4] E. Burton,[1] S. Woodman,[2] P. Hwu,[2] W. Hwu,[2] S. Patel,[2] H. Tawbi,[2] M. Davies,[2] A. Diab,[2] I. Glitza,[2] R. Bassett,[1] J. Cormier,[1] J. Gershenwald,[1] J.E. Lee,[1] A. Lucci,[1] R. Royal,[1] M. Ross,[1] J.A. Wargo.[1] *1. Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; 2. Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; 3. Genomic Medicine, University of Texas MD Anderson Cancer Center, Houston, TX; 4. Pathology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: There have been major advances in the treatment of metastatic melanoma through the use of targeted therapy and immune checkpoint blockade, and trials incorporating these agents are now being extended to patients with earlier-stage disease. The current SOC treatment for high-risk resectable melanoma (stage IIIB/IIIC) is upfront surgery and SOC adjuvant therapy; however, relapse rates are high (~70%). We reasoned that treatment with neo + adjuvant dabrafenib + trametinib (D+T) in this patient population would result in lower relapse rates and prolonged survival over SOC. Methods: To test this hypothesis, we designed a randomized clinical trial (NCT02231775) in patients with resectable Stage IIIB/C or oligometastatic stage IV BRAF-mutant melanoma. Enrolled patients were randomized 1:2 to SOC (Arm A) versus neo + adjuvant D+T (Arm B, 8 wks neoadjuvant + 44 wks adjuvant). The primary endpoint was relapse-free survival (RFS) with additional secondary endpoints. Importantly, results were validated in a similar cohort of patients treated with off-protocol neoadjuvant D+T (n=21). Results: 21 of 84 patients were enrolled (arm A=7, arm B=14). Arms were matched, and perioperative complication rates were similar between the groups. Toxicity to targeted therapy was limited. RECIST response rate to 8 wks D+T was 77%, with a pathologic complete response rate (pCR) of 58%. Early analysis revealed a significantly higher RFS in the D+T arm over SOC ($p<0.0001$), substantiating early stoppage of the trial. Similar results were seen in a validation cohort. Putative immune mechanisms of resistance to therapy were identified, with high T cell exhaustion markers (PD-1, Tim-3, and Lag-3) in baseline tumors of patients who did not achieve a pCR ($p < 0.05$). Conclusion: Neoadjuvant + adjuvant D+T is associated with a high pCR rate and improved RFS over SOC in patients with high-risk resectable metastatic melanoma. Results gained from this trial and correlative studies may yield insights into how to improve responses to this regimen, and may help change SOC.

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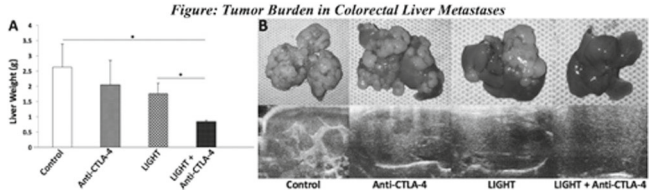
Combining Targeted Immunotherapy with Checkpoint Blockade Inhibits Formation of Colorectal Liver Metastases A.V. Maker,* N. Kunda, G. Qiao, J. Qin, B.S. Prabhakar. *University of Illinois at Chicago, Chicago, IL.*

Introduction: We have demonstrated improved survival for patients with resected colorectal liver metastases (CRLM) whose tumors contained increased numbers of tumor-infiltrating lymphocytes and expression of the cytokine LIGHT (TNFSF14). Increasing LIGHT in the tumor microenvironment may increase lymphocyte infiltration. The effect of LIGHT overexpression and checkpoint blockade on lymphocyte infiltration and tumor regression in CRLM remained to be determined. Methods: CT26LIGHT+ Balb/c syngeneic colorectal cancer cells were utilized in an immunocompetent isolated liver metastases model via splenic injection. Anti-CTLA-4 or isotype control were administered via intraperitoneal (IP) injection on days 4, 7, 10, and 13. Tumor growth was analyzed with transabdominal ultrasound biweekly. Tissues were harvested for analysis with flow cytometry, immunohistochemistry, & ImageJ Software. Results: LIGHT overexpression in the tumor microenvironment was associated with significantly decreased liver tumor weight ($p=0.001$) and metastatic burden ($p=0.04$), and correlated with increased $CD45^+$ tumor-infiltrating lymphocytes ($p=0.001$), $CD3^+$ T-cells ($p=0.02$), NK cells ($p=0.02$), and dendritic cells ($p=0.007$) compared to controls. When LIGHT overexpression was combined with anti-CTLA4 immune checkpoint blockade using an antibody to CTLA-4, combination treatment resulted in significantly decreased liver tumor burden ($p=0.03$, Figure A), and inhibition of liver metastases growth (42% vs 0.6%, $p=0.03$) compared to either treatment alone (Figure B, explanted liver, upper panel; in vivo ultrasound, lower panel). Conclusion: Increased LIGHT expression in the tumor microenvironment was associated with enhanced T-cell infiltration and significantly decreased formation of CRLM in a preclinical model. The anti-tumor immune response was further enhanced when combined with immune checkpoint blockade. In a malignancy where improved strategies are desparately needed, we demonstrate that combining targeted immunotherapy with checkpoint blockade can inhibit formation of colorectal liver metastases.

Figure: Tumor Burden in Colorectal Liver Metastases



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The First Demonstration of a Link Between the Microbiome and Recurrence in Colon Cancer: Results from a Prospective, Multicenter Nodal Ultrastaging Trial B. Bandera,[1]* A. Chan,[1] M. Sim,[1] J. Jansson,[2] A. Bilchik,[1] D. Lee.[1] *1. Surgery, John Wayne Cancer Institute, Santa Monica, CA; 2. Pacific Northwest National Laboratory, Richland, WA.*

Introduction: T cell immunoprofiling in colon cancer (CC) has recently been shown to be more prognostic than AJCC staging criteria. Improved disease-free survival (DFS) is associated with a higher expression of CD8 T cells. Microbes are in close contact with the tumor, and the link between the microbiome and CC is becoming increasingly clear. We hypothesized that the influence of the colonic microbiome on the tumor micro-environment may impact recurrence in CC. Methods: In a prospective NCI-sponsored multicenter trial evaluating ultrastaging in early CC,92 patients were randomly selected for analysis. 16S amplicon paired-end DNA sequencing of CC paraffin tissue was performed. Operational taxonomic units (OTUs) were grouped by 97% sequence similarity. Univariate analysis comparing recurrence to microbiome diversity, clinical, and immune profile was followed by multivariate analysis (MVA) incorporating parameters under an alpha threshold of 0.2. Results: DFS was influenced by six parameters: number of positive lymph nodes, Stage, CD8 staining, alpha diversity, and two microbiome principal components by MVA. Using the alpha and beta diversity to evaluate for the association with CD8 T cells an inverse correlation was seen($R=-0.41$). Beta diversity also showed an association with CD8 T cells ($p=0.007$). Analysis at the OTU level with false discovery correction revealed one OTU, Clostridia Clostridiales (class, order) to be associated with decreased CD8 T cells ($R=-0.35$) and increased recurrence (HR 3.06, CI-1.78 to 5.25). Conclusions: This study is the first to demonstrate an association of the microbiome and recurrence in CC. An increased abundance of Clostridia Clostridiales' was inversely associated with CD8 T cells and increased CC recurrence. The link between this microbe, CD8 T cells and DFS has not been previously shown. Further studies are warranted to examine the prognostic impact of the immune profile and the microbiome in colon cancer.

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Predicting Colorectal Cancer Recurrence by Utilizing Multiple-View Multiple-Learner Supervised Learning J. Castellanos,[1]* Q. Liu,[1] R. Beauchamp,[1] B. Zhang.[2] *1. Section of Surgical Sciences, Vanderbilt University Medical Center, Nashville, TN; 2. Baylor College of Medicine, Houston, TX.*

Colorectal Cancer (CRC) remains a leading cause of cancer-related mortality in the United States. A key therapeutic dilemma in the treatment of CRC is whether patients with stage II and stage III disease require adjuvant chemotherapy after surgical resection. Attempts to improve identification of patients at increased risk of recurrence have yielded many predictive models based on gene expression data, but none are FDA approved and none are used in standard clinical practice. To improve recurrence prediction, we utilize a machine learning approach to predict recurrence status at 3 years after diagnosis. A dataset was curated from six publically available microarray datasets, and multiple views were generated to include information from non-tumor tissue gene expression patterns, gene set structure, protein-protein interaction

network structure, previously curated molecular signatures, and identified tumor suppressor/driver mutations. These views were used to train a diverse pool of base learners using 10x 10-fold cross-validation. Stacked generalization was used to train an ensemble model, also known as a meta-learner, from the predictions of these base learners. The performance of microarray trained models was significantly better compared to models trained on clinical data (Paired Wilcoxon signed rank test, $p = 1.49 \times 10^{-8}$), demonstrating that molecular data predicts recurrence significantly better than basic clinical data. Review of the model training performances revealed that non-linear classifiers often outperform linear classifiers, and that ensemble methods can also enhance performance. We also demonstrate the feasibility of the multiple-view multiple learner (MVML) supervised learning framework to generate and integrate predictions across a diverse set of learners, with the performance of the meta-learner exceeding or matching that of the best base learners across all performance metrics (Table 1). This work represents the first effort to use ensemble learning to predict CRC recurrence and highlights the promise of ensemble learning to improve the performance of predictive models in order to realize the goals of precision medicine.

Detailed performance metrics of ensemble vs. selectBest methods on validation set

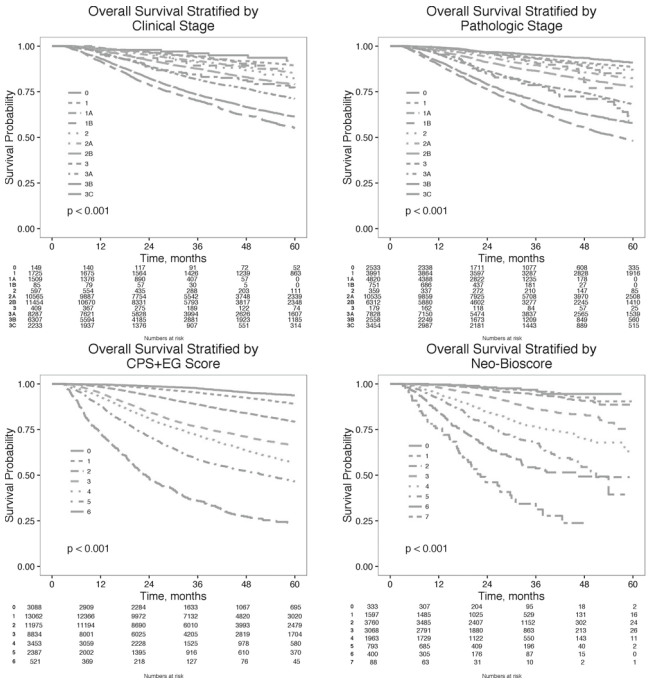
	Random Forest Ensemble	K-Nearest Neighbors Ensemble	selectBest
AUC	0.7860	0.7502	0.8388
Sensitivity	0.9474	0.7719	0.9298
Specificity	0.6495	0.6804	0.6598
Accuracy	0.7597	0.7143	0.7597
Positive Predictive Value	0.6136	0.5867	0.6163
Negative Predictive Value	0.9545	0.8354	0.9412
F Measure	0.7448	0.6667	0.7393

The results demonstrate that the random forest ensemble performed slightly superiorly or equivalently to the best base learner in all metrics aside from AUC, and actually exceeded the performance demonstrated in the test set in terms of F measure and accuracy.

8

CPS+EG and Neo-Bioscore are Superior Predictors of Overall Survival After Neoadjuvant Chemotherapy for Breast Cancer: A National Cancer Data Base Validation Study J.R. Bergquist,* B.L. Murphy, C.B. Storlie, E.B. Habermann, J.C. Boughey. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Improved staging systems which better predict survival for breast cancer patients who receive neoadjuvant chemotherapy (NAC) by accounting for grade, estrogen receptor, (CPS+EG) and ERBB2 status (Neo-Bioscore) have been proposed. We sought to validate these staging systems in a national cohort and compare their performance to each other and to AJCC 7th edition staging. Methods: The National Cancer Database (2008-2012) was reviewed for patients with invasive breast cancer who received NAC and survived ≥ 90 days after surgery. Overall survival for patients was stratified by four measures: clinical/pathologic AJCC 7th edition, CPS+EG, and Neo-Bioscore. Unadjusted Kaplan-Meier analysis and adjusted Cox proportional hazards modeling of overall survival (OS) were performed. Staging systems were compared on the basis of concordance and Integrated Discrimination Improvement (IDI). Results: From over 2 million patients available, 43,320 patients (5 year OS 76.0%, 95% CI 75.4%-76.5%) received NAC followed by surgery, met all inclusion criteria and had evaluable CPS+EG score, and 12,002 of these patients had evaluable Neo-Bioscore. Both CPS+EG and Neo-Bioscore improved staging stratification compared to clinical or pathologic AJCC staging (Figure). Concordance for CPS+EG (0.724, SE=0.003) and Neo-Bioscore (0.744, SE=0.008) were markedly improved relative to AJCC clinical (0.645, SE=0.003) and pathologic (0.676, SE=0.004) staging (all p<0.001). Both CPS+EG (IDI 4.7%, 95% CI 3.9-5.6%) and Neo-Bioscore (IDI 6.7%, 95% CI 5.2-8.5%) demonstrated superior discrimination when compared to AJCC pathologic staging. Comparison of CPS+EG to Neo-Bioscore yielded IDI of 1.0% (95% CI 0.5-1.5%), indicating Neo-Bioscore improved survival discrimination over CPS+EG. Conclusions: In a heterogenous national cohort of breast cancer patients, CPS+EG and Neo-Bioscore were found useful and substantially improved upon the AJCC 7th edition staging systems for patients treated with NAC. In cases where ERBB2 status was available, Neo-Bioscore provided superior staging discrimination to CPS+EG.



Overall Survival Stratified by AJCC Clinical/Pathologic Staging, CPS+EG, and Neo-Bioscore for Patients with Breast Cancer Who Received Neoadjuvant Chemotherapy Followed By Curative Intent Surgery.

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A Randomized Controlled Trial Evaluating the Impact of Web-based Information on Breast Cancer Patients' Knowledge of Surgical Treatment Options J.L. Tucholka,[2] D. Yang,[2] J.G. Bruce,[2] N. Steffens,[1] J.R. Schumacher,[2] C. Greenberg,[2] J. Steiman,[2] L. Wilke,[2] H.B. Neuman.[2]* *1. Denver Public Health, Denver Health and Hospital Authority, Denver, CO; 2. University of Wisconsin School of Medicine and Public Health, Madison, WI.*

Introduction: Providing breast cancer patients high quality treatment information prior to the surgical consultation prepares them to play an active role in decision making; however, delivering pre-consultation information can be challenging in clinical practice. We used a novel implementation strategy to deliver two different types of web-based information to patients prior to the surgical consultation, and compared the impact on patients' knowledge of their surgical options. Methods: We prospectively randomized stage 0-3 breast cancer patients to be emailed a link to standard web sites (National Cancer Institute, American Cancer Society, Breastcancer.org,) versus a decision aid (DA). Patients seeking second opinions, diagnosed by excisional biopsy, or without an email address were ineligible. Prior to meeting the surgeon, patients completed the Breast Cancer Surgery Decision Quality Instrument, which assesses knowledge on 5 key concepts. Differences in knowledge between the two arms were compared using univariate statistics. Logistic regression adjusted for age and education. Results: Of the 244 patients randomized, the median age was 59 (27-80), 99% were white, 65% had at least a college degree, and 74% used the internet multiple times a day, with no differences in demographic variables between study arms. Patients in both arms found the information highly beneficial (median score 8/10). Knowledge was higher in patients who received the DA (p=0.004), with significant differences on 3 individual questions (Table). In particular, DA patients were more likely to know that waiting a few weeks to make a treatment decision would not affect survival. On adjusted analysis, receipt of DA (p=0.002) remained associated with higher knowledge. Conclusion: Although patients found both types of information beneficial, the DA improved knowledge on key concepts relevant to patient decision making. Effectively conveying that there is time to make a breast cancer surgery decision may be especially valuable by decreasing the urgency patients feel. This may increase the quality of patient-surgeon interactions and patients' decision-making.

Key Knowledge Concepts Relevant to Decision Making for Breast Cancer Surgery

	% Correct		P value
	Decision Aid	Standard Websites	
Overall percent correct (mean)	70%	60%	0.004
How much would waiting a few weeks to make a treatment decision affect survival?	69%	48%	<0.01
With treatment, how many women diagnosed with early breast cancer will eventually die of breast cancer?	87%	77%	0.05
After which surgery is it more likely that women will need to have another operation to remove more tumor cells?	68%	64%	0.6
On average, will women with early breast cancer live longer after mastectomy or lumpectomy with radiation?	79%	66%	0.03
On average, will women have a higher chance of having breast cancer come back in the breast that has been treated after mastectomy or lumpectomy with radiation?	46%	40%	0.3

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Are We Choosing Wisely: When Should We Omit Sentinel Lymph Node Surgery in Women ≥70 Years with Hormone Receptor Positive Breast Cancer? J.L. Welsh,* T. Hoskin, C. Day, E.B. Habermann, M.P. Goetz, J.C. Boughey. *Surgery, Mayo Clinic, Rochester, MN.*

BACKGROUND: One SSO Choosing Wisely recommendation is don't routinely use sentinel lymph node (SLN) biopsy in clinically node negative (cN0) women ≥70 years of age with hormone receptor (HR) positive invasive breast cancer. We sought to evaluate factors impacting nodal positivity (pN+) in these patients (pts). METHODS: With IRB approval we queried our institutional breast surgery database (IBSD, 2008-2016) and the National Cancer Database (NCDB, 2004-2013) for all women ≥70 yrs with HR+ cN0 invasive disease. Recurrent and M1 disease were excluded. Rates of pN+ were based on women with axillary surgery. Pts were stratified by clinical T stage and tumor grade to compare risk of pN+ across strata; differences were tested using chi-square tests and estimated with relative risk ratios. RESULTS: Of 773 cases in 754 pts in our IBSD and 153,500 cases in the NCDB, 68 (8.8%) and 21,212 (13.8%) respectively had no axillary surgery; these pts were older (median 83 vs. 75 yrs, p<0.001, IBSD; 83 vs. 76 yrs, p<0.001 NCDB). pN+ rates were 14.3% (101/705, IBSD) and 15.2% (19,607/129,216, NCDB). Tumor grade and clinical T stage were associated with pN+ (See Table). Combining these two factors, low-risk criteria were defined as clinical T1a-b, grade 1-2 or clinical T1c, grade 1 and accounted for 54.3% (IBSD) and 43.2% (NCBD) of pts. Within this low-risk group, pN+ rates were 7.6% (IBSD) and 7.4% (NCDB). Pts not in the low-risk group had pN+ rates of 22.4% (IBSD) and 23.0% (NCDB) or relative risk of 2.95 (95% CI: 1.97-4.42) and 3.11 (95% CI: 2.99-3.23) respectively, each p<0.001. CONCLUSIONS: Risk of nodal involvement in women ≥70 years with HR+ invasive breast cancer is 14-15%, supporting that SLN surgery may be avoided in many of these low risk women. Addition of tumor size and grade to age and HR status can further stratify women at lowest risk (<8%) of nodal involvement for omission of SLN surgery. Women not meeting low risk criteria had a 3-fold increased rate of pN+ and for these cases nodal staging is important in guiding duration of systemic therapy and regional nodal irradiation.

Rates of pN+ in Women ≥70 Years with HR+ cN0 Invasive Breast Cancer Undergoing Axillary Surgery

	Our institution (IBSD)		National Cancer Database (NCDB)	
Overall pN+	101/705	(14.3%)	19,607/129,216	(15.2%)
Stratified by Clinical T Stage				
T1mic	0/9	(0%)	30/619	(4.9%)
T1a	0/39	(0%)	365/7,573	(4.8%)
T1b	21/242	(8.7%)	1,678/24,875	(6.8%)
T1c	42/271	(15.5%)	5,167/35,711	(14.5%)
T2	31/129	(24.0%)	6,922/25,349	(27.3%)
T3	4/11	(36.4%)	909/2,218	(41.0%)
T4	3/4	(75.0%)	502/1,085	(46.3%)
Stratified by Grade				
I	33/319	(10.3%)	3,954/40,543	(9.8%)
II	60/317	(18.9%)	10,340/62,138	(16.6%)
III	8/68	(11.8%)	4,338/19,457	(22.3%)

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Can Standard Pathologic Features be Used to Identify a Subset of Estrogen Positive HER2 Negative Tumors Likely to Benefit from Neoadjuvant Chemotherapy? O.A. Petruolo,* M.L. Pilewskie, S. Patil, M. Stempel, A.V. Barrio, M. Morrow. *Surgery, Memorial Sloan Kettering Cancer Center, NY, NY.*

Introduction: Patients with estrogen receptor positive (ER+) HER2- breast cancers are the least likely to have a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC), and the benefit of NAC in invasive lobular cancer (ILC) is uncertain. Our aim was to determine if histology, grade, differentiation, and progesterone receptor (PR) status can identify subsets likely to benefit from NAC. Methods: Patients with stage I-III ER+, HER2- breast cancer receiving NAC were retrospectively reviewed. Endpoints were downstaging to breast conservation (BCT) and nodal pCR post NAC. Patients were grouped based on PR status and grade/differentiation (high grade or poor (HP) vs non-HP). Statistical comparisons were performed using the chi-square test. Results: From 2007-2016, 402 ER+, HER2- cancers in patients receiving NAC were identified. Median age was 50 and 98% were clinical stage II-III (75% cN+; 68% cT2-3). Overall pCR rate was 5%; breast pCR in 7% and 15% nodal pCR in cN+ patients (p<.0001). Patients with ILC deemed ineligible for BCT at presentation (n=56) were less likely to downstage than those with ductal carcinoma (n=183), 16% vs 48% (p=<.0001); a similar trend was seen in the axilla (p=.086). PR status and HP predicted downstaging in both the breast and axilla. In those initially requiring mastectomy, rates of BCT eligibility post NAC were highest in ER+PR-/HP (62%) and lowest in ER+PR+/non-HP (29%) patients (p= .005). Overall rates of pN0 varied significantly within these groups (p<.0001), and nodal pCR among cN+ patients (n=301) ranged from 0-35% (p<.0001) and was most frequent in ER+PR-/HP patients (table). Conclusions: Patients with ILC have a low likelihood of downstaging in the breast or axilla following NAC, while lack of PR expression and HP identify a group with the highest likelihood of benefit. Given the decreasing use of adjuvant chemotherapy in ER+ patients, these features can be used to identify subsets of ER+ patients most likely to benefit from NAC.

Rates of breast and axillary downstaging based on tumor histology, receptor status, and grade or differentiation

Tumor characteristic	Eligible for downstaging to BCT (n=239)	P-value	Axillary pCR in cN+ patients (n=301)	P-value
	BCT Candidate after NAC			
Histology		<0001		0.086
Ductal	88/183 (48%)		40/245 (16%)	
Lobular	9/56 (16%)		4/55 (7%)	
Receptor/grade/differentiation		0.005		<0001
ER+PR+/HP	37/85 (44%)		16/117 (14%)	
ER+PR+/non-HP	24/82 (29%)		8/98 (8%)	
ER+PR-/HP	26/42 (62%)		17/48 (35%)	
ER+PR-/non-HP	8/23 (35%)		0/29 (0%)	

BCT: Breast conserving therapy; NAC: Neoadjuvant chemotherapy; pCR: pathologic complete response; cN+: clinically node positive; ER: estrogen receptor; PR: progesterone receptor; HP: high grade or poor differentiation

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Outcomes of Short Course Neoadjuvant Endocrine Therapy in Breast Cancer J.P. De Andrade,* M. Schroeder, J. Leone, S.L. Sugg, L. Erdahl, R. Weigel, I. Lizarraga. *Surgery, University of Iowa, Iowa City, IA.*

Introduction Neoadjuvant endocrine therapy (NET) for ≥3 months has been shown to decrease tumor size in hormone receptor-positive (HR+) invasive breast cancer (IBC) and allow breast conservation therapy (BCT). Short term NET is sometimes used for patients experiencing delay to surgery, but the incidence and efficacy of this is unknown. Methods The National Cancer Database (NCDB) was reviewed for women who had surgery for stage 1-3 HR+ IBC from 2004-13. Patients receiving neoadjuvant chemotherapy were excluded. 530,009 patients met inclusion criteria. Primary outcomes were time to surgery, NET duration, and whether pathologic stage at surgery was lower than clinical stage (downstaging). Results 9,631 (1.8%) patients received NET. Patients prescribed NET had higher clinical T stage (p < 0.001) and N stage (p < 0.001), although 40% receiving NET were clinical stage I. 5,225 (54%) NET patients received <3 months of therapy: 2,798 (29%) <1 month; 1,575 (16%) 1-2 months; and 852 (8.8%) 2-3 months. Of patients not receiving NET, 51% had a delay >1 month to surgery after diagnosis, 14% a >2 month

delay, and 1.5% >3 month delay. In the no NET group, tumor downstaging (cT>pT) occurred in 4.4% and nodal downstaging (cN+→pN0) in 0.5%. For patients receiving NET, the rate of cT>pT by duration of therapy was: 5.5% for <1 month, 9.7% for 1-2 months, and 17.2% for 2-3 months. When corrected for age, stage, and time to surgery, NET for 1-2 months and 2-3 months were significantly associated with cT>pT (OR 1.5 and OR 2.4, both p<0.001), but NET <1 month was not (OR 1.1, p=0.5). In those undergoing BCT, this was associated a lower risk for re-excision with NET >1 month (1-2 months: OR 0.82, p=0.02; 2-3 months: OR 0.40, p<0.001). There was no reduction in mastectomy rates or rate of cN+→pN0 for patients receiving NET <3 months. Discussion More than half of women with stage 1-3 HR+ IBC in the NCDB have primary surgery ≥1 month after diagnosis. Short course NET of 1-3 months is associated with tumor downstaging and lower rates of re-excision after BCT, with no benefit seen in treatment <1 month. Women with HR+ breast cancer with anticipated delays to surgical resection could be considered for short course NET.

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Directed Sentinel Lymph Node Biopsy (d-SLNB) Using Radioactive Seed Localization Establishes Axillary Status in Node Positive Breast Cancer After Neoadjuvant Chemotherapy E.J. Diego,[1]* P.F. McAuliffe,[1] M. Hankins,[2] A. Soran,[1] M. Bonaventura,[1] R.R. Johnson,[1] G.M. Ahrendt.[1] *1. Magee Womens Hospital of UPMC, Pittsburgh, PA; 2. University of Pittsburgh, Pittsburgh, PA.*

Introduction Neoadjuvant chemotherapy (NAC) downstages the axilla in up to 80% of patients (pts) depending upon breast cancer phenotype. Accurately identifying these pts is critical to reduce morbidity associated with axillary dissection. ACOSOG Z1071 demonstrated that tracer-guided sentinel lymph node biopsy (tr-SLNB) has a false negative rate (FNR) >10%, but tr-SLNB combined with resection of the node marked with a clip at initial presentation decreases FNR. Directed SLNB (d-SLNB) with I-125 seed localization of biopsy proven lymph node metastasis may enable less invasive targeted axillary staging. We hypothesize that d-SLNB alone can establish axillary status after NAC. Methods A prospective NAC database at a single institution was retrospectively reviewed to identify pts with US guided biopsy proven axillary lymph node metastasis pre-NAC. Patients received NAC and underwent combined d-SLNB and tr-SLNB between May 2013 and February 2016. All pts received technetium and blue dye for tr-SLNB and had I-125 seed localized d-SLNB. Demographics, clinicopathologic features and surgical outcomes were evaluated. Results 97 pts were identified. Mean age was 50, and mean tumor size was 3.6 cm. Mean number of lymph nodes retrieved was 1 for d-SLNB and 4 for tr-SLNB. In 77 pts for whom tracer uptake status of the d-SLNB was reported, 5 (6%) had no technetium or blue dye uptake. d-SLNB was successful in 96/97 pts. 40 (41%) and 51 (53%) pts had a pathologic complete response (pCR) in the breast and axilla, respectively. Of the 46 pts who did not have have axillary pCR, 43 were persistently node positive on d-SLNB, and 3 had no residual disease in the clipped node but had other positive axillary lymph nodes identified on tr-SLNB. Therefore, d-SLNB alone accurately characterized the axilla in 93/96 (97%) pts. The false negative rate was 3/46 (6.5%). Conclusion d-SLNB alone results in accurate staging of the axilla following NAC with a FNR <10%. d-SLNB instead of in combination with tr-SLNB, may be a reasonable alternative for axillary staging with potential for decreased morbidity. A larger study is warranted.

Patient Characteristics/ Surgical Outcomes N=97

Age(years)	Mean=50	Range 27-75
Follow-up(months)	Mean=21	Range 1-39
AJCC Stage	II	72(74%)
	III	25(26%)
Histology	Invasive Ductal Carcinoma	93(96%)
	Invasive Lobular Carcinoma/Metaplastic Carcinoma	4(4%)
Phenotype	Luminal	28(29%)
	HER2 positive	36(37%)
	Triple Negative	33(34%)
d-SLNB post-NAC	Lymph node confirmed retrieval with specimen radiograph/biopsy site changes	96(99%)
	tr-SLNB Mapping Outcomes	
	Concurrent uptake of technetium/blue dye	72
	No technetium/blue dye uptake	5
	Unknown status of technetium/blue dye uptake	18
	Pathologically Negative	54
	d-SLNB+tr-SLNB only	52
	d-SLNB+tr-SLNB, completion ALND	2
	Post-operative XRT	39
	Non d-SLNB positive node/ False negative d-SLNB	3
	Pathologically Positive	43
	d-SLNB+tr-SLNB only	9
	d-SLNB+tr-SLNB, completion ALND	34
	Post-operative XRT	42
	Additional non-d-SLNB positive node	20
Number of Additional LNs excised in whole group	Mean=8	Range 2-25
Number of Additional LNs excised in tr-SLNB	Mean=4	Range 1-8

d-SLNB: directed sentinel lymph node biopsy, tr-SLNB: tracer guided sentinel lymph node biopsy, ALND: axillary lymph node dissection, XRT: radiation therapy, LN: lymph node

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Factors Impacting the Accuracy of Targeted Axillary Dissection A. Caudle,* W. Yang, S. Krishnamurthy, E.A. Mittendorf, S. DeSnyder, I. Bedrosian, D.M. Black, M. Teshome, K.K. Hunt, H. Kuerer. *Breast Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Breast cancer staging is enhanced by axillary ultrasound (US) and biopsy of abnormal lymph nodes. When clips are placed in nodes with metastases, they can be evaluated for response to neoadjuvant chemotherapy (NAC). Targeted axillary dissection (TAD) includes selective removal of clipped nodes in addition to sentinel nodes (SLNs) with improved accuracy of axillary staging over SLND alone. The goal of this study was determine if clinical features impact the accuracy of TAD. Methods: Patients with clinical T0-4b, N1-2 breast cancer with biopsy–confirmed involved nodes marked with a clip who completed NAC were identified from a prospective registry and surgery schedules. All patients underwent TAD (including SLND and removal of clipped node) and ALND. Clipped nodes were localized using I^{125} seeds. Pathologic findings of the TAD procedure were compared to other nodes to determine false negative rate (FNR). Results: TAD was performed in 134 patients with 48 (36%) achieving nodal pCR. The FNR of TAD was 2.3% (2/86, 95% CI 0.3-8.2). Clinical T stage did not impact the FNR of the clipped node: FNR of T1 9.1% (1/11), T2 0% (0/50), T3 5% (1/20), T4 0% (0/5) (p=0.06). However, the number of abnormal nodes seen on pre-treatment US did impact the FNR. In 98 patients with <4 abnormal nodes, there were no false negative TAD results (0/61, 95% CI 0-5.9%). In 36 patients with ≥4 abnormal nodes on US, the TAD FNR was 8% (2/25, 95% CI 1.0-26%). There were no false negative results for patients with hormone receptor (HR)+/HER2- tumors (0/63, 95% CI 0-5.7%). Small sample size limits evaluation of other subgroups. Conclusions: While clinical T Stage does not impact the reliability of this assessment, initial extent of nodal disease should be considered in determining which patients should undergo TAD. TAD is a reliable method for axillary staging in patients with low volume nodal disease and patients with HR+/HER2- tumors. More data is needed to assess the reliability in patients presenting with ≥4 abnormal nodes and to determine if tumor subtype influences accuracy.

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Eliminating Axillary Surgery in Exceptional Responders to Neoadjuvant Chemotherapy with Documented Pathologic Complete Response in the Breast A. Tadros,[2]* W. Yang,[1] S. Krishnamurthy,[3] G. Rauch,[1] B. Smith,[5] V. Valero,[4] D.M. Black,[2] A. Caudle,[2] A. Lucci,[2] S. DeSnyder,[2] M. Teshome,[2] C. Barcenas,[4] M. Miggins,[2] T. Moseley,[1] B. Adrada,[1] R. Hwang,[2] K.K. Hunt,[2] H.M. Kuerer.[2] *1. UTMD Anderson Cancer Center, Department of Diagnostic Radiology, Houston, TX; 2. UTMD Anderson Cancer Center, Department of Breast Surgical Oncology, Houston, TX; 3. UTMD Anderson Cancer Center, Department of Pathology, Houston, TX; 4. UTMD Anderson Cancer Center, Department of Breast Medical Oncology, Houston, TX; 5. UTMD Anderson Cancer Center, Department of Radiation Oncology, Houston, TX.*

Introduction: Pathologic complete response (pCR) defined as no residual invasive or in situ disease in the breast and nodes occurs in at least 1/3 of patients (pts) with HER2+ and triple negative (TN) cancers treated with neoadjuvant chemotherapy (NCT). Imaging of the breast has a poor negative predictive value for pCR but preliminary results of feasibility studies of large-bore vacuum-assisted biopsy for documentation of pCR are promising. The rationale for managing the axilla when no surgery is performed among exceptional responders in the breast is evaluated. Methods: A prospective database identified 527 pts treated in 2010-14 with initial T1/T2, N0 or N1 (FNA/core documented), TN/HER2+ pts treated with NCT w/wo trastuzumab and/or pertuzumab followed by standard breast and nodal surgery. All pts underwent axillary nodal ultrasound (US) with biopsy of suspicious nodes. Associations between breast and nodal pCR were compared between groups. Results: Overall, 35.1% pts had a breast and nodal pCR and pCR was not significantly different between TN/HER2+ subtypes (Table). Among 290 pts with initial US documented N0 disease and a breast pCR (n=116), 100% had no evidence of axillary lymph node metastases after NCT at surgery. Among 237 pts with FNA/Core documented N1 disease and a breast pCR (n=77), 89.6% of patients had no evidence of axillary metastases. Pts presenting with documented N1 disease were less likely to have a breast pCR compared with initial N0 (32.5% vs. 40%, P=0.08) and among pts without a breast pCR and initial N1, 57.5% of pts had residual nodal disease. Conclusion: Trials will soon commence designed to eliminate surgery in exceptional responders with NCT. Response in the breast is highly correlated with nodal status and among those cases with a documented breast pCR and initial normal nodal US; the risk of missing nodal metastases without axillary surgery is extremely low. This data provides a strong rationale for these pts to proceed without axillary surgery after large-bore vacuum-assisted biopsy documents a breast pCR. Pts on trial will proceed with standard whole-breast radiotherapy.

Axillary status in patients with and without breast pCR following NCT

Breast pCR		# of Nodes Positive on Final Pathology(%)			
		0	1	2	≥3
Her2+	T1N0	6 (100%)	0	0	0
	T1N1	10 (77%)	2 (15%)	1 (7%)	0
	T2N0	46 (100%)	0	0	0
	T2N1	27 (93%)	1 (3%)	0	1 (3%)
Triple Negative	T1N0	12 (100%)	0	0	0
	T1N1	6 (100%)	0	0	0
	T2N0	52 (100%)	0	0	0
	T2N1	26 (90%)	2 (7%)	0	1 (3%)
Her2+ & Triple Negative	T1N0	18 (100%)	0	0	0
	T1N1	16 (84%)	2 (11%)	1 (5%)	0
	T2N0	98 (100%)	0	0	0
	T2N1	53 (91%)	3 (5%)	0	2 (3%)
No Breast pCR		# of Nodes Positive on Final Pathology(%)			
		0	1	2	≥3
Her2+	T1N0	8 (100%)	0	0	0
	T1N1	10 (71%)	1 (7%)	1 (7%)	2 (14%)
	T2N0	71 (99%)	1 (1%)	0	0
	T2N1	36 (48%)	7 (9%)	16 (21%)	16 (21%)
Triple Negative	T1N0	6 (86%)	1 (14%)	0	0
	T1N1	3 (33%)	0	3 (33%)	3 (33%)
	T2N0	79 (91%)	8 (9%)	0	0
	T2N1	19 (31%)	4 (6%)	16 (26%)	23 (37%)
Her2+ & Triple Negative	T1N0	14 (93%)	1 (7%)	0	0
	T1N1	13 (57%)	1 (4%)	4 (17%)	5 (22%)
	T2N0	150 (94%)	9 (6%)	0	0
	T2N1	55 (40%)	11 (8%)	32 (23%)	39 (28%)

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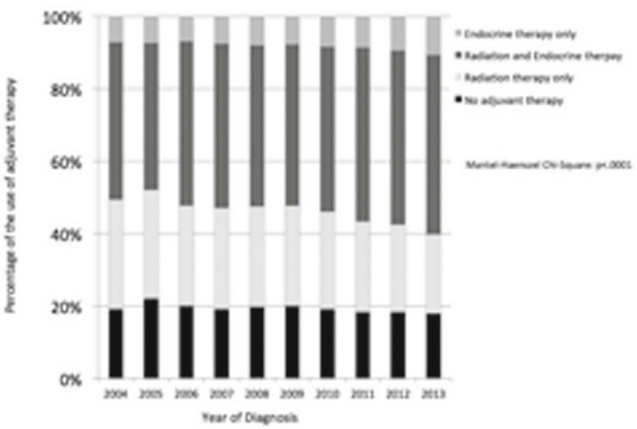
Trends in Adjuvant Radiation and Endocrine Therapies After Breast-Conserving Surgery for Ductal Carcinoma In Situ: Findings from the National Cancer Data Base, 2004-2013 Y. Sagara,[1]* R.A. Freedman,[4] F. Aydogan,[3] S.M. Wong,[2] A. Nguyen,[1] W.T. Barry,[4] M. Golshan.[1] *1. Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA; 2. McGill University Health Centre, Montréal, QC, Canada; 3. Istanbul University, Istanbul, Turkey; 4. Dana-Farber Cancer Institute, Boston, MA.*

Purpose: Breast-conserving surgery (BCS) followed by radiotherapy (RT) with or without endocrine therapy (ET) is a standard treatment option for ductal carcinoma in situ (DCIS). Temporal trends and factors influencing the use of adjuvant therapy in DCIS are not well-studied. We sought to investigate recent patterns in adjuvant therapy receipt after BCS for DCIS. Patients and Methods: Using data from the National Cancer Data Base (NCDB), we identified patients diagnosed with DCIS and treated with BCS between 2004 and 2013. We used multivariable logistic regression to estimate the odds of receiving adjuvant therapy after BCS, controlling for clinicopathologic demographic, and hospital characteristics. Result: We identified 65,455 patients who underwent BCS for DCIS, of which 50,147 were hormone receptor (HR) positive. Overall, 19% received no adjuvant treatment, 71% received RT, and 66% received ET. In adjusted analyses, among the patients with HR-positive DCIS, the odds for RT decreased in 2013 vs. 2004 (odds ratio [OR]: 0.86, 95% confidence interval [CI]: 0.78-0.93) while the odds of ET increased (OR: 1.4, 95% CI: 1.3-1.5) (Figure 1). Patients who chose RT were more likely to receive ET (OR: 3.4, 95% CI: 3.3-3.6), but there was a significant time-trend in choosing ET among patients who received RT (p= 0.006). Older age, positive margin status, and Medicare insurance were associated with lower odds of adjuvant RT and ET following BCS. Higher tumor grade and treatment at community cancer programs were associated with higher odds of both RT and ET. Increasing comorbidity and lack of insurance were associated with lower odds of RT only. We also observed geographic variation in receipt of adjuvant therapies. Conclusion: Although the proportion of women receiving no adjuvant therapy for HR-positive DCIS remained relatively stable over time, ET receipt increased and RT receipt decreased. This suggests a possible shift in patterns of care, which was also impacted by clinicopathologic and demographic factors.

Figure 1. Use of Adjuvant Therapy after Breast Conserving Surgery for HR positive DCIS Over Years (n=50,147)



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Nipple-Sparing Mastectomy is Not Associated with Delay of Adjuvant Treatment E. Albright,* M. Schroeder, S.L. Sugg, L. Erdahl, R. Weigel, I. Lizarraga. *University of Iowa, Iowa City, IA.*

Background Nipple sparing mastectomy (NSM) for breast cancer is increasing with excellent outcomes reported from single institutions. NSM is now offered to patients with more advanced disease but national data is sparse. We wished to determine if NSM, a more technically demanding operation compared to skin sparing mastectomy (SSM), was associated with adverse short term outcomes, especially delay in adjuvant therapy. Methods The National Cancer Database (NCDB) was queried for all female patients

undergoing unilateral mastectomy with immediate reconstruction (UM-R) from 2004-2013 for stage 0-3 breast cancer. Demographic and tumor characteristics and short-term outcomes of surgical margin status, length of stay and 30-day readmission rates were compared between NSM and SSM using Chi-square analysis. Time to adjuvant therapy was compared using a log-rank test. Results: Of 129,951 patients with UM-R, 8173 (6.3%) underwent NSM. NSM use increased from 2.5% in 2008 to 16% in 2013 (p<0.001). Patients with NSM were younger (p<.001) and had a lower clinical stage (Tis/T1: 62% v. 51.1%, p<0.001 and N0: 78.5% v. 65.3%, p<0.001). NSM patients were less likely to receive chemotherapy (37.4 vs 43.4%, p<0.001) or post mastectomy radiation (PMRT) (16.6 vs 17.7%, p<0.001). Chemotherapy in NSM patients was more likely to be neoadjuvant (NAC) than in SSM patients (34% vs 21%, p<0.001). Both groups were equally likely to receive PMRT after NAC (4.7% vs 4.9%). The rate of positive margins was equal for NSM and SSM patients (3.9%). More SSM patients had a post-operative length of stay ≥ 3 days (23.7% v. 17.6%, p<0.001) and 30 day re-admission (5.9% v. 4.4%, p<0.001). There was no difference in time from surgery to adjuvant chemotherapy in NSM vs SSM (mean 46.8 vs 47.3 days after surgery, p=0.589). Time from diagnosis to PMRT was not different between groups regardless of whether patients received NAC (mean 253.2 vs 257.7 days, p=0.186) or adjuvant chemotherapy (mean 235 days vs 238.2 days, p=0.703). Conclusion: Use of NSM for breast cancer in the NCDB is increasing. NSM is not associated with worse short term outcomes or delay to adjuvant chemotherapy and radiation, even in patients with more advanced disease.

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Delay in Radiation Therapy is Associated with Increased Risk of Recurrence in Women with Ductal Carcinoma In Situ E. Shurell,* C. Olcese, S. Patil, K.J. Van Zee, M.L. Pilewskie. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Adjuvant radiation therapy (RT) is associated with a 50% risk reduction of ipsilateral breast tumor recurrence (IBTR) among women with ductal carcinoma in situ (DCIS) undergoing breast-conserving surgery (BCS). The risk of a delay in RT initiation is unknown. We sought to examine the association between risk of IBTR and timing of adjuvant RT in women with DCIS undergoing BCS. Methods: Women with DCIS treated with BCS and RT from 1980-2010 were identified from a prospectively maintained database. IBTR rates were compared between those who began RT ≤8 weeks, >8 weeks to 12 weeks, and >12 weeks after completion of surgery. Time to IBTR was measured from completion of RT. Association between time to RT and IBTR was evaluated by Kaplan-Meier and log-rank analysis; a Cox model was used to adjust for 4 variables different between the groups and/or univariately associated with IBTR: menopause status, surgical excisions, endocrine therapy use, and presentation (clinical vs radiologic). Results: 1363 women were identified. Median age was 56 years. There were 127 IBTR events, of which 54% were DCIS, 43% were invasive, and 3% unknown. Median follow-up was 6.4 years. Time to RT following surgery was as follows: 832 (61%) ≤8 weeks, 399 (29%) >8 to 12 weeks, and 132 (10%) >12 weeks. 5- and 10-yr IBTR rates for women by RT timing were: 5.6% and 12.4% RT starting ≤8 weeks, 4.1% and 8.0% RT >8 to 12 weeks, and 8.9% and 24.0% with RT delayed >12 weeks after surgery, respectively (p=0.004). On multivariable analysis, in addition to premenopausal status (HR 1.9, p=0.0002) and lack of endocrine therapy (HR 2.0, p=0.004), timing of RT remained significantly associated with risk of IBTR (with RT ≤8 weeks as reference: RT >8 to 12 weeks HR 0.8, p=0.3; RT >12 weeks HR 2.0, p=0.006). Conclusions: Delay in RT >12 weeks is associated with a significantly higher risk of IBTR in women undergoing BCS for DCIS. Efforts should be made to avoid delay and ensure that RT begins within 12 weeks of surgery to minimize risk.

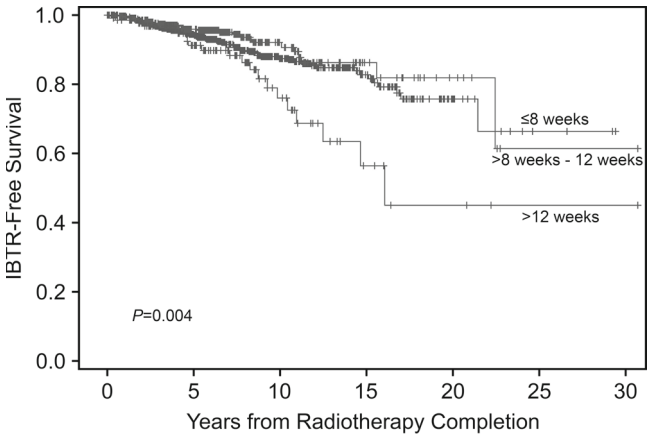

Figure 1. Ipsilateral breast tumor recurrence-free survival stratified by timing of adjuvant radiation.

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Impact of Morphological Status on Long-term Outcome Among Patients Undergoing Liver Surgery for Intrahepatic Cholangiocarcinoma F. Bagante,[2] G. Spolverato,[2]* M. Weiss,[3] S. Alexandrescu,[4] H.P. Marques,[5] L. Aldrighetti,[6] S.K. Maithel,[7] C. Pulitano,[8] T.W. Bauer,[9] F. Shen,[10] G. Poultsides,[11] A. Guglielmi,[2] J. Marsh,[12] E. Itaru,[17] B. Groot Koerkamp,[16] G. Martel,[15] O. Soubrane,[14] T. Gamblin,[13] T. Pawlik.[1] *1. Surgery, The Ohio State University, Columbus, OH; 2. University of Verona, Verona, Italy; 3. Johns Hopkins Hospital, Baltimore, MD; 4. Fundeni Clinical Institute, Bucharest, Romania; 5. Curry Cabral Hospital, Lisbon, Portugal; 6. Ospedale San Raffaele, Milan, Italy; 7. Emory University, Atlanta, GA; 8. Royal Prince Alfred Hospital, Sydney, NSW, Australia; 9. University of Virginia, Charlottesville, VA; 10. Eastern Hepatobiliary Surgery Hospital, Shanghai, China; 11. Stanford University, Stanford, CA; 12. University of Pittsburgh Medical Center, Pittsburgh, PA; 13. Medical College of Wisconsin, Milwaukee, WI; 14. Beaujon Hospital, France, Clichy, France; 15. University of Ottawa, Ottawa, ON, Canada; 16. Erasmus University Medical Centre, Rotterdam, Netherlands; 17. Yokohama City University School of Medicine, Yokohama, Japan.*

Background: The influence of morphological status on long-term outcome of patients undergoing liver resection for intrahepatic cholangiocarcinoma (ICC) is poorly defined. We sought to study the impact of morphological status on long-term overall survival (OS) of patients undergoing curative intent resection for ICC. Methods: A total of 1,166 patients who underwent curative-intent liver resection for ICC at one of the 16 participating institutions between 1990-2016 were identified. Data on clinicopathological characteristics, operative details, and morphological status, were recorded and analyzed. Results: Overall, 978 (83.9%) ICC were mass-forming (MF), 35 (3.0%) intraductal growth (IG), 59 (5.0%) periductal-infiltrating (PI), and 94 (8.1%) mass forming plus periductal-infiltrating (MS+PI). Median OS was 3.1 years (95% CI, 1.2-8.6), while 5-year OS was 38.1% (95% CI, 34.6-41.7), respectively. According to the AJCC 7th edition staging system, 546 (46.8%) patients were stage I, 132 (11.3%) stage II, 174 (14.9%) stage III, 85 (7.3%), stage IVa and 229 (19.7%) stage IVb. Several clinicopathological variables were independent predictors of OS, including tumor size (HR 1.06, 95% CI 1.04-1.09), nodal status (HR 1.13, 95% CI 1.03-1.25), major vascular invasion (HR 1.33, 95% CI 1.06-1.66), and multifocal disease (HR 1.63, 95% CI 1.34-1.98; all p <0.01). Of note, morphological subtype was the strongest predictor of OS (HR 1.75, 95% CI 1.39-2.19; p <0.001). Specifically, 5-year OS for MF and IG was 40.3% (95% CI 36.2-44.3) versus 24.2% (95% CI 16.4-32.8) for PI and MF+PI (p<0.01). Conclusion: For patients undergoing resection of ICC, morphological status is an important predictor of long-term outcome. In particular, patients with PI or MF+PI ICC had roughly a 75% increased risk of death compared with patients who had a MF or IG ICC.

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Actual 5-Year Survivors Following Resection of Hilar Cholangiocarcinoma T. Tran,[1]* C.G. Ethun,[2] J.A. Norton,[1] T. Pawlik,[3] S. Buettner,[4] K. Idrees,[5] C. Isom,[5] R. Fields,[6] B. Krasnick,[6] S.M. Weber,[7] A. Salem,[7] R.C.G. Martin,[8] C. Scoggins,[8] P. Shen,[9] H.D. Mogal,[9] C. Schmidt,[3] E. Beal,[3] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] G. Poultsides.[1] *1. Department of Surgery, Stanford University, San Francisco, CA; 2. Emory University, Atlanta, GA; 3. The Ohio State University, Columbus, OH; 4. John Hopkins Hospital, Baltimore, MD; 5. Vanderbilt University, Nashville, TN; 6. Washington University in St. Louis, St. Louis, MO; 7. University of Wisconsin, Madison, WI; 8. University of Louisville, Louisville, KY; 9. Wake Forest University, Winston Salem, NC; 10. New York University, New York, NY.*

Background: Although several studies have reported on actuarial survival outcomes following resection of hilar cholangiocarcinoma, the characteristics of patients who actually reached the 5-year milestone have not been adequately described. Methods: Patients who underwent resection for hilar cholangiocarcinoma from 2000-2015 in 10 US academic institutions participating in the Extrahepatic Biliary Malignancy Consortium were analyzed. Patients alive at last encounter with less than 5 years of follow-up were excluded. The clinicopathologic characteristics, perioperative, and long-term outcomes of actual 5-yr survivors and of patients who died within 5 years were compared. Results: Of 328 patients explored, 257 (78%) underwent curative resection and had an actuarial 5-year survival of 17%. After excluding 63 survivors with < 5 years follow-up, 194 patients were further classified as 5-year survivors (n=23, 12%) and non-5-yr survivors (Table). None of the 5-yr survivors had preoperative systemic biliary sepsis, portal vein embolization, T3 tumors with unilateral portal vein or hepatic artery invasion, or T4 tumors necessitating main portal vein or hepatic artery resection. However, actual 5-year survival was still achieved in the setting of bile duct resection only, R1 margins, poor differentiation, lymphovascular or perineural invasion, nodal metastasis, intraoperative blood transfusion, and serious postoperative complications. Five-year survival did not equal cure, as five 5-year survivors experienced disease recurrence, 2 before and 3 after the 5-year mark. There were ten actual 7-year survivors and four actual 10-year survivors. Conclusions: Although nodal metastasis, poor differentiation, and R1 margins are established predictors of poor outcome for hilar cholangiocarcinoma, the mere presence of these factors does not preclude patients from achieving a 5-year survival. In contrast, preoperative biliary sepsis, T3 or T4 stage, and the necessity for vascular resection and reconstruction appear to be prohibitive in reaching the 5-year milestone. This information can be utilized in the perioperative counseling of patients with this challenging malignancy.

	Dead within 5 years (n=171)	Alive > 5 years (n=23)	P value
Age (median, IQR)	66 (59-73)	60 (56-72)	0.088
ASA > 3 (n=165)	88 (61%)	15 (73%)	0.311
Peak bilirubin (median, IQR)	4.9 (2.1-11.8)	5.5 (2.4-9.8)	0.516
CA19-9 (median, IQR)	166 (52-514)	34 (15-64)	0.001
Portal Vein Embolization	13 (8%)	0 (0%)	0.171
Type of Resection			
Bile Duct Resection only	44 (26%)	6 (26%)	0.647
Hemihepatectomy	58 (35%)	10 (44%)	
Trisectionectomy	66 (39%)	7 (30%)	
Caudate lobe resection	52 (30%)	5 (22%)	0.391
Portal vein resection	15 (9%)	0 (0%)	0.139
Hepatic artery resection	6 (4%)	0 (0%)	1.000
R1 margins	67 (39%)	4 (17%)	0.001
Grade (n=179)			
Well	30 (19%)	4 (21%)	0.706
Moderate	91 (57%)	12 (63%)	
Poor	39 (24%)	3 (16%)	
Lymphovascular invasion (n=149)	59 (45%)	4 (22%)	0.066
AJCC T Stage (n=150)			
T1	12 (9%)	4 (24%)	0.047
T2	85 (64%)	13 (76%)	
T3	28 (21%)	0 (0)	
T4	8 (6%)	0 (0)	
Positive Lymph Node (n=174)	64 (42%)	3 (15%)	0.027
Any complication (n=170)	98 (66%)	14 (64%)	0.812
Grade 3 or 4 complication (n=170)	36 (22%)	3 (14%)	0.268
Neoadjuvant Chemotherapy (n=179)	7 (4%)	0 (0%)	0.597
Adjuvant Chemotherapy (n=160)	88 (63%)	10 (50%)	0.270
Readmission (n=123)	37 (35%)	6 (33%)	0.876

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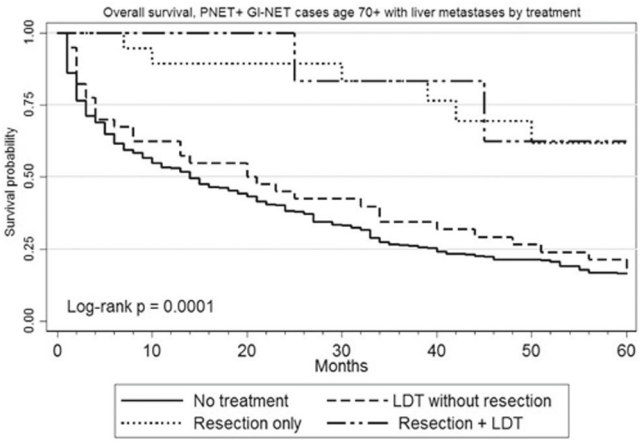
Is it Worth Resecting Gastrointestinal Neuroendocrine Tumors in Patients Above the Age of 70? Z. Jutric,* A. Lewis, M. Raoof, P.H.G. Ituarte, D. Li, G. Singh. *Surgical Oncology, City of Hope, Duarte, CA.*

Introduction There is little data to support aggressive surgical debulking of the primary gastrointestinal-neuroendocrine tumors (low to medium grade-pancreas, small bowel, colorectal) (GI-NETs), in patients above the age of 70 years. We aim to answer this using a large database. Methods Patients age 70 with a diagnosis of GI-NETs were identified using the California Cancer Registry (2000-2012). Linkage to patient discharge records provided information including resection of primary site (RPS), resection of liver metastases (LR), and liver directed therapy (LDT). Treatment group effects on overall survival (OS) were compared by Cox proportional hazard models. Results A total of 2,039 patients were identified. Among the 1,661 patients without metastases, 74% (n = 1,234) received RPS and demonstrated improved survival (HR 0.50, p<0.001) compared to those without RPS. Of the 378 number of patients with liver metastases, LDT alone (n = 23) was not significantly associated with survival (HR 0.65, p = 0.082). Reduced risk was similar for RPS alone (n = 149; HR 0.44, p < 0.001) or when paired with LDT (n = 17, HR 0.45, p = 0.007). RPS with LR, either with or without LDT, indicated the greatest impact in survival risk (n = 25; HR 0.14, p < 0.001). Conclusion We found a substantial benefit from surgical management of primary tumor and liver metastases in patients over the age of 70 with GI-NETs. Contrary to past logic, we propose surgery should be offered to patients above 70, provided satisfactory performance status.



*LDT = liver directed therapy

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An Analysis of Perioperative Chemotherapy in Resected Pancreatic Cancer: Identifying the Number and Sequence of Chemotherapy Cycles Needed to Optimize Survival I. Epelboym,* M.S. Zenati, J. Steve, K. Lee, N.S. Bahary, M. Hogg, H.J. Zeh, A.H. Zureikat. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Receipt of 6 cycles of systemic adjuvant therapy (AT) is standard of care in resected pancreatic cancer (PDA). Neoadjuvant chemotherapy (NAC) is being increasingly used, however the optimal number of chemotherapy cycles needed alone or in combination with AT remains unknown. We sought to determine the optimal number and sequencing of chemotherapy cycles in resected PDA. Methods: Retrospective review of all resected PDAs from 2008-2015 at a single institution. Total number of chemotherapy cycles received and their sequence (no chemo, AT only, NAC only, and NAC+AT) was evaluated. Overall survival (OS) was compared across groups using log-rank tests. Cox-proportional hazard modeling was used to determine adjusted hazard ratios. Results: 522 patients were analyzed: NAC alone =71(13.6%), NAC +AT= 166 (31.8%), AT alone= 222(42.5%), no chemo= 63(12.1%). For the entire cohort, median number of total received cycles was 6 (range 0-15), while follow-up and OS was 45.8 and 27.9 mos. Median OS based on total cumulative cycles was 13mos for 0 cycles (n=63, 12.1%), 18.5mos for 1-5 cycles (n=150, 29%), and 36.9mos for ≥6 cycles (n=309, 59%)

(p<0.05). Median survival with ≥6 AT cycles was comparable to ≥6 cycles of mixed NAC+AT(37vs 35.1 mos, p=0.856). On MVA(P <0.0001), compared to 0 cycles, receipt of a minimum of 6 cycles either as AT only (HR 0.34, CI 0.24-0.48) or as combined NAC+AT (HR 0.33, CI 0.23-0.47) was independently associated with improved OS, whereas higher tumor stage (HR 1.52, CI 1.22-1.88), positive nodal disease (HR 1.67, CI 1.30-2.15), positive resection margin (HR1.85, CI 1.40-2.45), and lower Charlson Comorbidity Index (HR 1.15, CI 1.04-1.26) were associated with decreased survival. Receipt of < 6cycles (in any combination) was not associated with survival (HR, 0.74, CI 0.53-1.03) on MVA. Conclusion: This analysis suggests receipt of 6 or more cycles of NAC+AT or AT alone is associated with equivalent and optimal survival in resected PDA. Neoadjuvant and adjuvant chemotherapy effects appear to be additive, suggesting those receiving NAC may need a shorter course in the adjuvant setting.

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Timing of Surgical Resection Following Neoadjuvant Chemoradiation in Localized Pancreatic Adenocarcinoma: Is Longer Better? R.J. Louie,* A.M. Olofson, A.J. Lambour, M. Hill, A. Fisher, R.J. Barth, A. Suriawinata, K. Smith. *Dartmouth-Hitchcock Medical Center, Lebanon, NH.*

For patients with pancreatic adenocarcinoma (PDAC) treated with neoadjuvant chemoradiation, the optimal interval between therapy completion and surgical resection is unknown. We aim to determine the optimal interval to surgery maximizing treatment response and oncologic outcomes. This was a retrospective cohort study of all patients with biopsy-proven PDAC who completed neoadjuvant chemoradiation and R0 surgical resection (tumor cells > 1 mm from the margin) at our institution from 1/1/2004-12/31/2015. We grouped patients according to time from chemoradiation completion to surgery: 6-8, 8-10 and >10 weeks. A GI pathologist, blinded to patient outcomes, classified tumor response by Evan's criteria and Ryan Scheme for Tumor Regression. We defined partial response (PR) as > 51% tumor destruction/fibrosis and determined recurrence by reviewing surveillance CT imaging. We excluded patients without available surveillance imaging. Primary outcomes were pathologic response, disease free survival (DFS) and overall survival (OS). Statistical analysis was performed with STATA. Of the 128 patients who met criteria, 9 (7%) patients had a pathologic complete response (CR) with recurrence in 4 (55%) patients (average DFS: 17 months/OS: 35 months). 31 (24%) patients had PR with recurrence in 21 (68%) patients (average DFS: 16 months/OS: 36 months). Of the 26 patients resected within 6-8 weeks of chemoradiation, 3 had CR (11%), 7 had PR (27%), and 61% of patients recurred (average DFS: 20 months). Of the 58 patients resected within 8-10 weeks, 4 had CR (7%), 41 had PR (71%), and 62% of patients recurred (average DFS: 17 months). Of the 44 patients resected within 10-13 weeks, 2 had CR (5%), 27 had PR (61%), and 61% of patients recurred (average DFS: 14 months). We observed improved PR in the 8-10 week group, but there were no statistical significance in distribution (p=0.17), DFS (p=0.71) and OS (p=0.19). Allowing more time from neoadjuvant therapy completion to surgical resection may improve the pathologic response. Larger studies are needed to determine if the time interval to surgical resection has oncologic benefit for these patients.

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Microscopic Lymphovascular Invasion is an Independent Predictor of Survival in Resected Pancreatic Ductal Adenocarcinoma J. Epstein,[4]* G. Kozak,[1] Z. Fong,[2] J. He,[3] A. Javed,[3] U. Joneja,[1] W. Jiang,[1] C. Ferrone,[2] K.D. Lillemoe,[2] J. Cameron,[3] M. Weiss,[3] H. Lavu,[1] C.J. Yeo,[1] C. Fernandez-del Castillo,[2] C. Wolfgang,[3] J. Winter.[1] *1. Thomas Jefferson University Hospital, Philadelphia, PA; 2. Massachusetts General Hospital, Boston, MA; 3. Johns Hopkins Hospital, Baltimore, MD; 4. Sidney Kimmel Medical College, Philadelphia, PA.*

PURPOSE: Despite its routine description in pathologic reports of resected pancreatic ductal adenocarcinomas (PDA), lymphovascular invasion (LVI) is not well characterized as a prognostic factor. METHODS: We performed a retrospective review of 2,640 patients who underwent a pancreatectomy for PDA at Thomas Jefferson University Hospital, Massachusetts General Hospital and Johns Hopkins Hospital (2003-2014). Original pathology reports were used to extract clinicopathologic information. RESULTS: The median post-resection survival for the total cohort was 19.2 months with a 5-year survival rate of 15.2%. There was an association between LVI and regional lymph node metastases in resected specimens: 86% of patients with LVI had N1 disease (vs. just 48% without LVI, p<0.001). In a multivariate Cox proportional hazards model, LVI was an independent predictor of survival (HR= 1.14, p = 0.017). In a stratified Kaplan-Meier survival analysis, patients with N0, LVI- PDA had a significantly improved overall survival, compared to N0, LVI+ patients (median 31 vs. 24 mo, p = 0.020); similarly, patients with N1, LVI- PDA had better survival as compared to patients with N1, LVI- disease (18.6 vs. 16.5 mo, p=0.001). Thus, stratification by lymph node status and LVI yielded four patient subgroups (LVI-, N0; LVI+, N0; LVI-, N1; LVI+, N1) with distinct median overall survivals as demonstrated in the figure. DISCUSSION: This represents the first focused study on LVI in PDA, and demonstrates that the routinely reported pathologic feature is a bona fide adverse prognostic factor after resection, independent of regional lymph node metastases. Thus, LVI represents an additional metric of lymphatic burden, similar to positive lymph node count and lymph node ratio. These findings have potential implications for pathologic staging and perhaps adjuvant therapy, and support a recommendation for meticulous assessment of LVI in resected specimens.

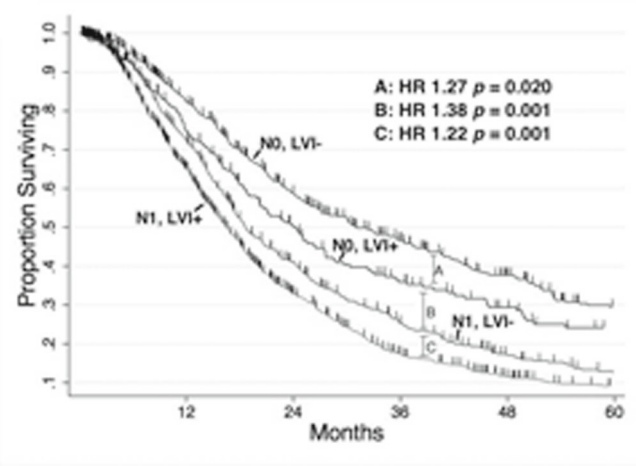

Fig. Kaplan-Meier survival curves stratified by regional nodal metastases status and LVI

Fig. Kaplan-Meier actuarial survival curves for patients undergoing PD for ductal adenocarcinoma of the pancreas according to lymphovascular invasion and regional lymph node metastases status. For N0, LVI- disease (n=520): median survival = 31.0 months, 1-year survival = 82%, 2-year survival = 59% and 5-year survival = 29%. For N0, LVI+ disease (n=211): median survival = 24.0 months, 1-year survival = 74%, 2-year survival = 50% and 5-year survival = 24%. For N1, LVI- disease (n=480): median survival = 18.6 months, 1-year survival = 72%, 2-year survival = 41% and 5-year survival = 12%. For N1, LVI+ disease (n=1270): median survival = 16.5 months, 1-year survival = 65%, 2-year survival = 33% and 5-year survival = 9%.

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A KRAS P53 P16 Genetically Engineered Mouse Model Demonstrates Robust Onset and Penetrance of Pancreatic Ductal Adenocarcinoma B. Schmidt,* G. Herrera, J. Yeh. *Surgical Oncology, University of North Carolina, Chapel Hill, NC.*

Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains a leading cause of cancer death. Genetically engineered mouse models (GEMMs) provide a test platform for experimental therapy and are increasingly important as immunotherapy and other therapeutics interacting with the tumor microenvironment emerge. GEMMs are challenging in their tractability due to variable penetrance and onset of adenocarcinoma. The commonest mutations in human PDAC are KRAS, P53 and P16. We decided to investigate if a GEMM incorporating all three pancreas specific mutations would develop tumors at a rate conducive to further studies of experimental therapy. Methods: Tumor specific survival and patterns of metastasis were evaluated in a GEMM with pancreas-specific, Cre mediated activation of a mutant KRAS allele, and deletion of P16 and P53 alleles. Mice were euthanized when they became moribund in accordance with institutional animal care and use committee guidelines. Results: Median PDAC specific survival was 21.4 +/- 1.2 weeks for all mice, with 71% harboring pancreatic adenocarcinoma at autopsy. In our study, P53

had the greatest impact on survival with a disease specific median survival of 40.0 +/- 12.7 weeks in $P53^{+/+}$ mice v 25.3 +/- 2.5 weeks in $P53^{+/lox}$ mice v 10.2 +/- 0.9 weeks in $P53^{lox/lox}$ mice (p=0.006). The impact of P16 genotype on disease specific survival was less dramatic with a modest but significant decrease in survival associated with $P16^{lox/lox}$ genotype (16.7 +/- 2.9 weeks v 22.7 +/- 2.9 weeks in non-$P16^{lox/lox}$ mice, p=0.02) P16 genotype did not correlate with the presence of metastatic disease at time of autopsy (p=0.92). A strong association between P53 genotype and the presence of metastatic disease was observed, with 0/5 of $P53^{+/+}$ mice (0%), 15/28 of $P53^{+/lox}$ mice (53.6%), and 7/8 of $P53^{lox/lox}$ mice (87.5%) with metastatic disease at the time of evaluation. Conclusion: This model may have a more tractable disease onset than previous GEMMs of PDAC. Within this model, the presence of one or more P53 mutations appears to be a necessary condition for the development of metastatic disease.

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Role of Cyclin Dependent Kinase 4/6 Inhibitors in Modulating the Immune Microenvironment in Pancreas Cancer R. Panni,* J. Herndon, B. Knolhoff, R. Fields, W. Hawkins, d. Denardo. *Washington University in St. Louis, St. Louis, MO.*

Introduction: Inhibition of cyclin dependent kinase (CDK) 4/6 is a therapeutic strategy to treat solid tumors. CDKs help regulate the cell cycle during the transition from G1 to S phase. Dysregulation of the CDK 4/6 retinoblastoma pathway has been identified in many cancers including pancreas cancer (PC) and contributes to cell cycle progression and unrestrained growth. PC has a unique resistance pattern to multiple therapies due to the dense immunosuppressive stroma which is predominantly composed of immune infiltrate. The role of CDK 4/6 has been established in tumor growth but its effect on tumor stroma has never been studied. We hypothesized that CDK 4/6 inhibitors play an important role in stromal proliferation in PC. We studied the effect of CDK 4/6 inhibitors on tumor stroma in a murine model of PC. Methods: Using a genetically engineered murine model of PC, KPC (p48-Cre; LSL-KrasG12D; Trp53flox/flox), we evaluated the effect of selective CDK 4/6 inhibitor 'Palbociclib' on tumor growth and immune infiltrates. After detection of tumors, the KPC mice were randomized to treatment with Palbociclib or vehicle. The tumors were harvested and analyzed for elevation of stromal fibrosis, proliferation and changes in the tumor immunity. Results: We analyzed the tumors for downregulation of stromal cell proliferation and found that Ki-67 activity was significantly decreased, predominantly in tumor stroma of KPC mice that received Palbociclib as a single agent. We also noticed changes in the fibrosis pattern and immune cell infiltrate and found significant differences in myeloid cell proliferation when compared to the vehicle group. These changes in tumor stroma after CDK 4/6 inhibitor therapy suggest that CDK 4/6 activity is an important regulator in stromal desmoplasia, which promotes tumor growth and resistance to therapy in PC Conclusion: CDK 4/6 inhibitors have emerged as a new modality in cancer therapy and our data suggest that this pathway has an important role in regulating stromal proliferation and fibrosis in PC. CDK 4/6 inhibition in addition to immunotherapy has the potential to overcome the barrier to T cell infiltration in PC.

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Selective Tumor Labeling of Pancreatic Cancer in an Orthotopic Mouse Model Using Humanized Anti-CEA Antibody Conjugated with a Near-Infrared (NIR) Dye T. Lwin,[1]* T. Murakami,[2] P.J. Yazaki,[3] R. Hoffman,[2] M. Bouvet.[1] *1. University of California San Diego, La Jolla, CA; 2. Anticancer, San Diego, CA; 3. City of Hope Beckman Research Institute, Duarte, CA.*

Introduction Pancreatic cancer is an aggressive malignancy with a poor survival rate. Curative treatment for pancreatic cancer is surgical resection with negative margins. However delineation of tumor margins is challenging in practice. Fluorescence-guided surgery with tumor-specific fluorophores can help surgeons enhance visualization of the tumor and margins in-situ. In the present study, we show that the use of a humanized anti-CEA antibody conjugated to an 800nm NIR fluorescent dye (Anti-CEA-800) can selectively label pancreatic cancer in an orthotopic xenograft mouse model. Materials/Methods BxPC3-GFP pancreatic cancer cells were injected into flanks of nude mice. Tumors were allowed to grow for 4 weeks. Tumors fragments (2 mm^3) were grafted onto the pancreatic tail of recipient mice to create an orthotopic xenograft model. After the tumors developed for 4 weeks, 600 ug of Anti-CEA-800 dye injected into the tail-vein (LI-COR 800 CW IRDye®, Lincoln, NE). Mice were imaged via the Maestro CRI imaging system (Perkin Elmer, Waltham, MA) at 24 and 48 hours after injection. Images were obtained at 510nm (GFP wavelength) and 800nm (Anti-CEA-800 wavelength). Results Images obtained after fluorescent antibody injection showed anti-CEA-800 clearly labeled the tumor with an adequate tumor to background ratio at 24 hours (calculated relative intensity value-CRI= 910.55). At 48 hours, tumor labeling was still present, but with decreased fluorescence (CRI= 655.13). Images obtained using the GFP filter showed fluorescence at CRI of 1751.46. However GFP wavelength had poor penetration if covered by overlying tissue which was not an issue with the Anti-CEA-800 dye. Conclusions Humanized anti-CEA-800 tumor-specific dye specifically labeled orthotopically implanted pancreatic cancer xenografts. The dye successfully co-localized with GFP tagged tumor cells. The longer wavelength allowed for deeper tissue penetration. Humanized anti-CEA antibody conjugated to a radio-labeling agent and LI-COR 800 dye is already in Phase I/II trials. Humanized anti-CEA conjugated with an IR-800 dye is promising for future clinical FGS applications.

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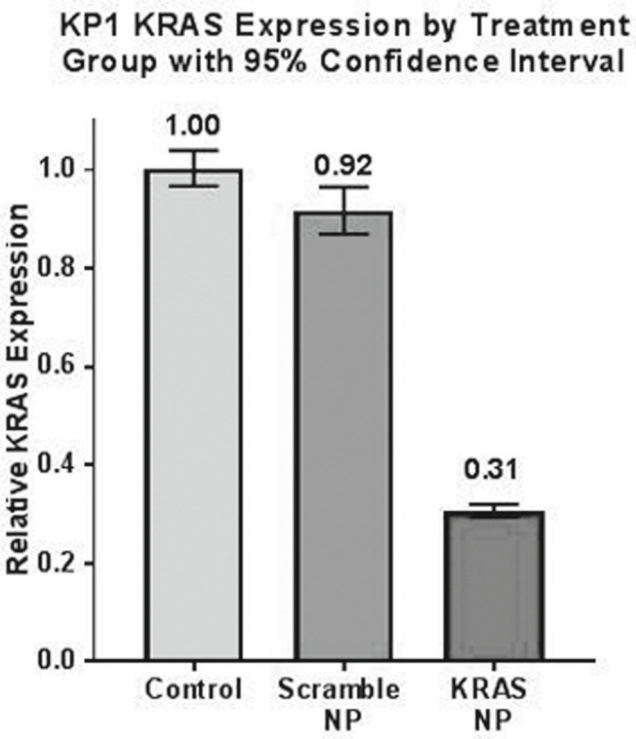
Precision Delivery of RAS-Inhibiting siRNA to Pancreatic Cancer via Peptide-Based Nanoparticles M. Strand,* H. Pan, B. Krasnick, X. Zhang, P. Goedegebuure, T. Fleming, d. Denardo, W. Gillanders, W. Hawkins, S.A. Wickline, R. Fields. *Washington University in St. Louis, Saint Louis, MO.*

Introduction: Greater than 95% of pancreatic adenocarcinomas (PDACs) are driven by KRAS activation; yet, despite decades of work, no RAS inhibitors have reached the clinic. Furthermore, the delivery of therapeutic agents of any kind to PDAC has been hindered by the extensive desmoplasia that accompanies these tumors. Herein, we show that serum-stable and pH-sensing nanoparticles (NPs) are taken up by PDAC cells, can deliver KRAS-specific siRNA into the cytoplasm and inhibit KRAS expression, thereby causing cell death. We go on to use a spontaneous model of pancreas cancer to show that this system can effectively deliver siRNA to stroma-rich tumors. Methods: The murine PDAC cell line KP1 was tested for NP uptake in vitro utilizing fluorescent siRNA NPs (fNPs) in combination with confocal microscopy and flow cytometry. KP1 cells were treated with KRAS-siRNA NP, and KRAS expression and cell viability were assessed with RT-PCR and CellTiter-Glo, respectively. Mice bearing subcutaneous KP1 tumors and KPPC mice with spontaneous PDAC were injected with fNP, and tumor fluorescence was assessed using an in vivo imaging system and fluorescence microscopy. Results: KP1 cells take up fNP in vitro, with >99% of cells positive for fluorescent signal at 24 hours. Treatment with KRAS-siRNA NP of KP1 cells reduced KRAS expression by 69% (see Figure) and reduced cell viability by 45% compared to untreated and scramble-siRNA treated controls. Gemcitabine demonstrated an additive effect with anti-KRAS therapy. Tumors from KP1 cells grown in mice, and tumors from KPPC mice, were strongly fluorescent 24 hours after IV injection of fNP. Fluorescence microscopy showed successful delivery of fNP to tumors. Conclusions: Our NP system can precisely deliver siRNA to KP1 cells and spontaneous PDAC, overcoming the predominant stromal component in these tumors. KRAS-siRNA delivery downregulates KRAS expression, leading to cell death. This represents a novel treatment for PDAC. Furthermore, with its ability to deliver siRNA into the tumor microenvironment and suppress a known oncogene, this platform could be used to target other putative drivers of tumor progression across various cancer types.



Expression of KRAS by treatment group as assessed by RT-PCR

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Predictors for Use of Sentinel Node Biopsy and the Survival Impact of Performing Nodal Staging in Melanoma Patients T.D. Murtha,[1]* G. Han,[2] D. Han.[1] *1. Yale School of Medicine, New Haven, CT; 2. Texas A&M University, College Station, TX.*

Background. Guidelines recommend sentinel node biopsy (SNB) in patients with melanomas ≥1 mm. However, it is unknown how many melanoma patients ultimately undergo SNB or if there is a therapeutic effect from performing SNB. This study evaluates prognostic factors for the use of SNB and assesses the survival impact of performing SNB in melanoma patients. Methods. The Surveillance, Epidemiology, and End Results database was queried for clinically node-negative melanoma cases treated between 2010-2012. Clinicopathologic factors were correlated with SNB use and with overall survival (OS) and melanoma-specific survival (MSS). Results. The study included a total of 34,135 cases. SNB was performed in 10,013 cases overall (29.3%), and in 3269 of 23,770 thin cases (13.8%), 5810 of 8524 intermediate thickness cases (68.2%), and 916 of 1743 thick cases (52.6%). Depth was unknown in 98 cases overall and in 18 SNB cases. On multivariable analysis, age ≥70 years, depth >4 or <1 mm, lentigo maligna histology, location on face, scalp, ear, or trunk, education and income levels all significantly predicted for not performing SNB ($P < 0.05$). SNB patients in the thin, intermediate thickness, and thick groups all had significantly ($P < 0.05$) improved OS and MSS compared with non-SNB patients in the corresponding groups. On multivariable analysis, use of SNB significantly predicted for improved OS and MSS ($P < 0.0001$ and $P = 0.01$, respectively). Other significant ($P < 0.05$) predictors for OS included age, gender, race, marital status, depth, ulceration, mitotic rate, and histologic subtype, and for MSS included age, marital status, depth, ulceration, mitotic rate, and histologic subtype. Conclusions. Only 68.2% of intermediate thickness melanoma patients are treated with SNB, which decreases to 52.6% for thick cases. Age, depth, histologic subtype, tumor location, and socioeconomic factors appear to influence whether or not SNB is performed. This data becomes even more relevant with the finding that use of SNB is correlated with improved OS and MSS. Further studies are needed to determine ways to improve adherence to guidelines regarding use of SNB in melanoma patients.

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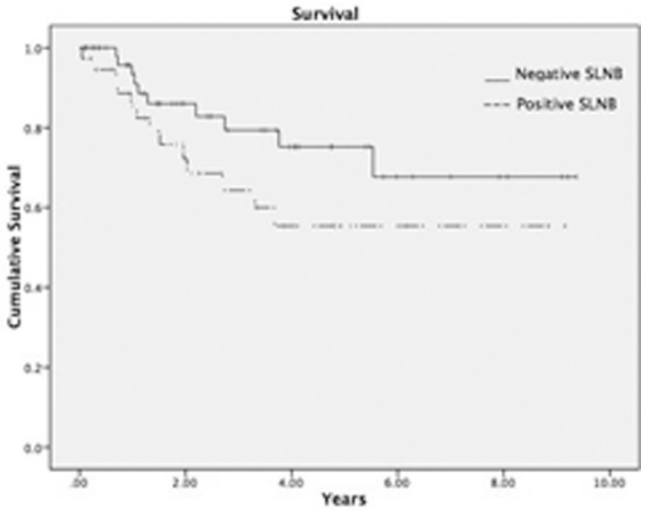
Multicenter Study of the Prognostic Value of Sentinel Lymph Node Biopsy in the Management of Recurrent Melanoma G. Beasley,[4]* Y. Hu,[1] L. Youngwirth,[2] R.P. Scheri,[2] A. Salama,[2] K. Rossfeld,[4] S.K. Gardezi,[1] D. Agnese,[4] J.H. Howard,[4] D. Tyler,[3] C.L. Slingluff,[1] A. Terando.[4] *1. University of Virginia, Charlottesville, VA; 2. Duke University, Durham, NC; 3. University of Texas Medical Branch, Galveston, TX; 4. The Ohio State University, Columbus, OH.*

Background: Sentinel lymph node biopsy (SLNB) for primary cutaneous melanoma can provide prognostic information and a possible therapeutic benefit. However, limited data exist for SLNB in the management of locally recurrent (LR) or in-transit (IT) melanoma. Methods: Data from 3 centers performing SLNB for LR/IT melanoma from 1997-present were reviewed. Aims were to 1) assess the feasibility of SLNB on LR/IT melanoma, 2) describe the rate of SLNB positivity, and 3) evaluate the prognostic value of SLNB in this population. Results: Among the 107 patients in the study cohort, 52% (56/107) had a prior SLNB at time of primary melanoma (PSLNB), 10/56 (18%) had a positive PSLNB, and 11/107 (10%) had prior LN dissections (LND). In the present study, 48 patients underwent SLNB for IT disease (45%) while 59 had LR melanoma (55%). A SLN was removed for pathologic examination in 96% (103/107) of LR/IT cases. Lymphoscintigraphy (LS) failures occurred in 2 patients with recurrent melanoma who had PSLNB. Two patients with LR disease and prior inguinal LNDs had iliac nodes identified on LS but no node found intra-operatively. The rate of SLNB positivity for LR/IT disease was 40% (41/103, 95% CI 31.5-50.5). Eighty-five percent (35/41) of patients with a positive SLNB had completion LND with 37% (13/35) having additional positive nodes. Among 44 patients with negative PSLNB, 12/44 (27%) had a positive SLNB at the time of surgery for LR/IT melanoma. Median time to disease progression was 1.4 years (95% CI, 0.75 to 2.0) for patients with LR/IT and a positive SLNB versus 5.9 years (95% CI, 1.7 to 10.2) in LR/IT SLNB negative patients (p=0.18). Figure 1 shows a trend towards improved overall survival for patients with IT/LR melanoma and a negative SLNB (p=0.06). Conclusion: SLNB can be successful in patients with LR/IT melanoma even if prior SLNB was performed. Both the rate of positive SLNB in this setting and the rate of non-sentinel node metastases exceeded the rates for patients with intermediate thickness melanomas. The status of the SLNB in IT/LR melanoma may have important implications for guiding subsequent therapeutic decisions.



Kaplan Meier Plots for Recurrent Melanoma SLNB negative (solid) versus SLNB positive (dash). (p=0.06)

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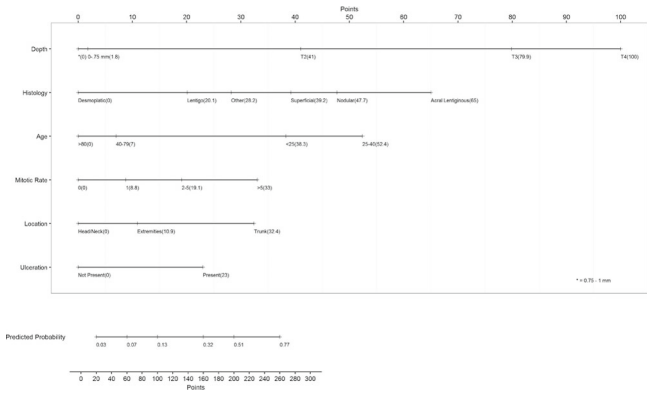
A Contemporary Nomogram for the Prediction of Sentinel Lymph Node Metastasis in Melanoma N. de Rosa,* N.A. Hein, L.M. Smith, J.M. Foster, D.J. Dimaio, A.S. Marr, J.A. Kozel, A.O. Wahl, C. Zhang, M.A. Kessinger, S.P. Thayer, E. Silva-Lopez. *Surgical Oncology, University of Nebraska Medical Center, Omaha, NE.*

Background: While it is widely accepted that tumor biology is multifactorial, current indications for sentinel lymph node biopsy (SLNB) are based primarily on tumor thickness. In 2010, the American Joint Committee on Cancer integrated mitotic rate (MR) as a high-risk feature for T1 lesions. The study aims are: 1) to develop a contemporary nomogram to more accurately predict the presence of SLN metastasis relative to tumor thickness alone; 2) to analyze the utilization of SLNB since 2010. Methods: The 2014 Surveillance, Epidemiology, and End Results database was queried for melanoma ICD-O-3 codes (C44.0-C44.7). The percentage of SLNB performed for thin, intermediate, and thick tumors was calculated from 2004-2013. SLNB performed from 2010-2012 were included in the nomogram construction, based on the inclusion of MR as a variable. Simple randomized selection allocated 70% of data for derivation and 30% for validation sets. Predictors of SLN positivity were selected using chi-square tests. A nomogram was derived using a multivariate logistic regression model. Results: From 2009-2013, SLNB in thin, intermediate, and thick melanomas increased (1.1% to 11.3%; 11.8% to 61.7%; 15.9% to 49.8%, respectively). From 2010-2012, 2,793 SLNB were performed. Patient majorities were white (97.7%), male (60.3%), and age 40-79 (78.2%). On univariate analysis age, thickness, MR, ulceration, primary tumor location, and histopathologic type were associated ($p < 0.05$) with a positive SLN and were included in the nomogram. The likelihood that an individual had a positive SLN was no different for MR of 1 compared to 0, after controlling for all other covariates. Increasing MR carried a higher risk, with MR 2-5 of borderline significance and MR of >5 significantly associated with the presence of a positive SLN. The concordance index was 0.71 (95% CI 0.67-0.75) for the validation set, indicating excellent calibration. Conclusion: Using commonly available clinicopathologic and patient demographics, we developed a nomogram to accurately predict the probability of occult SLN metastasis. This model should improve patient counseling, minimize clinical practice variation, and optimize hospital resources.



Nomogram for the Prediction of Sentinel Lymph Node Metastasis in Melanoma

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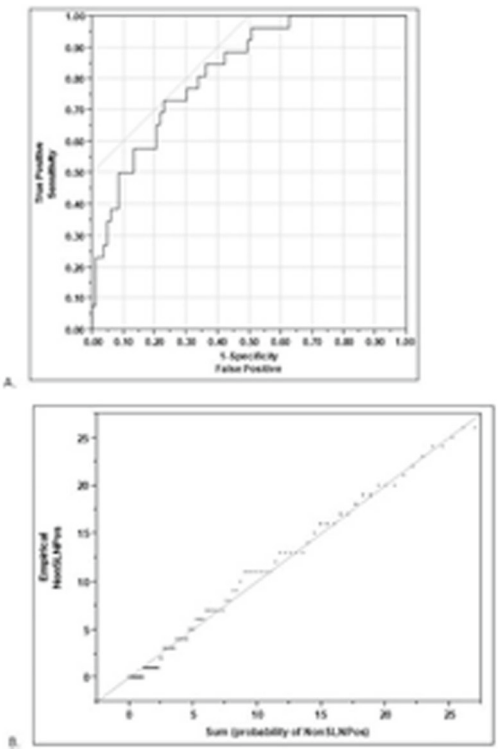
Predicting Non-Sentinel Node Positivity in Melanoma Patients with a Single Positive Sentinel Lymph Node N. Bhutiani,[1]* M.E. Egger,[2] A.J. Stromberg,[3] R.C.G. Martin,[1] C. Scoggins,[1] M. Ross,[2] J. Gershenwald,[2] K.M. McMasters.[1] *1. University of Louisville Department of Surgery, Louisville, KY; 2. University of Texas MD Anderson Cancer Center, Houston, TX; 3. University of Kentucky Department of Statistics, Lexington, KY.*

Background: Scoring systems of non-sentinel node (NSN) positivity include patients with >1 tumor-positive sentinel lymph node (SLN); many surgeons consider >1 positive SLN to be a relative indication for completion lymph node dissection (CLND). We evaluated predictors of NSN positivity among patients with a single positive SLN and developed a predictive model in this population of patients that creates the greatest dilemma regarding CLND. Methods: A combined Sunbelt Melanoma Trial and University of Louisville Melanoma Database was queried for patients with a primary cutaneous melanoma and single positive SLN who underwent CLND. Factors associated with NSN positivity were identified and used to construct a regression model for predicting NSLN positivity. The model was validated both internally using the index dataset and externally using a data set from MD Anderson Cancer Center (MDACC). Results: Overall, 111 patients had a single positive SLN. Of these, 27 were found to have positive NSN on CLND (24.3%). Patients with positive NSN were older ($p=0.03$) and more likely to have primary tumors with Breslow thickness ≥ 2.77 mm ($p=0.04$). 63% of patients with positive NSN had multiple SLN tumor deposits compared to 42% with negative NSN ($p=0.05$). Patients with positive NSN were also less likely to have subcapsular tumor deposits and more likely to have diffuse deposits throughout the SLN (40.7% vs. 61.9%, $p=0.05$; 44.4% vs. 19.1%, $p=0.008$). SLN tumor deposit diameter ≥ 0.4 mm ($p=0.007$) and area >0.1 mm2 ($p=0.004$) as well as cells in perinodal lymphatics ($p=0.05$) were associated with NSN positivity. Validation studies of the regression model yielded an area under the ROC curve of 0.82 and a fairly linear cumulative logistic probability distribution (Figure 1). Sensitivity and specificity of the model were 83% and 59% for the index dataset and 85% and 20% for the MDACC dataset (n=223). Conclusions: Patient, primary tumor, and SLN characteristics can help predict NSN positivity in melanoma patients with a single positive SLN. Our NSN positivity model can help surgeons identify patients with low risk of harboring tumor deposits in NSN and spare them the morbidity of CLND.

Figure 1: ROC and Cumulative Logistic Probability Curves



(A) Receiver Operating Curve (ROC) and (B) Cumulative logistic probability distribution for NSN positivity model validation with index dataset.

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Limb Salvage in Patients with Unresectable Recurrent Melanoma and Sarcoma with the Hyperthermic Isolated Limb Perfusion Technique L. Kerivan,* C. Reintgen, M. Reintgen, E. Reintgen, S. Shivers, D.S. Reintgen. *Surgery, University of South Florida, Morsani School of Medicine, Tampa, FL.*

Introduction: Hyperthermic isolated limb perfusion (HILP) is a surgical procedure for the regional delivery of heat and high doses of chemotherapy and biologic agents to the extremity. The procedure is employed as a limb salvage technique for locally advanced primary malignancies or recurrent cancers

confined to the extremity that are unresectable. Methods: From 1987-2016, 247 patients with unresectable recurrent melanoma (95%), sarcoma or Merkel Cell Carcinoma underwent HILP for limb salvage of the affected extremity after staging was negative for Stage IV disease and disease was confirmed to be confined to the extremity. All patients underwent regional node dissection to gain access to the vascular supply of the extremity and to clear any regional nodal disease. Patients were then perfused with Melphalan at a dose of 0.8 mg/kg and 1.2 mg/kg for upper and lower extremity HILP, respectively for a duration of 1 hour. Systemic therapies that included chemotherapy and immunotherapy were employed when patients recurred systemically or when complete responses were not obtained. Results: All patients had limb salvage with this protocol. Patients were clinically negative in their regional basin at the time of perfusion but 40% of the patients had evidence of regional nodal disease in their nodal dissections. Immediate responses (within 3 months) on the extremity to the HILP were as follows: Complete responses of 66%, PR of 20%, 10% stable disease and 4% progressive disease. With a mean follow-up period of 5 years, 61.5% of the patients have recurred with 68.4% of the recurrences being systemic, 21% regional nodal, 7.2% Intransit and 3.3% local-regional soft tissue. Conclusions: HILP is an effective strategy for limb salvage in patients with unresectable, locally advanced cancers confined to the extremity. The treatment was associated with a high rate of complete responses on the extremity. Most patients recurred with distant metastases emphasizing the need for better systemic therapies for these malignancies.

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Isolated Limb Infusion: A Single-Center Experience with 200 Infusions C. O'Donoghue,* J.E. Mullinax, D. Hardman, S. Sileno, P. Matthew, S. Naqvi, Y. Kim, J.S. Zager. *Moffitt Cancer Center, Tampa, FL.*

Introduction: Isolated limb infusion (ILI) is a minimally invasive technique to deliver regional chemotherapy to an extremity for patients with locally advanced cutaneous malignancies and sarcoma. Methods: A single-institution prospectively collected database of patients was analyzed for intention to treat with ILI. Analysis included intraoperative and postoperative outcomes including overall response rate at 3 months and infield progression free survival (PFS). Results: From May 2007 to June 2016, a total of 158 patients underwent 200 ILI procedures (196 successfully completed). The mean age was 73 years old (range 27-94 years old). The majority of patients were female (59.5%). Four disease types were treated: melanoma (72.5%), sarcoma (23.1%), squamous cell carcinoma (2%), and Merkel cell carcinoma (2.5%). The median creatinine phosphokinase peak was 411.0. Median length of stay was shorter for UE (4 days) than for LE (6 days) ($p<0.0001$) but LOS did not differ between initial and repeat ILIs ($p=0.15$). A median grade II Wieberdink Toxicity Score was observed for initial and repeat ILIs; the score was not associated with the overall response rate ($p=0.82$). Median follow up was 18.1 months. Overall response rate (ORR) defined as either complete response (CR) or partial response (PR) for the entire cohort was 55.9%. The table below shows CR and PR rates by histology, initial vs repeat ILI and UE vs LE. The ORR did not differ between initial and repeat ILIs ($p=0.64$). For those who had a CR/PR response, the median infield progression free survival (PFS) for melanoma was 361 days, sarcoma was 368 days, SCC was 97 days, and MCC was 510 days. Melanoma infield PFS did not significantly differ between initial vs repeat ($p=0.69$) or UE vs LE ($p=0.16$). Sarcoma patients had an overall limb salvage rate of 68.4%. Conclusion: Over 50% of patients had a treatment response at 3 months. Infield PFS was approximately 1 year for those who had a response. Repeat ILI is a reasonable treatment for patients who had an initial response. Sarcoma limb preservation was 68.4%. ILI is a safe and well tolerated procedure for patients with locally advanced melanoma, sarcoma and other cutaneous malignancies.

Isolated Limb Infusion Response Data

RESPONSE DATA	CR	PR	SD	PD
Overall Response All Disease (N=188)	22.9%	33.0%	13.8%	30.3%
Overall Response Melanoma (N=138)	26.1%	32.6%	13.0%	28.3%
UE (N=24)	33.3%	45.8%	8.3%	12.5%
LE (N=114)	24.6%	29.8%	14.0%	31.6%
Initial ILI Melanoma (N=108)	27.8%	30.6%	13.9%	27.8%
UE (N=20)	40.0%	35.0%	10.0%	15.0%
LE (N=88)	25.0%	29.5%	14.8%	30.7%
Repeat ILI Melanoma (N=30)	20.0%	40.0%	10.0%	30.0%
UE (N=4)	0.0%	100.0%	0.0%	0.0%
LE (N=26)	23.1%	30.8%	11.5%	34.6%
Overall Response Sarcoma (N=40)	12.5%	32.5%	12.5%	42.5%
UE (N=10)	10.0%	30.0%	10.0%	50.0%
LE (N=30)	13.3%	33.3%	13.3%	40.0%
Initial ILI Sarcoma (N=34)	8.8%	32.4%	11.8%	47.1%
UE (N=8)	0.0%	25.0%	12.5%	62.5%
LE (N=26)	11.5%	34.6%	11.5%	42.3%
Repeat ILI Sarcoma (N=6)	33.3%	33.3%	16.7%	16.7%
UE (N=2)	50.0%	50.0%	0.0%	0.0%
LE (N=4)	25.0%	25.0%	25.0%	25.0%
Overall Response Merkel Cell Carcinoma (N=5)	40.0%	20.0%	20.0%	20.0%
UE (N=3)	33.3%	0.0%	33.3%	33.3%
LE (N=2)	50.0%	50.0%	0.0%	0.0%
Initial ILI Merkel Cell Carcinoma (N=3)	66.7%	0.0%	33.3	0.0%
Repeat ILI Merkel Cell Carcinoma (N=2)	50.0%	50.0%	0.0%	0.0%
Overall Response Squamous Cell Carcinoma (N=4)	0.0%	50.0%	50.0%	0.0%
UE (N=2)	0.0%	50.0%	50.0%	0.0%
LE (N=2)	0.0%	50.0%	50.0%	0.0%
Initial ILI Squamous Cell Carcinoma (N=3)	0.0%	66.7%	33.3%	0.0%
Repeat ILI Squamous Cell Carcinoma (N=1)	0.0%	0.0%	100.0%	0.0%

CR, complete response. PR, partial response. SD, stable disease. PD, progressive disease.

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Immune Regulatory Genes Predict Survival After Resection of Metastatic Melanoma M. Gainsbury,[1]* D. Kauffman,[1] K. Gong,[2] N. Deng,[1] R. Essner.[1] *1. Cedars Sinai Medical Center, Los Angeles, CA; 2. David Geffen School of Medicine at UCLA, Los Angeles, CA.*

Introduction: Five-year survival rates for metastatic melanoma remain <20% even with the FDA approval of anti-CTLA4 and anti-PD1 therapies. The aim of this study was to identify which immunomodulatory genes were associated with improved survival among immunotherapy-naïve metastatic melanoma patients undergoing surgical resection. Methods: Twenty-nine patients underwent surgical resection for curative intent of metastatic melanoma. Tumor specimens were obtained to generate cDNA for microarray analysis. Differential expression of 79 immune regulatory genes were compared between patients who survived less than 5 years with those who survived 5 or more years. Results: Of the 29 patients with metastatic melanoma, 15 (51.7%) survived <5years while 14 (48.3%) survived >5years. Average survival time from primary diagnosis was 31.0 versus 117.3 months between the two groups ($p<0.01$). Mean survival from metastatic diagnosis was 9.0 versus 29.9 months ($p<0.01$), respectively. Most common sites of metastasis were intraabdominal (41.4%), subcutaneous (31.0%), and lung (13.8%). There was no difference in patient age, gender or metastatic site between the two groups. No patients received immunotherapy for metastatic disease. Five genes of the 79 selected were identified as significantly differentially expressed between <5 year and >5 year survivors. CD27 and CD40, both members of the TNF receptor family, were significantly overexpressed in those surviving >5 years (differential expression fold change (DEFC) of 2.08 and 1.29 respectively, $p=0.04$ and $p=0.02$). RAP1B, member of the RAS oncogene family, and ACTA2 (alpha-actin-2) were also significantly overexpressed (DEFC 1.81, $p=0.03$ and DEFC 1.16, $p=0.01$) in long term survivors. VEGF-A was significantly under expressed (DEFC 0.38, $p=0.03$) in patients surviving > 5 years. Conclusion: We identified five immune regulatory genes that are differentially expressed in the microenvironment of resected metastatic melanoma. These genes may play an important role in the host response to the metastases and may be useful for guiding selection of patients for resection.

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Internal Pathology Review for Melanoma: Improvement in Care or Redundancy? C. Isom,* M. Hooks, R. Kauffman. *General Surgery, Vanderbilt, Nashville, TN.*

Background: Previous studies have shown significant variability between dermatopathologists in the histopathologic analysis of invasive melanoma. Many tertiary care centers routinely subject all outside pathology to internal review, incurring a cost burden to both the institution and the patient. We sought to evaluate discordance of histopathologic diagnosis and staging parameters of invasive melanoma between external and internal review, and subsequent impact on staging and surgical management. Methods: A retrospective review was performed of cases of invasive melanoma referred to an NCCN-designated cancer center from August 2015 to August 2016. Per policy all external pathology was reviewed internally prior to surgical resection. Outside and institutional dermatopathology reports were compared. Patients that presented with recurrences, distant metastases, or multiple primaries were excluded. Results: A total of 188 patient were identified. The cohort was 61.2% male with an average age of 60.5 years. Shave biopsies were performed in 72.9%, excisional biopsy in 13.3%, punch biopsy in 10.6% and 3% did not have biopsy type reported. Mitotic rate was the most frequently discordant variable, with 17% having an increase in reported mitotic rate and 18.6% with a decrease. Tumor thickness was increased in 10.1% and decreased in 12.2% after internal review. Ulceration was changed to "present" in 3.7%, and from "present" to "absent" in 2.7%. Overall, 36% had change in their mitotic rate, 22.8% had change in the melanoma depth and 6.9% had a change in ulceration status. Internal review led to a change in stage in 12.7%, with 6.4% being upstaged and 5.9% downstaged. Staging change altered surgical treatment in 5.9% of the entire cohort, and 47.8% of those whose stage was changed after internal review Conclusions: This preliminary study has shown a high degree of variability between pathologists reviewing invasive melanoma specimens. More than 10% of patients had a change in their stage after internal review, leading to clinically relevant changes in surgical management. Additional study is warranted to examine the cost burden of internal review in regards to overall cost of care and surgical outcomes.

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Optimization of Isolation and Expansion of Memory CD8+ T-Cells for Use in Adoptive Cell Transfer M.V. Beems,[1]* A. Contreras,[1] A. Tatar,[1] P. Srinand,[1] S. Sen,[2] T.K. Luther,[3] C. Cho.[3] *1. University of Wisconsin, Madison, WI; 2. Duke University, Durham, NC; 3. Univerity of Michigan Hospital, Ann Arbor, MI.*

Background Adoptive cell transfer (ACT) is a promising strategy for cancer immunotherapy that remains ineffective for a large subset of patients. Our laboratory and others have shown that ACT with memory cells is superior to traditional ACT with effector cells. However, memory T cell-based approaches to ACT will require the large-scale procurement of tumor-specific memory T cells from patients. We hypothesized that modifications to current isolation and expansion protocols could produce more memory-like T cells and improve ACT efficacy. Methods C57BL/6 mice were inoculated with B16GP33 melanoma flank tumors, and lymphocytes isolated from tumors, tumor draining lymph nodes (TDLNs), and spleens were characterized by flow cytometry. Lymphocytes were stimulated and expanded in vitro in the presence of various cytokines. Expanded lymphocytes were characterized by flow cytometry and transferred into melanoma-bearing mice to test their efficacy for ACT. Results TDLNs were found to be enriched for memory-like CD8+ T cells compared with spleens and tumors. In vitro culture in the presence of IL7 and IL15 exhibited optimal expansion of memory CD8+ T cells, with 145-fold proliferative expansion and enriched differentiation of memory phenotype at 56% of all cells. TDLN-derived CD8+ T cells and CD8+ T cells expanded in the presence of IL-7/IL-15 appeared to be optimal for use in ACT. Conclusion The isolation of lymphocytes from TDLNs combined with expansion in the presence of IL7 and IL15 promoted a memory phenotype and improved the efficacy of ACT. This methodology may provide a basis for actualizing the potential therapeutic advantages of memory T cells for ACT. Current studies are examining the ability of in vivo preconditioning therapies and in vitro immunomodulatory conditions to further enhance memory T cell yield and therapeutic efficacy.

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Predicting Cancer Risk in Patients with Atypical Ductal Hyperplasia at the Genomic Level K. Shaffer,* E.E. Abbott, Z. Hothem, B. Thibodeau, R. Keidan. *General Surgery, William Beaumont Hospital, Royal Oak, MI.*

Background: The current treatment of atypical ductal hyperplasia (ADH) diagnosed on core needle biopsy (CNB) is excisional breast biopsy due to the risk of finding invasive cancer or in situ disease. Upstaging of ADH may occur 10-20% of the time, meaning unnecessary surgical procedures are performed in up to 90% of patients. Several studies have examined clinical features to distinguish those patients more likely to benefit from excision, but few studies describe variation within oncologic genes. The purpose of this study was to identify genetic variation associated with the risk of upstaging in patients with ADH on CNB. Methods: 35 samples total, 21 ADH and 14 DCIS were examined, comparing samples with ADH on both CNB and excision with ADH on CNB but DCIS on excision. DNA was isolated and libraries made for next generation sequencing using the TruSeq Amplicon–Cancer Panel on the Illumina NextSeq 500. NextGENe and Ingenuity Variant Analysis software was used for alignment and variant calling. This was also used to determine the Overall Mutation score to estimate the likelihood the mutation is real. Results: Genetic analysis studied 160 oncologic genes. Five tumor-specific variants were found in > 50% of DCIS patients. Unfortunately, these variants were also found in more than half of the ADH samples. At the gene level, two genes had variants in > 50% of the DCIS group, ATRX and KMT2D. Again these variants were seen in the ADH group as well. Genes containing variants occurring in at least 5 of the DCIS patients but no more than one ADH patient included APC, BRCA1, and CDK12, and all of these variants have some evidence of being deleterious. The BRCA1 variant at position 41,246,401 using genome build GRCh37 was present in 80% of the DCIS patients containing any BRCA1 variation and also has evidence of being deleterious. Conclusion: On analyzing 160 different oncologic genes for variation between ADH on both CNB and excisional biopsy, versus ADH on CNB and DCIS on excisional biopsy, no genetic variants were found to be unique to the DCIS group. Consequently, in patients with ADH on CNB, surgical excision remains a reasonable treatment.

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Population-Based Analysis of Secondary Malignancies and Survival Outcomes in Women Diagnosed with Lobular Carcinoma In Situ S.M. Wong,[1]* T. King,[2] M. Golshan.[2] *1. Surgery, McGill University Health Centre, Montreal, QC, Canada; 2. Dana-Farber/Brigham and Women's Cancer Center, Boston, MA.*

Purpose: Lobular carcinoma in situ (LCIS) is associated with an increased risk of developing breast cancer, although little data exist on long-term outcomes of patients, including those who develop subsequent malignancies. Methods: Using the Surveillance, Epidemiology, and End Results database, we identified 19,462 women diagnosed with LCIS between 1983-2013. We examined the incidence and clinical features of subsequent malignancies, and using the Kaplan-Meier method and Cox proportional hazards regression, obtained breast-cancer specific survival (BCSS) estimates for women with LCIS according to age at diagnosis, clinical characteristics, and treatment of LCIS. Results: The mean age at LCIS diagnosis was 53.7 years (range, 19-95 years), with a 10- and 20-year cumulative incidence of subsequent breast malignancy of 11.3% (95% CI; 10.7-11.9%) and 19.8% (95% CI; 18.8-20.9). At a mean follow up of 9.3 years (range, 0-30.9 years) a total of 1,837 second primary breast cancers were diagnosed, of which 55.2% were diagnosed in the ipsilateral breast, and 44.5% contralateral. Most secondary breast cancers were intermediate grade, hormone receptor positive, and diagnosed in early stages. Of subsequent malignancies, invasive ductal carcinoma (IDC) distributed equally across both breasts, whereas invasive lobular carcinoma (ILC) was more likely to present in the ipsilateral breast (ipsilateral presentation; 69.0% ILC vs. 49.2% IDC, $p<0.001$). On multivariable analysis, age at LCIS diagnosis and race were significant predictors of BCSS, while type of surgical treatment for LCIS had no affect on long-term survival ($p=0.44$). The 10- and 20-year BCSS for women with LCIS was 98.9% (95% CI; 98.7-99.1%) and 96.3% (95% CI; 95.6-96.8%), respectively. Conclusion: Women with LCIS who are diagnosed with a subsequent primary breast cancer are often diagnosed in early stages and have excellent BCSS. While management should be tailored to reduce the risk of subsequent breast cancer, patients should also be counselled on their excellent long-term outcomes.

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Mammographic Breast Density Decreases After Bariatric Surgery
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Introduction Breast density (BD) is an important risk factor for breast cancer, and is under myriad influences including genetics, hormonal effects, and body habitus. Bariatric surgery provides a reliable and durable method of weight loss for patients who are morbidly obese. Very little is known, however, regarding the impact of surgical weight loss on BD. The loss of body fat may lead to an increase in breast density, though it is also possible that significant weight loss may reduce breast density and indirectly reduce breast cancer risk. Our hypothesis is that weight loss after bariatric surgery is associated with a significant change in mammographic BD. Methods From the electronic medical record of a multi-hospital health system, women 40 years of age or older who underwent gastric bypass or gastric sleeve from 1/1/2010 to 12/31/2014 were identified. Mammographic BI-RADS density data for both pre- and post-operative mammograms were collected from a database containing breast imaging data from all health system-associated radiology facilities from 2009 – 2015. These patients' change in BMI and change in BD were analyzed with paired t-tests. Results Of the 1098 women undergoing bariatric surgery, pre- and post-operative mammography data were available for 111 patients. The mean time between surgery and post-operative mammogram was 21.4 months, and 29.4 months between mammograms. The mean decrease in BMI between surgery and the post-operative mammogram was 9.69 ($p<0.001$), and 9.99 between mammograms ($p<0.001$). BI-RADS density decreased by one in 21 patients and by two in 2 patients; it increased by one in 10 patients. Overall, post-operative BD was significantly less than pre-operative BD (Table 1). Conclusions In this cohort of women undergoing bariatric surgery, BI-RADS BD significantly decreased, which suggests that metabolic change secondary to weight loss may impact BD more than the loss of body fat. Our results suggest that bariatric surgery may indirectly reduce breast cancer risk by reducing BD, and warrant additional studies to elucidate the biochemical association between bariatric surgery and breast density.

Table 1. Frequency of mammographic BI-RADS density before and after bariatric surgery.

	BI-RADS density Frequency (%)				p-value
	1	2	3	4	
Pre-operative	28 (25.2)	66 (59.5)	17 (15.3)	0 (0)	0.008
Post-operative	41 (36.9)	57 (51.4)	13 (11.7)	0 (0)	

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Obesity-related Breast Cancer Showed Higher Response to Combination Therapy of Immune Modulator FTY720 and Doxorubicin
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INTRODUCTION: Recently we have demonstrated that sphingosine-1-phosphate (S1P), a signaling lipid mediator, link inflammation and cancer in colitis-associated colon cancer. FTY720, a functional antagonist of S1P signaling, is an immune-modulator that dramatically reduces peripheral lymphocyte counts and other inflammatory cells. We hypothesized that addition of FTY720 thus suppress the effect of obesity-mediated inflammation should enhance anti-cancer effect of doxorubicin, which is one of the most commonly used anti-cancer drug for breast cancer as part of the standard of care. METHODS: Female B6.cg-Lepob (ob/ob) mice fed with high fat diet for 2 weeks prior to orthotopic implantation of murine mammary adenocarcinoma E0771 cells were used as an obesity model, and litter mate control mice fed with normal diet were used as a control. Both ob/ob and control mice were randomized into 4 groups in each group; vehicle, Doxorubicin, FTY720 and Combination of Doxorubicin and FTY720. RESULTS: The body weight of obesity model was significantly heavier than control mice at the time of cancer cell inoculation (44.1 g vs 19.4 g; $p < 0.001$). In non-treatment group, tumor weight in obesity group was significantly heavier than control mice (1232 mg vs 966 mg; $p = 0.049$), which is consistent with the dogma that obesity worsen cancer progression. As expected, tumor weight in non-treatment group was heavier than any treatment group, and that in combination treatment of doxorubicin and FTY720 was lightest in both of obesity group and control group. Interestingly, tumor reduction rate in obesity group compared with non-treatment group is significantly greater than control group (Doxorubicin: 83% vs 19%, $p=0.001$; FTY720: 80% vs 46%, $p=0.027$, Doxorubicin + FTY720: 93% vs 64%, $p=0.011$). Over 15% weight loss were seen in obesity doxorubicin group and obesity combination treatment group. CONCLUSIONS: Immune-modulator FTY720 enhanced the efficacy of doxorubicin particularly in obese mice, which implicate a novel approach to treat obesity-associated breast cancer.

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Final Analysis of the Phase IIb Trial of the HER2 Vaccines, AE37 or GP2+GM-CSF Versus GM-CSF Alone to Prevent Recurrence in High-risk Breast Cancer Patients
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Introduction HER2 is expressed at a detectable level in 60-70% breast cancers(BrCa). We completed a randomized controlled phase IIb trial of 2 HER2-directed peptides: GP2, a CD8+ T cell-eliciting peptide; AE37, a CD4+ T cell-eliciting peptide. Both were safe and effective in raising HER2-specific immunity, but neither showed a significant overall difference in disease free survival (DFS). Here, we explore the differing effect of these vaccines within pre-defined subgroups. Methods After completion of standard therapy, BrCa patients(pts) with any level of HER2(IHC 1-3+) were randomized to GP2+GM-CSF or GM-CSF alone if HLA-A2+ or AE37+GM-CSF or GM-CSF alone if HLA-A2-. Pts received 6 monthly doses of peptide+GM-CSF(VG) or GM-CSF alone (CG) and 4 semi-annual boosters. Demographic and DFS data were analyzed. Pts who recurred prior to completing the primary vaccine series or developed another malignancy were excluded from per-treatment (PT) analysis. Results A total of 301 pts were enrolled in the AE37 arm (VG:154, CG:147; median f/u 46.7mo) and 180 in the GP2 arm (VG:89, CG:91; median f/u 41.7mo). There were no clinicopathologic differences between groups. For AE37, the relative risk of recurrence (RRR) was lower for the VG in ER/PR-, HER2 1-2+, triple negative (TNBC) and advanced stage subsets. ITT analysis of AE37 pts with TNBC & advanced stage showed a trend toward improved DFS for the VG v CG (85.7% v. 31.3%, $p=0.054$). For GP2, the RRR was lower for the VG in low T stage, ER+, and HER2 overexpression (OE) subsets. PT analysis of GP2 pts with HER2 OE showed a trend toward improved DFS VG v CG (100% v. 87.2%, $p=0.052$). Discussion In this trial of two different peptide vaccines, we found benefits in differing subsets for each vaccine. AE37, a CD4-eliciting vaccine showed improved DFS in advanced stage, TNBC pts, a group with few treatment options currently. In contrast, GP2, a CD8-eliciting vaccine showed improved outcomes in HER2 OE pts; the combination of GP2 and trastuzumab is being studied. These two vaccines could be given separately to specific subsets of pts or used broadly as a multi-epitope vaccine.

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Intratumoral Injection of Chimeric Antigen Receptor (CAR) T-Cells Directed Against C-Met in the Treatment of Breast Cancer is Safe: Results of Phase I Trial NCT018376
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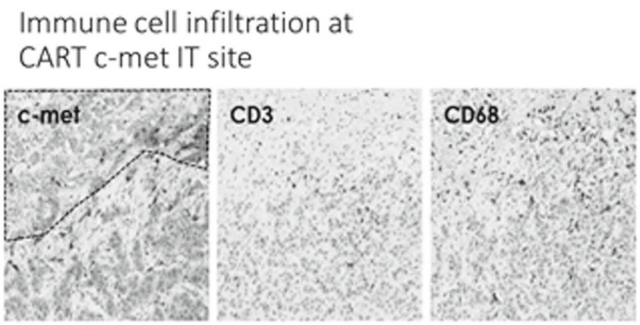
Introduction: CAR T cells (CART) are "supercharged" effector immune cells genetically modified to carry out tumoricidal functions upon CAR/antigen (e.g. CD19) binding. CART have demonstrated unprecedented effectiveness in the treatment of hematologic malignancies. However the effectiveness of CART in the treatment of solid tumors remains uncertain. Barriers include 1) on-target/off-tumor effects due to the presence of tumor associated antigens on normal tissues; and 2) an immunosuppressed tumor microenvironment limiting access and potency of CART within the tumor. We have developed a CART (c-Met CART) against c-Met, an oncodriver, expressed in >50% of all breast cancer regardless of subtypes. Our preclinical data confirmed the effectiveness of c-Met CART in eradicating tumor xenografts. We have designed a first in human phase I clinical trial to evaluate c-Met CART in patients with

c-Met+ metastatic breast cancer (NCT01837602). Two safety measures were used: 1) instead of transfection with DNA vector, RNA CAR transcripts were electroporated into T cells to ensure transient (5 days) CAR expression; and 2) intratumoral (IT) injection limits CART extravasation and allows evaluation of direct tumor effects of CART. Methods: Patients with c-Met+ tumors received a single IT injection at 1 of 2 c-Met CART dose levels: $3x10^7$ (cohort 1) and $3x10^8$ (cohort 2) (n=3 per cohort). Tumors treated with IT c-met CART were excised and analyzed using IHC. Results: IT c-Met CART was well tolerated. Patients only reported mild subjective myalgia as adverse events (AE) (grade I), which resolved within 24 hours. The higher IT dose $3x10^8$ c-Met CART was well tolerated in all 3 patients. Examination of resected tumor revealed tumor necrosis, including abundant c-Met^+ cellular debris, surrounded by myeloid-derived CD68+ cells at the leading edge of necrotic zone (Figure). CART was not detected in peripheral blood post IT injection. Conclusion: IT c-Met CART is feasible, safe and evokes significant inflammatory response within tumors. A phase 1 trial to assess safety of systemic c-met CART treatment of breast cancer is planned.



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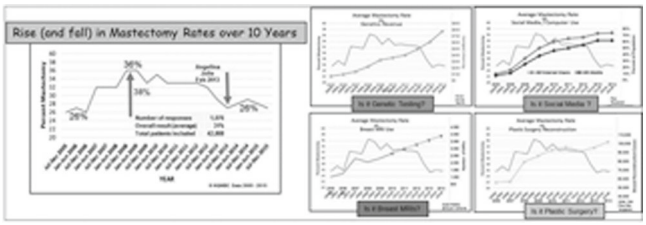
Increasing Rates of Mastectomy: Has the Pendulum Swung Back? Data from the National Quality Measures for Breast Centers - NQMBC C.S. Kaufman,[1]* B.S. Rosen,[2] T. Heckel,[3] F.L. Tucker,[4] E. Kim.[5] *1. Surgery, University of Washington, Bellingham, WA; 2. Advanced Surgical Care, Barrington, IL; 3. Catholic Healthcare Initiatives, Colorado Springs, CO; 4. Virginia Biomedical Laboratories, Roanoke, VA; 5. Sutter Health, Roseville, CA.*

BACKGROUND: Mastectomy for early stage breast cancers has increased in the United States compared with prior years. Agents associated with this change may be a) use of genetic testing, b) use of breast MRI, c) options for reconstructive surgery, and d) anxiety prompted by social media. The National Quality Measures for Breast Centers (NQMBC) program measures the use of breast conserving surgery (BCS) for early stage breast cancer. We present these data of frequency of use of mastectomy (in contrast to BCS) from 2005 through 2015, and timely associations to understand these changes. METHODS: Centers may participate in the NQMBC by entering their data on any of 31 quality measures and immediately compare themselves with results from other similar centers. Over 500 centers have participated over the last 10 years. We report on the use of mastectomy over the 10 year period. We also look at the use of those four associations during this time. RESULTS: The overall average use of mastectomy was 30.8%. This was calculated from 1,076 individual submissions representing 42,888 patients. The percentage receiving mastectomy varied over time (Figure). We saw a 10.5% increase in use of mastectomy between 2005 and 2009 (25.8% to 36.3%) which is a relative 38% increase from baseline levels. From 2009 to 2012 the rate of mastectomy remained high across all geographic regions submitting data. After 2012 there was an absolute 7% decrease in mastectomy use, with levels of mastectomy by 2014 falling to their 2006 baseline values (25.6%). We note that all the external factors (genetic testing, breast MRI, plastic surgery, and use of social media) showed increased use over this time period. Over this time period, social media went from a trusted new source of information to the recognizing not everything on the internet is true. CONCLUSIONS: The NQMBC quality program has monitored the use of BCS and mastectomy over 10 years 2005 to 2015. The NQMBC has seen a relative 38% increase in mastectomy but also a return to baseline levles in recent years. Further research will be necessary to identify causative agents which may influence trends in mastectomy use.



Left graph shows increasing rates of mastectomy, rising til 2009, being level til 2013 than decreasing back to baseline. The right four graphs show increase use of the four potential causative agents related to the mastectomy changes.

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A Systematic Review of the Surgical and Ablative Management of Breast Cancer Liver Metastasis K. Yoon-Flannery,[1]* S.A. Blankenship,[2] C.S. Fisher,[1] R.E. Mustafa,[1] N. Nocera,[1] J. Tchou,[1] B.J. Czerniecki,[3] L. De La Cruz.[1] *1. University of Pennsylvania, Philadelphia, PA; 2. Washington University in St. Louis, St. Louis, MO; 3. Moffitt Cancer Center, Tampa, FL.*

Background: When breast cancer spreads to the liver, it is considered a systemic disease and associated with poor prognosis. Isolated liver metastasis occurs in 5-18% of breast cancer patients. Systemic therapy is still considered the first line treatment for these patients, although the survival is still poor. There is increasing interest in surgical management of breast cancer liver metastasis (BCLM) to yield better survival. We aim to assess oncologic outcomes after two types of local management in patients with BCLM. Methods: A systematic literature review identified peer-reviewed articles in PubMed evaluating oncologic outcomes for surgical resection (SR) and ablative therapies (AT) for the management of BCLM. Selected studies reported the following oncologic outcomes: disease-free survival (DFS), overall survival (OS), overall survival rate (OSR) at 1, 2, 3 and/or 5 years, complication rate (CR) and/or mortality rate (MR). Results: The search yielded 3,028 articles; 67 met the inclusion criteria and collectively evaluated 2,357 patients with a median age of 49.7 years (range 45.2-62.5) over a mean follow-up of 32.4 months. Most common tumor histology was invasive ductal carcinoma (77.3%) with extrahepatic disease (EHD) present in 30.1% (SR 15.5% vs. AT 39.5%). Weighted-averages for median length of OS and DFS were 43.7 and 22.8 months among the SR group and 40.6 and 23.4 months among the AT group. Local recurrence for the SR group was 51.4% vs. 13.9% for the AT group. CR and MR were 8.8% and 0.04% for AT vs. 17.7% and 0.37% for SR. OS at 1, 2, 3 and 5 years were 86.8%, 70.6%, 58.3% and 36.9% for SR, and 87.3%, 79.3%, 56.4% and 37.5% for AT. Among SR patients, length of OS did not significantly differ for patients with and without EHD (43.2 vs. 37.6 months, p=0.68). Conclusion: This study is the largest comprehensive literature review on the surgical and ablative management of BCLM to date. Our systematic review reveals favorable OS and DFS with low morbidity and mortality rates when patients undergo local management of their BCLM. While a clinical trial may not be feasible, surgery and ablative therapy should be considered for all patients with BCLM.

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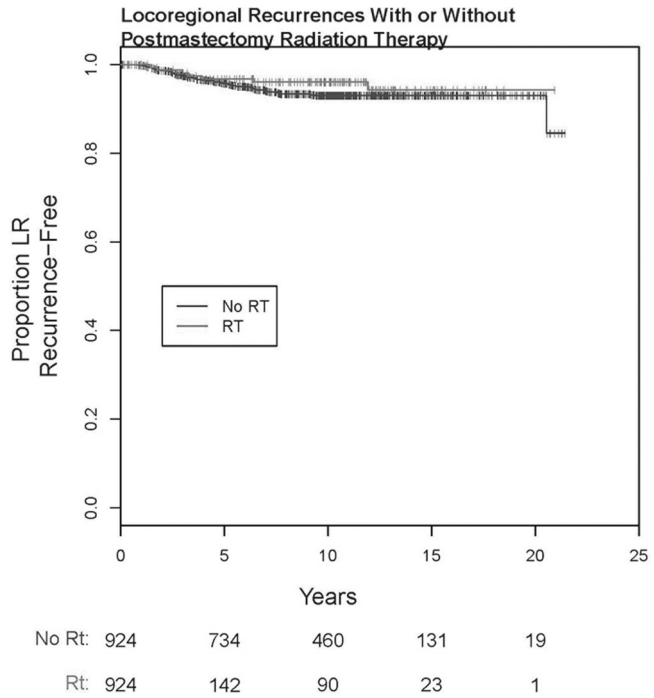
Most Breast Cancer Patients with T1-2 Tumors and 1-3 Positive Lymph Nodes Do Not Need Post-Mastectomy Radiotherapy S. Muhsen,* S. Patil, M. Stempel, S. Powell, M. Morrow, M. El-Tamer. *Breast Surgical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Recently published guidelines concur that postmastectomy radiation (PMRT) in T1-2 tumors with 1-3 positive (+) lymph nodes (LN) decreases locoregional recurrence (LRR). They have advised limiting PMRT to patients with highest risk of LRR to balance against potential harms. The purpose of this study is to identify risk factors for LRR after total mastectomy (TM) in patients with T1-2 tumors and 1-3 + LN, treated with modern chemotherapy, with a 10-year follow-up to evaluate the safety of limiting PMRT in high risk patients. Method: From 1995-2006, patients who underwent TM with sentinel and/or axillary lymph node dissection were identified. Patients receiving neoadjuvant chemotherapy, T3-4 tumors, or >3 + LNs were excluded. Patients were categorized based on receipt of PMRT. Molecular

subtypes (MST) were defined as Luminal A/B (HR+/Her2-), Luminal Her2 (HR+/Her2+), Her2 (HR-/Her2+) and Basal (HR-/Her2-). Chi-squared test was used to compare clinicopathologic features. Kaplan-Meier and Cox regression analysis were used to examine associations between PMRT or MST and LRR, Recurrence-free Survival (RFS), and Overall Survival (OS). Results: 1087 patients (924 no PMRT, 163 PMRT) were included. Median follow-up was 10.8 yrs (Range,0-21). In the entire cohort, 63 LRRs occurred (56 no PMRT, 7 PMRT). The 10-yr risks of LRR with and without PMRT were 4% and 7%, respectively (Graph-1). Patients receiving PMRT had larger tumors (p=0.013), higher histologic grade (p=0.03), more + LNs (p<0.0001), LVI (p<0.0001), extranodal invasion (p<00001), macroscopic axillary LN metastases (p<0.0001), and age ≤50yrs (p=0.001). PMRT and no-PMRT groups did not differ in LRR, RFS or OS (p>0.3). There was no association between MST and LRR. On multivariate analysis, age ≤50 years (p=0.0011) and presence of LVI (p<0.0001) were predictors of LRR in those who did not receive PMRT. Conclusions: Our data is consistent with the new guidelines. With careful selection, 85% of patients with T1-2 tumors and 1-3 + LN were spared PMRT, while maintaining low LRR and survival equivalent to those who received PMRT. Age ≤50 years and presence of LVI are significant predictors of LRR.



Locoregional Recurrences With or Without Postmastectomy Radiation Therapy

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Axillary Micrometastases are Not an Indication for Post-Mastectomy Radiotherapy in Stage 1 and 2 Breast Cancer

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Background: Randomized trials demonstrate equivalent locoregional control with sentinel node biopsy (SNB) or axillary dissection (ALND) for T1-2, micrometastatic (T1-2N0i+/N1mi) breast cancer, but include few mastectomy patients. Consensus is lacking on indications for post-mastectomy radiotherapy (PMRT) in this population, which is underrepresented in most radiotherapy trials. We sought to evaluate locoregional recurrence (LRR) in an unselected, modern cohort of T1-2N0i+/N1mi patients having mastectomy. Methods: We retrospectively identified patients with T1-2N0i+/N1mi breast cancer treated with mastectomy from 1/2006-12/2011. Nodal deposits measured ≤2mm and included isolated tumor cells (ITCs). Recurrent, bilateral, and neoadjuvant cases were excluded. Clinicopathologic features and adjuvant therapies were assessed. The primary outcome of interest was LRR. Results: Of 352 patients who met inclusion criteria, 211 (60%) had ITCs and 141 (40%) had micrometastases. A single node was positive in 295 (84%) cases. 162 (46%) patients had SNB alone, with median 4 sentinel nodes (SNs) removed; the remainder had axillary dissection. 31 (9%) patients had PMRT. Table 1 summarizes characteristics of 321 patients treated without PMRT. 95% had systemic therapy. At median 6 years of follow-up, the overall LRR rate was 2.8% (n=9), with no axillary recurrences. The LRR rate was 4.4% among those with 1 positive node who had SNB alone. Those with LRR had median age 55yrs, median tumor size 1.7cm, and all ductal histology; 67% were multifocal/multicentric, 33% had medial/central tumors, 33% had lymphovascular invasion, and the majority were high grade (89%), estrogen receptor positive (78%), with 1 positive node (89%). By Kaplan-Meier estimation, there was no association between LRR and receipt of PMRT (p=0.4), SNB vs. ALND (p=0.2), or number of positive nodes (p=0.7). Conclusions: LRR was low at median 6 years of follow-up among T1-2N0i+/N1mi patients treated with mastectomy without PMRT, with no axillary failures. These results demonstrate excellent locoregional control in this population without PMRT or nodal radiotherapy.

Table 1: Clinicopathologic characteristics of T1-T2 N0i+/N1mi patients treated with mastectomy without PMRT, n=321

	n=321
	Median (Range)
Age (years)	50 (24–90)
Pathologic tumor size (cm)	1.5 (<0.1–4.8)
	n (%)
Histology	
Ductal	254 (79%)
Lobular or mixed	67 (21%)
Associated DCIS*	
<25%	197 (63%)
>25%	115 (37%)
Grade**	
Low	16 (6%)
Intermediate	133 (47%)
High	135 (48%)
Receptor status***	
ER+/HER2–	222 (71%)
ER+/HER2+	43 (14%)
ER–/HER2+	21 (7%)
ER–/HER2–	28 (9%)
Lymphovascular invasion	112 (35%)
Multifocal/multicentric	162 (50%)
Tumor location	
Medial or central	103 (32%)
Lateral	218 (68%)
# of positive lymph nodes	
1 node	272 (85%)
>1 node	49 (15%)

*Unknown in n=9 cases, percentages calculated among n=312 known
**Unknown in n=37 cases, percentages calculated among n=284 known
***Unknown in n=7 cases, percentages calculated among n=314 known

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Promoter DNA Hypermethylation of CDO1 Gene and High Chemosensitivity Through Modification of Mitochondrial Membrane Potential in Colorectal Cancer

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Background Cysteine dioxygenase type 1 (CDO1) has been recently demonstrated to be a tumor suppressor gene in human cancers and its expression is proved to be regulated frequently by its promotor DNA cytosine methylation. Otherwise, cysteine sulfinic acid (CSA, the metabolite of CDO1) was shown to be accumulated in high grade glioblastoma and its accumulation enables cancer cells to sustain mitochondrial membrane potential (MMP) that could affect chemoresistance. The aim of this study is to investigate the clinical significance of CDO1 gene in colon cancer. Material and methods We first investigated 90 adenoma and 107 colorectal cancer (CRC) tissues and corresponding normal mucosa tissues with regard to CDO1 methylation. We next investigated another 170 colon cancer patients with pathological Stage III who undertook colectomy. CDO1 promoter DNA methylation was assessed by quantitative methylation specific PCR as TaqMeth V. Analysis of the functional role of CDO1 gene was done by using a forced expression

model of CDO1 gene in CRC cell lines. Results (1) Mean TaqMeth V of CDO1 gene in normal mucosa, adenoma and primary CRC tissues were 4.3, 19.8 and 34.8 respectively, and there was a significant difference during CRC progression ($p<0.0001$). (2) Multivariate Cox proportional hazards model identified CDO1 methylation was independent prognostic factor, if restricted to 170 primary colon cancer with pStage III ($p=0.0341$). Surprisingly, the stage III colon cancer patients with high TaqMeth V showed significantly better prognosis than otherwise patients among those with adjuvant chemotherapy ($p=0.0361$). (3) In CRC cell lines, forced expression of CDO1 gene increased MMP. Furthermore, CDO1-expressed cells showed resistance to the chemotherapy with 5-FU. Conclusion Methylation of CDO1 gene promotor DNA was accumulated during adenoma-carcinoma sequence of CRC development. Conversely, hypermethylation of CDO1 gene may indicate high sensitivity of postoperative adjuvant chemotherapy in Stage III colon cancer from a prognostic point of view, putatively through the mechanism modifying MMP.

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Oncolytic Vaccinia Virus Expressing IL15/IL15Rα Fusion Protein Induces Immune Cell Infiltration into Tumor and Improves Anti-tumor Efficacy S. Kowalsky,* Z. Guo, R. Ravindranathan, D. Bartlett. *University of Pittsburgh Cancer Institute, Pittsburgh, PA.*

Background: Tumor-selective vaccinia virus (vvDD) has oncolytic properties, which can be improved by arming the virus with immune-stimulating molecules. Interleukin 15 (IL15) plays an important role in activation and proliferation of CD8+ T cells and NK cells. Fusing IL15 to its alpha receptor chain (IL15Rα) augments this activity and anti-tumor effects. Methods: We created a novel vaccinia virus expressing IL15/IL15Rα fusion protein (vvDD-IL15Rα). Immunologic effects of virus (vvDD-IL15Rα or vvDD vs PBS control) on tumor microenvironment (TME) were evaluated with quantitative real-time PCR analysis in a MC38 murine colon cancer. Immune cell infiltration and cytokine expression in TME was analyzed. Anti-tumor effects and survival were evaluated in a MC38 colon cancer carcinomatosis model. Results: After intravenous administration, vvDD and vvDD-IL15Rα both replicated in tumor tissue, and vvDD-IL15Rα expressed the fusion complex in TME at all time points (day 2, 4, and 6). vvDD-IL15Rα treatment significantly increased median relative expression of CD8 marker at each time point compared to vvDD. Viral IL15Rα fusion complex expression significantly enhanced NK cell marker NKp46 expression at day 6 (0.392 vs 0.011, $p<0.001$) and NKG2D expression at day 4 and 6. Suggesting activated cell infiltrate, granzyme B expression was significantly elevated at day 6 (9.48 vs 0.176, $p=0.001$). Immune-inhibitory TGFβ expression was significantly decreased at day 4 (8.80 vs 28.1, $p<0.001$). In murine colorectal carcinomatosis, intra-peritoneally delivered vvDD-IL15Rα significantly delayed tumor progression up to 30 days by in vivo imaging. Survival was significantly improved with vvDD-IL15Rα treatment, with 100% survival at day 48, compared to median survival of 36 days for vvDD-treated ($p<0.001$) and 18 days for control mice ($p<0.001$). Conclusions: Evaluation of TME suggests increased infiltration and activation of CD8+ T cells and NK cells with vvDD-IL15Rα treatment. Significant advantages in delayed tumor progression and improved overall survival were observed, suggesting immune cell recruitment to TME improved anti-tumor efficacy.

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Anti-KRAS siRNA Nanoparticles for Targeted Colorectal Cancer Therapy B. Krasnick,[1]* M.S. Strand,[1] Y. Bi,[1] P. Goedegebuure,[1] T. Fleming,[1] S.A. Wickline,[2] H. Pan,[2] R. Fields.[1] *1. Department of Surgery, Washington University School of Medicine, St. Louis, MO; 2. Department of Medicine, Washington University School of Medicine, St. Louis, MO.*

Introduction: Standard treatment for metastatic colorectal cancer (mCRC) is systemic chemotherapy with anti-EGFR treatment, depending on KRAS mutational status. However, tumors harboring a KRAS mutation do not respond to existing targeted therapy. Moreover, targeting mutant KRAS has, to date, not been possible. Herein, we explore using a KRAS inhibitory nanoparticle (NP), to directly knock down mutant KRAS. Methods: Utilizing fluorescent-labeled small interfering RNA (siRNA) NPs, uptake was assessed via fluorescent microscopy. KRAS mutant CT26 and wild-type MC38 CRC cell lines were incubated with either scramble (Sc) sequence siRNA NP, KRAS siRNA NP, or FOLFOX chemotherapy ± KRAS siRNA NP. Cell viability was assessed via a luminescent viability assay. KRAS and cleaved caspase 3 protein expression were assessed using western blotting. Results: Fluorescent NP uptake was demonstrated in CT26 cells as early as 260 minutes post treatment. Decreased cellular viability was seen with KRAS siRNA NP treated CT26 cells, as compared to both Sc siRNA NP and non-treated CT26 cells (both $p<0.0001$). Cell viability was significantly diminished with FOLFOX combined with KRAS siRNA NP as compared to FOLFOX alone for CT26 cells ($p=0.0003$), but not MC38 cells ($p=0.2259$). Western blot demonstrated decreased KRAS and increased cleaved caspase 3 expression in CT26 cells treated with KRAS siRNA NP. Conclusion: A KRAS siRNA tagged NP was internalized by the CRC cells in vitro, and induced cellular death via apoptosis in mutant type KRAS CRC. In addition, KRAS siRNA NP acted synergistically with FOLFOX chemotherapy to enhance cell death. We believe KRAS inhibition based NP treatment is a promising target for mutant type KRAS CRC.

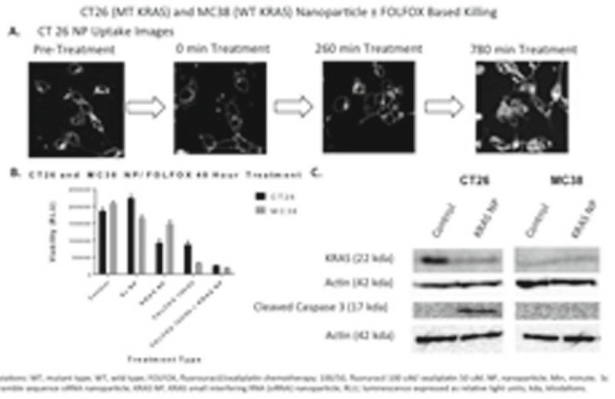

Figure. A. CT26 fluorescently tagged siRNA based NP (pink), with fluorescently tagged lysosomes (yellow) and cell membranes (cyan blue). Uptake is seen as early as 260 minutes post treatment, as seen here with intracellular speckling of fluorescent siRNA. B. Killing assay of CT26 and MC38 cells with NP ± FOLFOX chemotherapy. C. Western blot data demonstrating decreased KRAS expression in CT26 colorectal cancer cells, in addition to increased expression of cleaved caspase 3.

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Methylomic Classifiers of Anal Cancer Outcomes: An NRG Oncology/RTOG 98-11 Tissue Study E. Siegel,[2] S.A. Eschrich,[2] A.E. Berglund,[2] A. Ajidahun,[1] A.M. Magliocco,[2] R. Putney,[2] B. Riggs,[2] J. Moughan,[10] S. Hoffe,[2] J.P. Simko,[3] J. Ajani,[4] C. Guha,[5] G. Okawara,[6] J.W. Clouse,[7] M.J. Becker,[8] J.F. Pizzolato,[9] C.H. Crane,[4] D. Shibata.[1]* *1. Surgery, University of Tennessee Health Science Center, Memphis, TN; 2. Moffitt Cancer Center, Tampa, FL; 3. University of California San Francisco, San Francisco, CA; 4. M.D. Anderson Cancer Center, Houston, TX; 5. Montefiore Medical Center, New York, NY; 6. Juravinski Cancer Centre, Hamilton, ON, Canada; 7. Cancer Research for the Ozarks NCORP, Springfield, MO; 8. Columbus Community Clinical Oncology Program, Columbus, OH; 9. Mount Sinai Comprehensive Cancer Center, Miami, FL; 10. NRG Oncology, Philadelphia, PA.*

Background: Genome-wide epigenetic events appear to play a role in the development and behavior of HPV+ cancers. The value of adjuvant therapy following chemoradiation for localized anal cancer (AC) remains unclear. Molecular prognostication to identify patients (pts) who may be at higher risk for recurrence would be valuable. The goal was to define methylomic profiles predictive of disease-free (DFS) and overall (OS) survival in pts with AC. Methods: Genomic DNA was extracted, processed and methylation status at ~450,000 CpG loci was examined (Illumina HumanMethylation450 Array). A multistep bioinformatics methodology was applied to develop a prognostic methylomic classifier for OS and DFS: (1) feature selection for methylated regions (β-value interquartile range ≥ 0.2, ≥ 2 adjacent significant probes within a CpG Island and $p<0.05$ by univariate Cox proportional hazards) (2) selected features were entered into a supervised principal component analysis (PCA) and 3 components (PC1, PC2, PC3) were derived (3) classifier was built using forward selection multivariate regression models [PC1, PC2, PC3 alone and in combination with clinical features (size: >T2 vs. ≤T2, nodal status: N0 vs N+)]

using a 10-fold cross-validation (4) final model prediction risk score was generated, dichotomized and evaluated for prognostic values in Cox regression analysis. Results: A total of 121 AC specimens from RTOG 98-11 were examined. The methylomic-only classifier model trended towards statistical significance (log-rank p=0.05; HR=1.96; 95% CI 0.99-3.88) in DFS (PC1, PC3 selected). In the combined model with clinical features, the final classifier included T status and epigenetic features (PC1, PC3) and was strongly predictive for DFS (p<0.0001, HR=4.45; 2.02-9.76). Final OS classifier models [methylomic-only (p=0.28 HR=1.55; 0.70-3.44) or combined (p=0.013 HR=2.88; 1.20-6.89)] were not as accurate. Conclusions: Methylomic and clinical features synergize to predict DFS in AC. Multivariate modeling reveal independent contributions from clinical and methylomic variables. Epigenomic profiling may contribute to the identification of high-risk pts who may benefit from adjuvant strategies.

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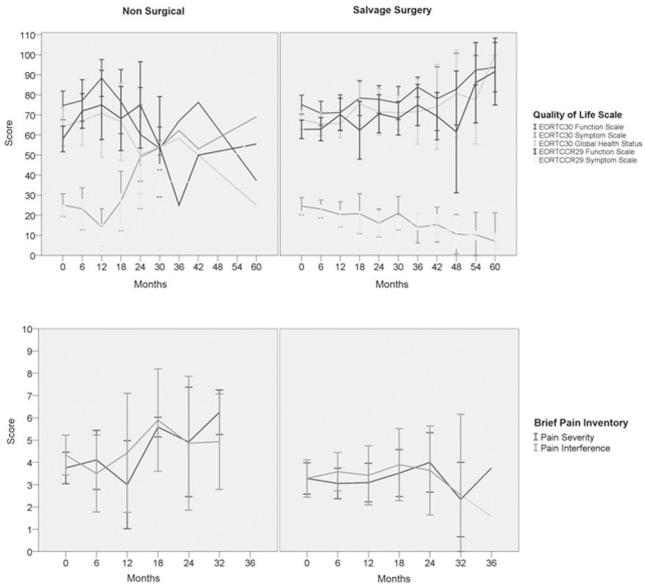
The Longitudinal Trajectory of Cancer Survivorship in Patients with Recurrent Rectal Cancer: Anatomy of Recurrence Impacts Prospective Quality of Life and Pain Severity T. Sammour,* S. Malakorn, G. Chang, M. Rodriguez-Bigas, B. Bednarski, C. Eng, P. Das, J.M. Skibber, Y. You. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction Multiple treatment modalities are utilized for patients with recurrent rectal cancer (RRC). While recurrent pelvic tumor can be highly symptomatic, treatments often carry significant morbidity risks. Patient-reported outcomes such as quality of life (QoL) and pain can supplement traditional clinical endpoints in assessing the effectiveness of salvage treatments, and thus aid in treatment decision making. We aimed to examine the longitudinal trajectory of cancer survivorship in RRC. Methods A prospective protocol enrolled patients diagnosed with RRC between 2008 and 2015. Participants prospectively self-reported QoL (measured by the validated EORTC QLQ-C30 and EORTC QLQ-CR29) and pain (measured by the Brief Pain Inventory, BPI), at presentation, and then every 6 months for 5 years. After accounting for repeated measures, trajectory of mean scores over time was assessed for patients amenable to surgical salvage vs those who were not, using linear mixed effect models. Results A total of 104 patients were enrolled of which 73 (70.2%) were amenable to salvage surgery with curative intent. Surgical salvage was associated with 30 day operative morbidity of 68.5% (13.7% and 5.5% Grade 3 and 4). Three year overall survival was 56.7% (68.5% in surgical and 29.0% in non-surgical patients). Mean baseline QoL scores did not differ between surgical vs. nonsurgical patients but were significantly impacted by the anatomical site of recurrent disease (lowest scores in posterior pelvic recurrence; P=0.012). On longitudinal analysis with a median followup of 33 months, surgically salvaged patients showed gradual sustained improvement in QoL but not pain scores (Figure 1). Anatomy of initial recurrence had an ongoing impact on QoL long term with posterior recurrences having the worst scores. Both QoL and pain scores worsened in patients not amendable to surgical salvage. Conclusion Disease anatomy determines QoL at baseline and long term in patients with RRC. Surgery improves QoL but not pain in selected resectable cases. Figure 1: Trajectory of QoL (EORTC30, EORTCCR29), and pain (Brief Pain Inventory)



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Causes of Death in Long-term Survivors of Colorectal Cancer A. Lewis,* P.H.G. Ituarte, K. Melstrom, S. Sentovich, J.Y. Kim. *Department of Surgery, City of Hope, Duarte, CA.*

Introduction: Prolonged survival and uncertainty after surviving cancer has led to an increased interest in survivorship. We analyzed causes of death (COD) in >5 year long survivors of CRC in an effort to optimize screening and treatment efforts. Methods: This retrospective study of patients with CRC queries the California Cancer Registry between 2000-2011 linked to inpatient records. COD were identified using ICD-10 codes, and death date was subtracted from diagnosis date. COD among patients dying within and surviving beyond 5 years (long-term survivors) were compared. Results: Of 139,743 patients with CRC, 97,604 (69.8%) originated from colon and 42,139 (30.2%) from rectum. The median age at time of presentation, 5 years and 10 years was 68, 70, and 74, respectively. The actual 5-year OS was 59.1% during which 94.9% of cancer-specific deaths occurred. The major COD within 5 years was CRC (n=38,992, 65.4%), then cardiovascular (CVD) (n=7,140, 12.0%), second primary cancer (n=3,775, 6.3%), neurologic disease (n=2,329, 3.9%), and pulmonary disease (n=2,307, 3.9%). In contrast, CVD is the major COD in long-term survivors (n=2,163, 24.0%); however, CRC still caused nearly as many deaths (2,094, 23.2%). This was followed by neurologic (n=1,174, 13.0%), secondary primary cancer (n=1,146, 12.7%), and pulmonary disease (n=765, 8.5%). CVD surpassed CRC as the major COD at 8 years (23.1% vs 22.6%, respectively) and by second primary cancer at 10 years (14.1% vs 13.8%, respectively). Conclusion: The majority of CRC deaths occur within the first 5 years. Over time, CRC is surpassed by CVD and second primary cancers as leading COD. While important in all patients post-treatment for CRC patients, control of CVD and screening for second primaries may be high target priorities in the follow-up care of long-term CRC survivors.

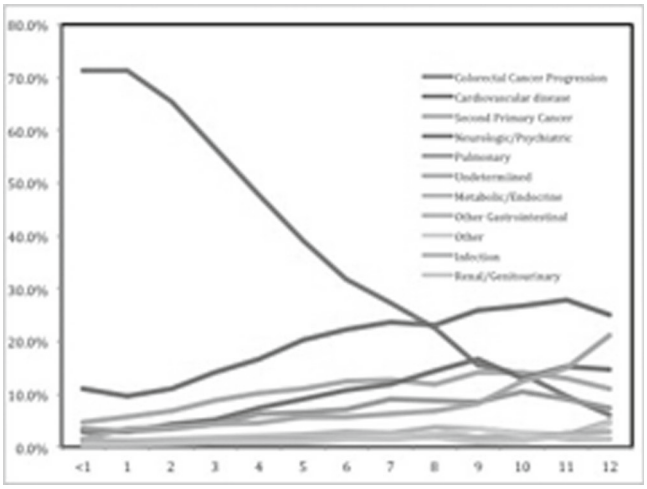

Figure 1. Proportional Causes of Death by Year in Colorectal Cancer.

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Management of Stage III Colon Cancer in the Elderly: Practice Patterns and Outcomes in the General Population S.J. Merchant,* K. Brennan, S. Karim, S. Patel, S. Nanji, C. Booth. *Surgery, Queen's University, Kingston, ON, Canada.*

Introduction: Clinical trials have established surgical resection and adjuvant chemotherapy (ACT) as standard management for stage III colon cancer; however, the extent to which the results of these trials apply to elderly patients in routine practice is not well known. Here we describe management and outcomes of elderly patients with stage III colon cancer in Ontario, Canada. Methods: All cases of surgically resected colon cancer in Ontario, Canada from 2002-2008 were identified using the population-based Ontario Cancer Registry. Linked records of treatment identified surgery and ACT utilization. Pathology reports were obtained for a 25% random sample of all cases; those cases with stage III disease constitute the study population. Management and outcomes were compared for elderly (70+ years) and non-elderly (< 70 years) patients. Cox proportional hazards model explored the association between ACT and cancer-specific (CSS) and overall survival (OS). Results: The study population included 2920 patients, 1521 (52%) of whom were elderly. Thirty and 90-day mortality increased with advanced age: <70 years, 2%/5%; 70-74 years, 3%/7%; 75-79 years, 5%/8%, 80+ years, 9%/16% (p<0.001). ACT was delivered to 48% (725/1521) of patients 70+ years and 81% (1136/1399) of patients < 70 years (p<0.001). ACT utilization rates remained stable over the study period. Factors independently associated with ACT utilization among the elderly were younger age (p<0.001), male sex (p=0.041), and no co-morbidity (p=0.001). Among patients 70+ years, ACT was associated with improved CSS (HR 0.73, 95%CI 0.60-0.88) and OS (HR 0.71, 95%CI 0.60-0.83); however, the magnitude of benefit in elderly patients was smaller than in patients < 70 years (CSS HR 0.53, 95%CI 0.42-0.67; OS HR 0.56, 95%CI 0.45-0.69). Conclusions: Half of patients 70+ years of age with stage III colon cancer do not receive ACT. Our results suggest that although the effect size is smaller than in younger patients, ACT is associated with improved long-term survival in elderly patients.

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Pathologic Response After Short Versus Long Course (chemo) Radiation Therapy in Rectal Cancer Patients A. Rombouts,[1]* N. Hugen,[1] M. Elferink,[2] P. Poortmans,[1] I. Nagtegaal,[1] H. de Wilt.[1] *1. Surgery, Radboud University Medical Center, Nijmegen, Netherlands; 2. Netherlands Comprehensive Cancer Organisation, Enschede, Netherlands.*

Background: Because of the level of morbidity associated with total mesorectal excision (TME) surgery, concerns have risen that radical surgery may not be the optimal method of treatment for rectal cancer. There is an ongoing quest for organ preserving treatment strategies and the goal of the current study was to evaluate and compare the pathological response rate between patients who received short course radiation therapy (SCRT) and long course chemoradiation therapy (CRT). Methods: All stage I-III rectal cancer patients who were diagnosed between 2005-2014 and received SCRT (5x5Gy; N=787) or CRT (25x2Gy + 5FU; N=1,214) followed by surgery after a treatment interval of 5-15 weeks were retrieved from the Dutch nationwide cancer registry. Characteristics were analysed using chi-square test, or in case of an expected cell count less than 5 the Fisher's exact test or Monte Carlo simulation was used. Logistic regression was used for multivariable analysis. Results: Median age for patients treated with SCRT was 76 years (range 28-92) compared with a median age of 64 years (range 23-86) in patients treated with CRTX (p<0.001). Patients treated with SCRT had a favorable cT- and cN-stage (Table 1). Treatment interval between neoadjuvant therapy and surgery was significantly shorter in patients treated with SCRT (p<0.001; Table 1). Complete pathologic response (ypT0N0) was found in 8.7% of patients treated with SCRT and 14.8% of patients treated with CRT (odds ratio [OR] 0.56, 95% confidence interval [CI] 0.33-0.94). A near complete pathologic response (ypT0-1N0) was found in 17.5% of patients after SCRT and 20.1% of patients after CRT (OR 0.86, 95% CI 0.56-1.23). Pathologic response was not associated with the length of treatment interval in either of the two treatment groups. Conclusion: Despite a worse clinical stage, complete pathologic response was more prevalent in patients treated with CRT compared to patients treated with SCRT. Prospective trials are needed to establish the difference between these two treatment regimens and the impact on organ preserving strategies.

Clinical and pathological characteristics

		SCRT (N=787)	CRT (N=1,214)	p-value
Age in years	Median (range) - <45 - 45-59 - 60-74 - >75	76 (28-92) 10 (1.3) 76 (9.7) 261 (33.2) 440 (55.9)	64 (23-86) 68 (5.6) 357 (29.4) 644 (53.0) 145 (11.9)	<0.001
Sex	- Male - Female	436 (55.4) 351 (44.6)	763 (62.9) 451 (37.1)	0.001
cT-stage	- cT0 - cT1 - cT2 - cT3 - cT4 - cTx	1 (0.1) 16 (2.0) 161 (20.5) 489 (62.1) 4 (0.5) 116 (14.7)	3 4 (0.3) 110 (9.1) 770 (63.4) 107 (8.8) 220 (18.1)	<0.001
cN-stage	- cN0 - cN1 - cN2 - cNx	347 (44.1) 112 (14.2) 50 (6.4) 278 (35.3)	271 (22.3) 276 (22.7) 195 (16.1) 472 (38.9)	<0.001
Treatment interval	- 5-8 weeks - 9-11 weeks - 12-15 weeks	379 (48.2) 265 (33.7) 143 (18.2)	408 (33.6) 508 (41.8) 298 (24.5)	<0.001
ypT-stage	- ypT0 - ypT1 - ypT2 - ypT3 - ypT4 - ypTx	78 (9.9) 72 (9.1) 218 (27.7) 368 (46.8) 2 (0.3) 49 (6.2)	194 (16.0) 77 (6.3) 302 (24.9) 532 (43.8) 23 (1.9) 86 (7.1)	<0.001
ypN-stage	- ypN0 - ypN1 - ypN2 - ypNx	483 (61.4) 12 (1.5) 5 (0.6) 287 (6.5)	800 (65.9) 61 (5.0) 32 (2.6) 321 (26.4)	<0.001
Differentiation	- Well - Intermediate - Poor - Unknown	20 (2.5) 295 (37.5) 35 (4.4) 437 (55.5)	26 (2.1) 378 (31.1) 63 (5.2) 747 (61.5)	0.023
Distance to anus	- 0-5 cm - 6-10 cm - >10cm - Unknown	342 (43.5) 278 (35.3) 104 (13.2) 63 (8.0)	459 (37.8) 376 (31.0) 131 (10.8) 248 (20.4)	<0.001
Histology	- AC - MC - SRCC - Other	726 (92.2) 56 (7.1) 4 (0.5) 1 (0.1)	1,088 (89.6) 111 (9.1) 10 (0.8) 5 (0.4)	0.201

SCRT, short course radiation therapy; CRT, chemoradiation therapy; cT-stage, clinical tumor stage; cN-stage, clinical node stage; ypT-stage, pathological tumor stage; ypN-stage, pathological node stage; AC, adenocarcinoma not otherwise specified; MC, mucinous adenocarcinoma; SRCC signet ring cell adenocarcinoma.

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Investigation of Usefulness of the Distance of Mesorectal: Extension (DME) in Preoperative MRI in Surgical Techniques Selection J. Mazaki,* S. Tsukamoto, D. Shida, H. Ochiai, Y. Kanemitsu, M. Miyake. *National cancer center hospital, Cyuo-ku, Japan.*

Introduction: In recent years, pathological infiltration distance of rectal tumor in mesorectum (distance of mesorectal extension, DME) has been suggested to affect the prognosis in lower rectal cancer. Objective: We aimed to investigate the usefulness of DME measured in preoperative MRI on operative

procedures selection of either intersphincteric resection (ISR) or abdominoperineal resection (APR) in lower rectal cancer. Method: A total of 447 patients with lower rectal cancer, who underwent either ISR or APR from 2000-2014 were reviewed retrospectively. There were 223 patients with preoperative cT3 or T4 rectal cancer of whom their DME could be measured in preoperative MRI. DME was defined as the maximum depth (mm) of invasion beyond the outer border of muscularis propria. The optimal prognostic cut-off point of DME for oncology outcome in term of recurrence prediction was determined using the receiver operating characteristic (ROC) curve and with reference to the previous reports. DME of 4mm was taken as the positive cut-off value of rectal tumor infiltration. Patients with a DME≥4mm were treated as DME positive group whereas patients with DME<4mm were analysed as DME negative group. Result: There were 74 cases of ISR and 149 cases of APR. The DME was 0-20mm (median 0mm) in ISR and 0-32mm (median 4.2mm) in APR. There were 102 DME positive patients and 121 DME negative patients. Background characteristics between the two groups (age, sex, distance from anal verge, preoperative CEA) were not significantly different. The 3-year recurrence-free survival of patients undergoing ISR and APR in DME negative group was 87.2% and 77.9% (p=0.2168), respectively meanwhile it was 52.7% and 69.5% (p=0.0442), respectively in DME positive group. Conclusion: Although surgical techniques selection of ISR or APR didn`t affect the prognosis in DME negative group, the 3-year recurrence-free survival of ISR patients was significantly lower than that of the APR group in DME positive group. DME measured in preoperative MRI is potentially useful in the selection of surgical procedures in lower rectal cancer.

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Phase II Trial of Liver Resection followed by Bevacizumab in Combination With CapeOX in Colorectal Cancer Patients With Liver Metastases (H2, H3) (NCCSG-05) Y. Takii,[1]* H. Kameyama,[2] S. Maruyama,[1] H. Nogami,[1] A. Nishimura,[3] M. Kawahara,[3] T. Yamazaki,[4] A. Iwaya,[4] T. Tani,[5] K. Akazawa,[2] T. Wakai.[2] *1. Gastroenterological Surgery, Niigata Cancer Center Hospital, Niigata, Japan; 2. Niigata University, Niigata, Japan; 3. Nagaoka Chuo General Hospital, Nagaoka, Japan; 4. Niigata City General Hospital, Niigata, Japan; 5. Japanease Red Cross Nagaoka Hospital, Nagaoka, Japan.*

<Background> We planned a phase II trial to evaluate the resection rate and safety of CapeOX + Bevacizumab (BV) therapy for unresectable or marginable resectable liver only metastasis from colorectal cancer (H2 and H3 in Japanese classification). Primary endpoint was resection rate of liver metastasis. Secondary endpoints included R0 resection rate, overall response rate, progression free survival (PFS), overall survival (OS), safety, etc.. <Methods> The study design was multicenter, single-arm, open-label phase II study. Eligible patients had to have H2 or H3 liver only metastasis with confirmed diagnosis of adenocarcinoma and without previous chemo-radiotherapy. Treatment was administered every 3 weeks until evidence of progression, unacceptable toxicity, patient refusal, or for a maximum of 9 cycles. During the treatment, image assessment was reported every 3 cycles, and if liver metastases could be resectable, liver resection was performed. <Results> From 01/2010 until 02/2014, 42 patients were enrolled. 42 patients were investigated. Overall response rete was 69.0%, and CR: 0%, PR: 69.0%, SD: 23.8%, PD: 4.8%, NE: 2.4%. Resection rate was 50.0% (21/42) in all patients included 6 resectable patients, 41.7% (15/36) in unresectable and marginal resectable patients, 33.3% (9/27) in unresectable patients. There is no intraoperative complication. Two cases had intraabdominal abscess and one case had intraabdominal bleeding, abscess, bile leakage and wound infection postoperatively. No cases needed reoperation. Median PFS is 17.1 month in R0 resected patients and 6.0 month in unresected patients. Median OS is 64.6 month in R0 resected patients and 21.0 month in unresected patients. <Conclusion> CapeOX+BV therapy for unresectable or marginal resectable liver only metastasis from colorectal cancer was safe and useful.

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Incidence and Predictors of Preoperative Venous Thromboembolism in Asymptomatic Patients Undergoing Major Oncologic Surgery M. Gainsbury,[1]* D. Taubman,[2] J. Mirocha,[1] F. Amersi,[1] A.W. Silberman.[1] *1. Cedars Sinai Medical Center, Los Angeles, CA; 2. Mount Sinai, New York, NY.*

Introduction: Approximately 1 in 5 cases of venous thromboembolism (VTE) is malignancy-related. Postoperative VTE is a leading cause of morbidity for cancer patients. The incidence of preoperative VTE remains unclear. The aim of this study was to evaluate risk factors associated with preoperative VTE in asymptomatic patients undergoing major oncologic surgery. Methods: Retrospective analysis of 412 patients identified from our prospectively maintained database of patients undergoing abdominopelvic oncologic surgery from 2009 to 2016. Records were reviewed for demographics, comorbidities, cancer site, metastatic disease, recurrent disease, history of prior VTE, hormonal therapy, anticoagulant medications, neoadjuvant chemotherapy, and postoperative complications. All patients received a lower extremity venous duplex scan (VDS) preoperatively. Results: The overall incidence of preoperative VTE found on screening VDS in asymptomatic patients undergoing major oncologic surgery was 8.0%. 33 patients found to have a preoperative deep venous thrombosis (DVT) were compared to 379 patients without. Patients with a history of prior VTE (PVTE) were significantly more likely to have a preoperative DVT versus those with no PVTE (75.0% vs 23.7%, p<0.01). Relative risk for PVTE was 3.2 (95% confidence interval (CI) 2.0-5.1). Older age was also significantly associated with preoperative VTE. Logistic regression modeling determined that patients were 1.3 times more likely to have a preoperative DVT for every 5-year increase in age (Odds ratio=1.3, 95% CI 1.1-1.6). All other clinical and pathological variables were not significantly associated with preoperative DVT. All patients with preoperative above-knee DVT received inferior vena cava filters prior to surgery. There were no postoperative pulmonary embolisms. Conclusion: Asymptomatic cancer patients undergoing major oncologic surgery have an 8.0% incidence of preoperative DVT. Increasing age and history of prior VTE are significantly associated with preoperative DVTs. This suggests high risk oncologic patients may benefit from screening lower extremity VDS prior to surgery.

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Incidence of Venous Thromboembolic Events Following Major Pelvic and Abdominal Surgery for Cancer P.E. Serrano,* K. Dhamanaskar, L. Elit, S. Parpia, L. Linkins, M. Simunovic, L. Ruo, M. Bhandari, M. Levine. *McMaster University, Hamilton, ON, Canada.*

Background: The recommendation to administer extended-duration (28 days) venous thromboembolic events (VTE) prophylaxis with low molecular weight heparin in patients undergoing abdominal and pelvic surgery for cancer has not been widely implemented mainly because most studies focus on asymptomatic events with unknown clinical significance. The objective of this study was to determine the post-hospital discharge VTE incidence in these patients who do not receive post-hospital discharge prophylaxis. Methods: Prospective cohort study of patients undergoing abdominal and pelvic operations for cancer within the gastrointestinal tract, hepatobiliary (HPB) system or gynecological organs, with surgery lasting >1 hour, post-operative stay <28 days, and not undergoing anticoagulant therapy. Patients were evaluated at 1, 3 and 6 months from index operation for the presence of VTE by means of a screening ultrasound at 28 days and a questionnaire at each follow-up. The proportion with 95%CI of VTE was calculated. Multivariable logistical regression was performed. Results: Of 284 patients, there were 79 (28%) colorectal, 97 (35%) HPB and 100 (35%) gynecology. All patients received pre- and postoperative in-patient prophylaxis. The proportion of VTE at 6 months was 0.070, 95%CI 0.044–0.107 (20 events). Most events occurred between 3-6 months, 0.046, 95%CI 0.0246– 0.077. Only one event occurred at one month after surgery (0.0035, 95%CI 0.0006–0.0197). 50% of the cohort had screening ultrasound, all of which were negative. Events were evenly distributed according to the type of surgery. The proportion of patients who died was 0.066, 95%CI 0.035–0.094 (17 patients, 2 of which had a VTE-related death). In the multivariable analysis, post-operative chemotherapy was significantly associated with VTE, odds ratio (OR) 2.74, 95%CI 1.07–6.99. Caprini score was also associated with VTE but was not significant when included in the multivariable analysis, OR 1.19, 95%CI 0.99–1.42. Conclusions: Incidence of VTE following abdominal cancer surgery is low. Most events occur between 3 – 6 months from surgery. Post-operative chemotherapy is significantly associated with post-hospital discharge VTE.

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Hospital Quality and Medicare Expenditures for Cancer Surgery
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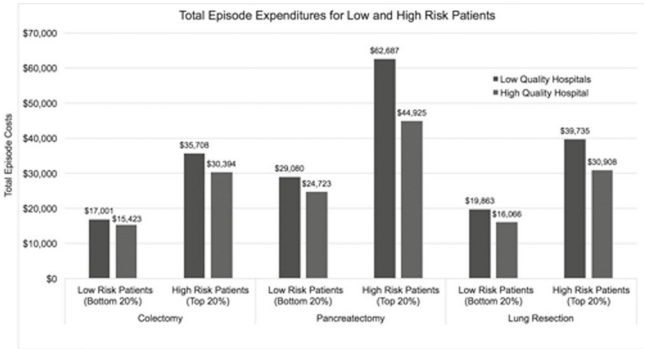
Introduction: Surgical resection is a mainstay of cancer treatment and accounts for a large portion of total cancer care expenditures. Cancer resections are performed in hospitals of widely varying quality and cost. Given increasing pressure to improve the value of healthcare delivery, we sought to explore the potential benefit of selective referral for cancer surgery based on quality and cost. Methods: Using 100% Medicare claims data for 2010-2013, we identified patients aged 65-99 years undergoing colectomy (Col), pancreatectomy (Panc), or lung resection (Lung) for cancer. We calculated Medicare payments for index hospitalization, physician services, post-acute care, and readmissions for the entire "surgical episode" from the index admission through 30 days after discharge. Risk- and reliability-adjusted hospital rates of serious complications and mortality were assessed using a hierarchical logistic regression model accounting for patient characteristics, comorbidities, and operation type. A similar model was used to stratify patients into highest and lowest risk quintiles. Results: There was no difference in patient characteristics between the highest and lowest quality hospitals for each of the procedures evaluated. There were substantial increases in expenditures for procedures performed at the lowest compared to highest quality hospitals for each procedure (Col: $24,406 vs $20,992, Panc: $45,731 vs $35,149; Lung: $27,638 vs $21,282) (Figure). Index hospitalization payments comprised 62-79% of the difference in total payments. Increased costs at lowest quality hospitals were found for all patient risk levels but were largest for the highest risk patients. Referring a high-risk patient from a lowest to highest quality hospital would generate a savings of $5,314 for Col, $8,827 for Lung, and $17,762 for Panc. Conclusion: We found that total episode expenditures for cancer resections were lower when care was delivered in low complication, high quality hospitals. Cost differences were particularly large for high-risk patients, suggesting that selective referral of high-risk patients to high quality centers may be an effective strategy to optimize value in cancer surgery.



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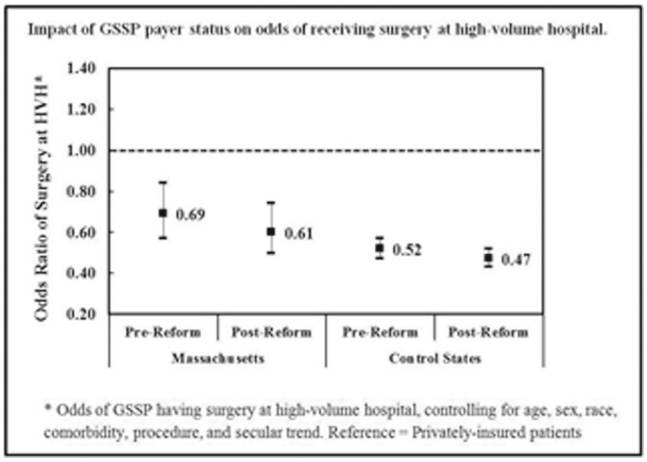
Health Reform and Use of High-Volume Hospitals for Complex Cancer Operations A.P. Loehrer,[1]* G. Chang,[1] D. Chang.[2]
1. Surgical Oncology, MD Anderson Cancer Center, Houston, TX;
2. Massachusetts General Hospital, Boston, MA.

Introduction High volume hospitals (HVH) are associated with better short and long-term outcomes for patients receiving complex cancer operations. Yet underinsured populations are less likely to receive surgery at HVH, contributing to disparities in care by insurance coverage. Little is known as to how recent health reforms, including the 2006 Massachusetts (MA) insurance expansion, will affect site of complex cancer surgery. Methods We used the Hospital Cost and Utilization Project State Inpatient Databases for MA and two control states (New York, New Jersey) to evaluate use of high-volume hospitals for resections of bladder, esophageal, pancreatic, rectal, or lung cancer between 2001 and 2011. HVH were defined by procedure and state as those in upper quartile of annual volume for all payers. We included all non-elderly, adult patients with private insurance or government-subsidized or self-pay (GSSP) coverage. Multivariable ordinary least square difference-in-differences models evaluated changes in probability of surgery at HVH associated with the 2006 MA health reform. Multivariable logistic models evaluated disparities in use of HVH by GSSP relative to privately insured patients. Results Our final cohort included 11,334 patients in MA and 33,824 patients in control states. HVH were associated with lower mortality compared to non-HVH in MA (OR 0.58; P=0.050) and control states (OR 0.58; P<0.001). Controlling for patient-level confounders and secular trends, the 2006 MA insurance expansion was not associated with a change in the probability of GSSP patients receiving surgery at HVH (0.8 percentage-point decrease; P=0.773) compared to control states. Disparities in the use of HVH by GSSP patients remained unchanged after the 2006 MA health reform in both MA and control states (Figure). Conclusions The 2006 MA insurance expansion, a model for the Affordable Care Act, was not associated with changed utilization of HVH for complex cancer operations and disparities in use of HVH persist in MA and control states. Additional studies are needed to understand patient decisions, referral patterns, and barriers to optimal site of complex cancer care in order to enhance expanded insurance coverage.



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Hospital Surgical Volume and Concordance with Adjuvant Chemotherapy Guidelines in Older Adults with Cancer L.V. Selby,* C. Atoria, B.R. Roman, P.B. Bach, E.B. Elkin. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: High-volume cancer centers have been shown to have improved quality and outcomes on multiple measures. We hypothesized that patients who received surgical resection at high-volume hospitals were more likely to receive guideline-concordant adjuvant chemotherapy than patients at low-volume hospitals. Methods: We identified all patients in SEER-Medicare from 2004-2012 with non-small cell lung, gastric, or colon cancer who had surgical resection and where NCCN guidelines recommended observation without adjuvant chemotherapy (early) or delivery of adjuvant chemotherapy (advanced). After excluding patients who received neoadjuvant chemotherapy or those with pre-operative metastatic disease, we investigated the impact of hospital volume on two endpoints observed within six-months of discharge: consultation with a medical oncologist and receipt of adjuvant chemotherapy. Results: There were 30,008 patients with early non-small cell lung, gastric, or colon cancer, for whom chemotherapy is not recommended, and 23,779 patients with advanced disease, for whom adjuvant chemotherapy is recommended. Controlling for demographic and disease characteristics, compared to patients treated at low-volume hospitals, patients with early disease operated on at high-volume hospitals were significantly less likely to have a post-discharge visit with a medical oncologist (lung: 32.3% vs 43.7%; gastric: 33.1% vs 45.6%; colon: 38.7% vs 42.6%) and less likely to receive adjuvant chemotherapy (lung: 4.8% vs 7%; gastric 2.8% vs 5.8%; colon 5.5% vs 7.5%) ($p < 0.05$ for all cancer types, both measures). For patients with advanced disease, volume did not affect either endpoint. Conclusion: Elderly patients with early non-small cell lung, gastric, or colon cancer are significantly more likely to have a post-operative visit with a medical oncologist and, against NCCN recommendations, receive adjuvant chemotherapy if they have surgery at low-volume hospitals. In patients with advanced disease volume does not appear to affect these measures. Treatment at low-volume hospitals may be associated with overuse of adjuvant chemotherapy in patients for whom it is not recommended.

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Compliance with Breast Quality Performance Measures Amongst Centers Accredited by the National Accreditation Program for Breast Centers and the Commission on Cancer

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Introduction: The National Accreditation Program for Breast Centers (NAPBC) was launched in 2008 as a quality improvement program for breast centers. Approximately one third of facilities accredited by the American College of Surgeons Commission on Cancer (CoC) are also accredited by the NAPBC. Methods: Utilizing National Cancer Data Base data, we compared compliance with six NAPBC performance measures between CoC-alone and NAPBC centers. Compliance was determined at the patient and facility level using multivariate analysis to adjust for patient, tumor, and facility factors. At the facility level, compliance at an 80% benchmark was measured for comparison between centers. Mixed effects modeling was used to account for variations in facility volume. Results: Of 1,231 facilities, 792 (64.3%) were CoC-alone accredited and 439 (35.7%) were NAPBC accredited in 2013, the most recent year of available data. Of 216,186 patients, 113,061 (52.3%) were treated at CoC-alone facilities while 103,125 (47.7%) were treated at NAPBC facilities. Compared with CoC-alone facilities, NAPBC facilities were more often academic centers and had higher patient volumes ($p<0.001$). At the patient and facility level, NAPBC facilities were significantly more likely to comply with all six quality measures than CoC-alone centers (Table 1) when adjusting for patient, tumor, and facility factors. For two measures, measure 2, needle/core biopsy prior to surgical treatment of breast cancer, and measure 4, post-mastectomy radiation considered or administered for four or more positive axillary lymph nodes, NAPBC facilities were more than twice as likely as CoC-alone facilities to perform at 80% compliance level (measure 2: OR 2.54, 95% CI 2.46-2.62, $p < 0.001$; measure 4: OR 2.17, 95% CI 1.93-2.43, $p = 0.002$). Conclusions: This is the first study to compare NAPBC and CoC-alone centers on breast cancer quality measures. NAPBC accreditation is associated with improved performance on all six quality measures. Ongoing analysis utilizing the date of accreditation will help determine a causal link between accreditation and improved performance.

Table 1: Summary of Performance on NAPBC Quality Measures at NAPBC vs. CoC Alone Facilities

	OR (95% CI) at Patient Level	OR (95% CI) at Facility Level
Measure 1: A target rate of 50 percent of all eligible patients diagnosed with early stage breast cancer (Stage 0, I, II) are treated with BCS.	--	1.15 (1.09-1.21) p < 0.001
Measure 2: Needle/core biopsy is performed prior to surgical treatment of cancer.	1.41 (1.36-1.46) p < 0.001	2.54 (2.46-2.62) p < 0.001
Measure 3: Radiation therapy is administered within one year (365 days) of diagnosis for women under age 70 receiving BCS for breast cancer.	1.10 (1.05-1.16) p < 0.001	1.11 (1.07-1.16) p = 0.009
Measure 4: Radiation therapy is considered or administered within one year (365 days) of diagnosis for women undergoing mastectomy for breast cancer with four or more positive nodes.	1.52 (1.33- 1.74) p < 0.001	2.17 (1.93-2.43) p = 0.002
Measure 5: Combination chemotherapy is considered or administered within four months (120 days) of diagnosis for women under age 70 with AJCC T1c, Stage II, or Stage III hormone-receptor-negative breast cancer.	1.17 (1.03-1.32) p = 0.014	1.31 (1.18-1.45) p = 0.002
Measure 6: Tamoxifen or third generation aromatase inhibitor is considered or administered within one year (365 days) of diagnosis for women with AJCC T1c, Stage II, or Stage III hormone-receptor-positive breast cancer.	1.29 (1.24-1.36) p < 0.001	1.73 (1.67-1.81) p < 0.001

BCS = Breast conserving surgery
OR > 1 indicates greater likelihood of compliance at NAPBC vs. CoC facilities

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Adherence to Current Guidelines for Nodal Evaluation in Thin Melanoma is Associated with Improved Survival

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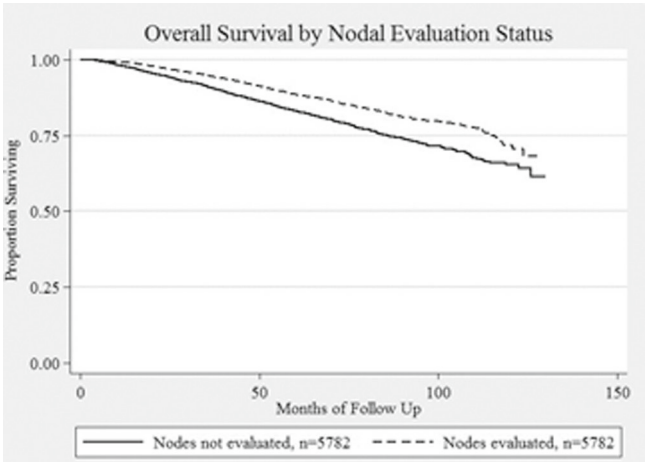
Background Current guidelines recommend consideration or performance of sentinel lymph node biopsy (SLNB) in T1 melanoma ≥0.76mm thickness based primarily on likelihood of identifying occult nodal disease, but impact of guideline adherence on outcome is uncertain. Here we study the association between nodal evaluation (NE) and overall survival (OS) in this patient cohort using a large national dataset. Methods Patients who underwent definitive treatment of clinically localized T1 ≥0.76mm thick melanomas (2004-2012) were identified using the National Cancer Data Base. NE was defined as any pathologic evaluation of nodes at time of wide excision (WE). OS was compared between patients who underwent NE and those with no NE (NNE) by multivariable Cox proportional hazards and Kaplan-Meier modeling. Multivariable logistic regression was performed to identify factors associated with NE, and survival comparison was subsequently repeated using a cohort matched 1:1 on propensity to receive NE. Results Among 20,293 patients with T1 tumors≥0.76mm undergoing WE, 13,944 underwent NE (68.7%). Among T1B patients specifically, NE rate was 76.7%. Factors associated with NE in multivariable analysis included: younger age, male gender, non-head and neck primary tumor, increasing thickness, higher Clark level, presence of mitoses, presence of ulceration, insurance status, and non-community cancer center. Nodal positivity rate was 3.9% among those undergoing NE. In a multivariable analysis of factors associated with OS, NE was found to be significant (HR 1.89, $p<0.001$) in addition to age, positive nodal status, male gender, mitogenicity, and lymphovascular invasion. Five year OS was 91.8% with NE compared to 81.6% with no NE. After propensity matching, OS remained worse in patients not undergoing NE (HR 1.44, $p<0.001$) with 5y OS 89.7% (95% CI 88.7-90.6%) for those with NE vs 84.8% (95% CI 83.7-85.8%) with no NE (figure). Conclusion NE in T1 melanoma ≥0.76mm for whom SLNB should be considered or offered is associated with a clinically small but statistically significant prolongation of OS. These outcomes data support current recommendations regarding consideration of SLNB in this group.



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New Persistent Opioid Use after Cancer Surgery

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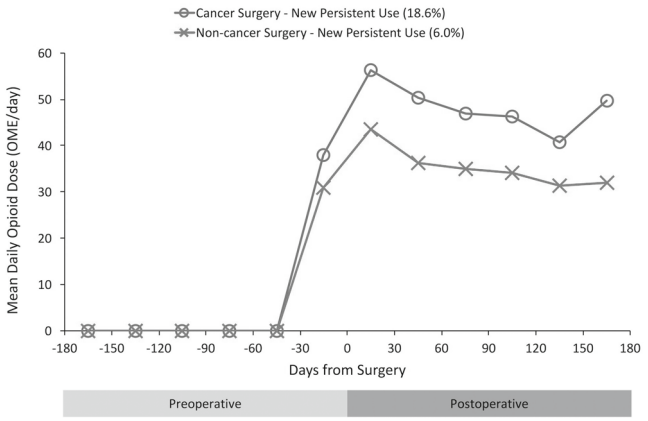
INTRODUCTION: Treating cancer pain is a crucial aspect of patient-centered cancer care. The recent rise in mortality from prescription opioids, however, has underscored the need for providers to utilize opioids appropriately. Patients undergoing cancer surgery may be particularly vulnerable to opioid dependence and diversion due to psychological distress, multiple invasive procedures, and uncoordinated prescribing from multidisciplinary providers. While cancer pain is well-studied, little is known about opioid use in naïve patients after cancer surgery. We hypothesized that opioid naïve patients undergoing cancer surgery would have higher rates of new persistent opioid use compared to non-cancer surgery. METHODS: Using national data from employer-based insurance claims, we identified opioid naïve patients who underwent surgery with claims linked to a cancer diagnosis (colorectal/pancreas/gastric/liver/lung resection; esophagectomy; mastectomy; wide local excision; cervical/axillary/inguinofemoral lymphadenectomy) from 2010 – 2013 (n=8,987). We also identified opioid naïve patients who underwent non-cancer general, hand, or gynecologic surgery (n=36,177). We excluded patients with subsequent operations within 180 days. Opioid prescriptions were

obtained from pharmacy claims and converted to oral morphine equivalents (OME). Our primary outcomes were new persistent opioid use 90 days after surgery and daily opioid dose. RESULTS: Opioid naïve patients undergoing cancer surgery had markedly higher rates of new persistent opioid use compared to non-cancer surgery (18.6% vs. 6.0%, p<0.0001). They also were prescribed higher daily doses up to 6 months after surgery (Figure 1), equivalent to 10 tablets/day of hydrocodone/acetaminophen 5/325, compared to 6 tablets/day for non-cancer surgery. CONCLUSIONS: Opioid naïve patients undergoing cancer surgery develop much higher rates of new persistent opioid use compared to non-cancer surgery, and are prescribed higher daily doses. While cancer pain from advanced disease must be treated aggressively, patients undergoing curative-intent surgery are at risk of developing new opioid dependence. Providers should remain aware of this during the surveillance and survivorship phases of care.

Figure 1. Trajectory of Daily Opioid Dose for New Persistent Opioid Users



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An Assessment of the Effect of a Randomized Controlled Trial: Preoperative Biliary Decompression in Patients with Periampullary Malignancy D. Kagedan,[1]* J. Mosko,[1] M. Dixon,[1] P. Karanicolas,[1] A.C. Wei,[1] N. Goyert,[2] Q. Li,[3] N. Mittmann,[4] N. Coburn.[1]
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Introduction: In 2010, a multicenter randomized controlled trial reported increased postoperative complications among pancreaticoduodenectomy (PD) patients undergoing preoperative biliary decompression (PBD). We sought to evaluate rates of PBD at the population level before and after publication. Methods: A retrospective population-based observational cohort study was performed. Patients undergoing PD for malignancy, 2005-2013, were identified and linked to administrative healthcare databases covering all medical services provided to a population of 13.5 million. Patients undergoing PBD within 6 weeks prior to surgery were identified using physician billing codes, and divided into those undergoing PD before and after publication (6 month washout period). PBD rates were compared using chi-square tests. Surgeon and/or gastroenterologist consultations prior to PD were identified using billing codes, and the interval between initial consultation and PD was calculated. Results: Of 2053 PD patients identified, 974 underwent surgery prior to article publication and 951 after (128 in washout period). Before publication, the rate of PBD was 47.4%, versus 40.8% after (p=0.003). The annual rate of PBD decreased from 52.5% (2005) to 40.4% (2013) (p=0.025). Among patients seen preoperatively by both a gastroenterologist and a surgeon, the median interval from initial consultation to surgery was 47 days (surgeon first), and 48 days (gastroenterologist first). Patients seen preoperatively only by a surgeon had a median interval of 30 days. Conclusions: Rates of PBD have significantly decreased following publication of a randomized trial. While preoperative consultation with multiple specialists increases the time interval to surgery, the order in which they are seen does not.

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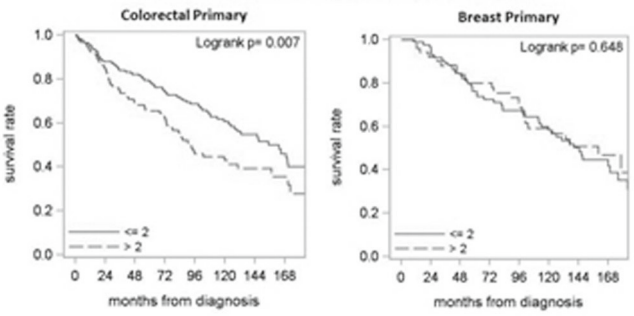
The Prognostic Value of FAK in 642 Patients with Colorectal, Breast, Gastric Cancer or Melanoma L. Davis,[1]* F. Lenzo,[1] L. Ylagan,[1] A. Omillian,[1] K. Attwood,[1] W. Cance.[2] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. University of Arizona Cancer Center, Phoenix, AZ.*

Intro: Focal adhesion kinase (FAK) is an attractive therapeutic target in solid cancers, but there is no method to identify high risk patients based on FAK expression nor biomarker for therapeutic response. Previous FAK expression studies were not standardized and showed varying correlations. This single-institution study aims to define FAK expression patterns among primary and metastatic (mets) tumor subtypes and correlate with patient outcomes. Methods: We analyzed 1056 samples from 642 patients using tissue microarrays stained for FAK and scored 0-3 by a single pathologist. We studied primary tumors with matching normal/mets from 298 patients with colorectal cancer (290/47), 134 with breast (0/70), 65 with gastric (0/7), and 60 primary melanoma and 85 unmatched melanoma mets. FAK expression and patient outcomes were evaluated using Kruskal-Wallis exact and Wilcoxon signed-rank tests. Results: FAK expression correlated with aggressive phenotype in colorectal primaries. Matching normal colon tissue had lower FAK than primaries (p<0.001). Higher primary tumor FAK expression was associated with higher tumor stage (p<0.001) and shorter overall survival (OS, p=0.007). FAK in colorectal mets did not correlate with OS (p=0.945). Breast primary tumors and lymph node mets had similar FAK expression. Locally recurrent tumors had higher FAK compared to tumors developing distant mets (p=0.012). There were no associations between FAK and OS (primaries or mets). Melanoma primaries and mets had significantly higher FAK compared to colorectal, breast, and gastric primaries and mets (p<0.01). Despite high expression, there were no associations between FAK in melanoma and aggressive phenotype or OS. Primary gastric ca had lower FAK compared to the other primaries (p<0.001). Conclusion: By standardizing FAK quantification, we determined FAK expression was heterogeneous across tumor types. For the first time, FAK expression correlated with outcome in colorectal cancer, identifying a high-risk subset of patients. Melanoma and locally recurrent breast ca have the highest FAK expression, suggesting FAK may be an important driver and therapeutic target in these tumors.

Figure 1: Overall survival in high versus low FAK expression



Overall Survival	FAK	Patients	10-yr OS (95% CI)	Median Follow-up (Range in Months)
Colorectal Primary	Total	298	0.53 (0.47-0.60)	123.3 (31.3 - 258.7)
	≤ 2	176	0.61 (0.52-0.68)	155.2 (124.2 – 196.0)
	> 2	122	0.43 (0.33-0.53)	90.9 (73.1 - 130.2)
Breast Primary	Total	134	0.58 (0.49 – 0.66)	161.9 (50.4 – 222.1)
	≤ 2	84	0.58 (0.46 – 0.68)	163.5 (55.1 – 222.1)
	> 2	50	0.59 (0.44 – 0.72)	156.2 (50.4 – 198.3)

High FAK expression in primary colorectal cancer is associated with shorter overall survival (p = 0.007). High FAK expression in primary breast cancer does not correlate with overall survival (p = 0.648).

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Pleomorphic and Dedifferentiated Liposarcomas Represent Two Molecularly Similar Subtypes of Liposarcoma with Similar Clinical Outcome N. Shannon,* M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Liposarcomas, despite being rare consist of a number of entities spanning low to high grade sarcomas. We aimed to compare molecular

profiles across different subtypes of liposarcoma. In particular with regards to similarities between pleomorphic liposarcoma and other subtypes which might aid treatment decisions for this rare subtype. Methods: We analysed data from three studies (GSE30929, GSE52390, GSE21122) representing subtypes of liposarcoma (well-differentiated WDLS n=52, de-differentiated DDLS n=98, pleomorphic PLS n=64, myxoid MLS n=57). Expression data was downloaded and used to segregate samples into molecularly distinct subgroups. The SEER database was utilised to compare staging information (TNM/AJCC 2010+), which was available for 2485 patients (n= 1080 WDLS, 654 DDLS, 204 PLS, 547 MLS). Results: In all studies PLS segregated as a heterogeneous group with DDLS whereas MLS emerged as a distinct molecular entity (Figure 1). In one study (GSE30929) which included WDLS, these segregated as a separate group. Consistently MLS demonstrated more homogeneity compared to other subtypes ($p<0.01$). WDLS were more homogenous than DDLS or PLS, but we were only able to make this comparison in one study. In the SEER database DDLS were the most likely to be metastatic at diagnosis (8%) compared to WDLS (1%), PLS (4%) and MLS (6%). In PLS, lung and bone were more common sites of metastasis (44% vs 33% and 33% vs 9% respectively compared to DDLS). Survival rates for PLS and DDLS were similar at 2 years (72%, 74%) and 5 years (53%, 54%) and lower than in WDLS and MLS (2 year survival 94% and 90%, 5 year survival 86% and 79% respectively) Conclusion: There is considerable overlap in molecular profiles of DDLS and PLS, although MLS and WDLS remain distinct molecular entities. Interestingly these two molecularly similar subtypes had similar rates of survival, with patients belonging to either group performing poorer than MLS or WDLS. Given these similarities, experience in dealing with DDLS has relevance in the management of the rarer subtype PLS in which clinical information is lacking.

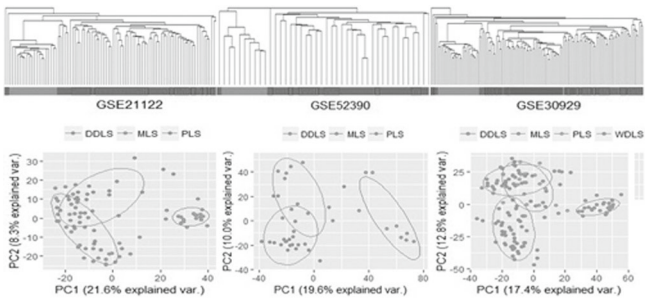

Figure 1. Clustering of liposarcoma samples (above) and principal components (below) across the three datasets utilised.

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Targeting MAPK and PI3K/mTOR Pathways in Myxofibrosarcoma and Undifferentiated Pleomorphic Sarcoma

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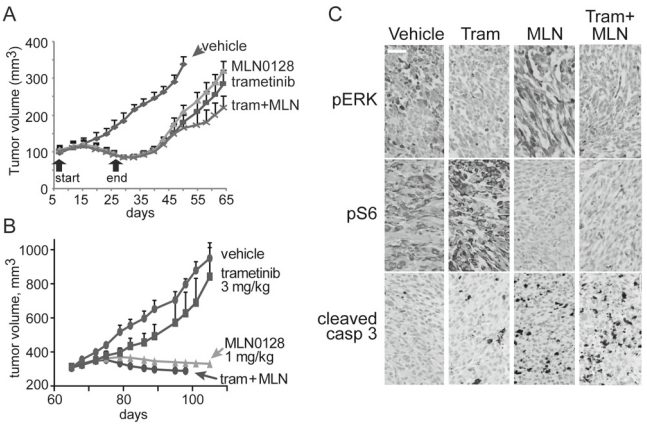
Introduction: Myxofibrosarcoma/undifferentiated pleomorphic sarcoma (MFS/UPS) is the most common and among the most deadly groups of soft tissue sarcomas. We sought to identify the oncogenic pathways driving MFH/UPS tumorigenesis and assess the efficacy of mTOR and MEK inhibitors in MFS/UPS cells and xenografts. Methods: Copy number alterations and mRNA expression were profiled in 94 primary untreated MFS/UPS samples using Agilent 1M CGH and Affymetrix U133A arrays. The most significant activated pathways were functionally evaluated in MFS/UPS cell lines and xenografts using trametinib (MEK inhibitor) and MLN0128 (mTOR inhibitor). Cell proliferation, cell signaling, apoptosis, and in vivo tumor growth were assessed. Results: Of the 94 MFS/UPS, 84 (89%) had alterations in MAPK and/or PI3K/mTOR pathways, such as amplification or overexpression of ITGA10, ETV1, JUN, or NTRK1 or deletion of NF1 or PTEN. Trametinib or MLN0128 inhibited proliferation of 3 MFS/UPS cell lines with IC50 values of 8-140 nM. Growth suppression and apoptosis were greater with the two drugs combined than with either alone ($p<0.001$). Treatment of MFS/UPS xenografts with trametinib, MLN0128, or both all suppressed tumor growth ($p<0.01$). After the end of treatment, tumors treated with the combination had the slowest regrowth rate (Fig 1A; $p<0.05$). Large, relapsed MFS xenografts also showed the most dramatic response to the combination (Fig 1B; $p<0.05$). Immunohistochemistry on the xenografts showed that trametinib suppressed pERK (MAPK activity) but increased pS6 (mTOR activity) (Fig 1C). MLN0128 suppressed pS6 but increased pERK. Combination therapy suppressed this compensatory upregulation and synergistically induced apoptosis compared to either drug alone (by % of cells positive for cleaved caspase 3; $p<0.01$). Conclusion: MAPK and PI3K/mTOR pathway alterations are common in MFS/UPS, and combined inhibition of both pathways suppresses compensatory signaling, inhibits growth, and synergistically induces apoptosis in MFS/UPS cells and xenografts. These results support the design of a phase I/II clinical trial of trametinib plus MLN0128 for patients with metastatic MFS/UPS.



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Tumor Grade & Preoperative Therapy Impact the Establishment of Soft Tissue Sarcoma Patient-Derived Orthotopic Xenografts (PDOX): UCLA Sarcoma Program Prospective Clinical Trial

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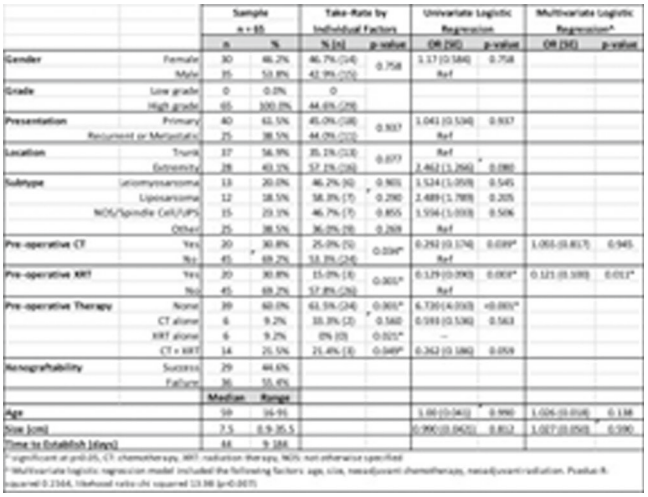
Objective: Given the diverse and often aggressive nature of soft tissue sarcomas(STS), there is a need for more precise therapy. Information obtained from the surgical specimen and propagated through murine models can provide a platform for personalized therapy. The aims of this trial were to determine the feasibility of establishing STS PDOX models in the clinical setting & identifying factors associated with PDOX establishment. Methods: From 5/2015-5/2016 all 107 patients with biopsy-proven or potential STS offered enrollment signed pre-operative consent. FCE obtained tumor in the OR which was transported immediately for surgical orthotopic implantation (SOI) in nude mice. Once a PDOX reached 500mm^3 and was passaged, it was considered established. PDOX with no growth at 6 months were classified as failed. No low grade STS established. To date, 65 high-grade(HG)-STS PDOX completed surveillance and were analyzed for factors contributing to establishment. Results: Of the 65 HG-STS, 29(47%) successfully established thus far(Table 1). Median establishment time was 44 days. Take-rates were similar by gender, presentation, location & histology, but varied by pre-operative therapy(preop-tx). Untreated patients (no preop-tx) had the highest take rate, 62%. On univariate analysis, preop chemotherapy(CT) and radiation(XRT) both impacted the likelihood of xenograft establishment (OR 0.29 with CT, OR 0.13 with XRT, $p<0.05$ for both). On multivariate analysis, only preop XRT significantly impacted likelihood of establishment (OR 0.12, $p=0.007$). Conclusion: In the largest PDOX study to date, we demonstrate a 62% establishment rate in untreated high-grade STS tumors, with median establishment time of 44 days. Preop therapy, most notably with XRT, significantly decreased the ability to establish a PDOX. This study demonstrates that PDOX is an option for personalizing therapy in the majority of patients with HG-STS, and that obtaining tumor prior to therapy will improve the likelihood of successful xenograft establishment.



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Treatment of Locally Advanced Soft Tissue Sarcoma by Hyperthermic Isolated Limb Perfusion, Preoperative Radiotherapy and Surgery (PRS) M. Stevenson,* J. Seinen, R. van Ginkel, B.L. van Leeuwen, B. Pras, A. Suurmeijer, L.B. Been, H.J. Hoekstra. *University Medical Center Groningen, Groningen, Netherlands.*

Introduction: Limb salvage treatment of locally advanced, primarily unresectable soft tissue sarcomas (STS) remains challenging. Hyperthermic Isolated Limb Perfusion (HILP) with Tumor Necrosis Factor α (TNFα) and Melphalan (with or without adjuvant radiotherapy) results in a 90% limb salvage rate. In this feasibility study, a new intensive treatment schedule consisting of HILP, PET-CT image guided preoperative radiotherapy (12x3 Gy) followed by surgical resection was explored. The goal was to reduce the overall treatment time while achieving comparable limb salvage rate, treatment morbidity and local failure rate. Methods: From 2011 to 2015, 10 patients with primarily unresectable high grade STS of the lower extremity were included in this new PRS treatment regime. This regime consists of HILP with TNFα and Melphalan, followed two weeks later by 12x3 Gy PET-CT guided external beam radiotherapy (EBRT). After radiotherapy, surgical resection with or without plastic surgical reconstruction was performed. After resection, histopathologic examination of the specimen was performed and the extent of response to neo-adjuvant treatment was determined. Results: The median overall treatment time was 57 (range 50-73) days. The limb salvage rate was 90%. One patient underwent amputation due to failure of the plastic surgical reconstruction. Histopathologic examination of the tumor showed 6 (60%) R0 resections, and 4 (40%) R1 resections. HILP and EBRT induced tumor necrosis was found to be excellent (>90%) in 4 (40%) patients, moderate (50-90%) in 3 (30%) patients, and poor (<50%) in 3 (30%) patients. After a median follow-up of 37 (range 21-51) months one patient (10%) developed a local recurrence. Five patients (50%) developed distant metastases, and three (30%) patients died during follow up. Conclusions: This intensive PRS treatment approach was feasible in all 10 patients with acceptable morbidity. A reduction of overall treatment time was achieved compared to conventional HILP treatment alone. Limb salvage rate was excellent and local failure rate was comparable to our conventional HILP series.

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The Prognostic Value of Pathologic Complete Response following Neoadjuvant Therapy in Soft Tissue Sarcoma C.G. Ethun,* A.G. Lopez-Aguiar, D.K. Monson, M.R. McInnis, N. Le, N.B. Reimer, S. Oskouei, K. Delman, C.A. Staley, S.K. Maithel, K. Cardona. *Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA.*

Background: Pathologic complete response (pCR) following neoadjuvant therapy has been associated with improved outcomes in several malignancies. The prognostic value of pCR in soft tissue sarcoma (STS) is not known. Methods: All patients who underwent curative-intent resections of primary, high-grade, truncal and extremity STS at a single institution from 2000-2015 were included. Patients who received adjuvant therapy were excluded. Primary outcome was overall survival (OS). Secondary outcome was locoregional recurrence-free survival (LR-RFS). Results: Of 1,227 resections, 302 (25%) were curative-intent for primary, high-grade, truncal/extremity STS, and in patients who did not receive adjuvant therapy. The majority of tumors were MFH/UPS (55%), >5cm (67%), and deep (86%). Neoadjuvant therapy was given in 165pts (55%): 105 (64%) only radiation, 22 (13%) only chemotherapy, and 32 (23%) both. 9pts (6%) had pCR on final pathology; 29 (18%) had >95% and 49 (30%) had >90% treatment effect. There were no differences in patient demographics, extent of resection, pathologic factors, or postoperative complications between patients with pCR and no pCR. Similarly, no differences were seen between groups when using 95% and 90% treatment effect cut-offs. Comparing pCR to no pCR, no association with OS (44mos vs MNR, p=0.81) or LR-RFS (MNR vs 121mos, p=0.97) was seen. There was also no difference in survival using either 95% (OS: 101mos vs MNR, p=0.21; LR-RFS: MNR vs 121mos, p=0.60) or 90% treatment effect cut-offs (OS: MNR vs MNR, p=0.71; LR-RFS: MNR vs 121mos, p=0.35). Among patients who received only neoadjuvant radiation, still no association with OS or LR-RFS was seen for pCR (n=7), or for 95% (n=17) and 90% (n=31) treatment effects. Conclusions: Pathologic complete response and extensive treatment effect following neoadjuvant therapy are not associated with improved overall or locoregional recurrence-free survival in patients with primary, high-grade, truncal and extremity soft tissue sarcomas. Alternative pathologic characteristics and novel biomarkers that may indicate a favorable therapeutic response and translate to improved survival should be investigated.

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Management of Desmoid Tumors: A Population Based Analysis of Observation Versus Surgery as Initial Management B. Turner,* M.A. Alghamdi, J. Henning, E. Kurien, D. Morris, A. Bouchard-Fortier, S. Puloski, M. Monument, D. Itani, L.A. Mack. *University of Calgary, Calgary, AB, Canada.*

Introduction: Desmoid tumors represent an uncommon pathology associated with an unpredictable course. More recently, conservative management or minimally aggressive treatment, which may include tamoxifen and NSAIDs or observation alone, has been advocated. In this retrospective cohort study, we sought to compare patients initially observed to those treated with surgery upfront. Methods: All patients within the Alberta Cancer Registry diagnosed with desmoid tumor August 2004-September 2015 were identified. Patient demographics and tumor characteristics, treatment, recurrence and progression data were collected by primary chart review. Results: 117 patients were identified. Median follow-up was 34.9 months. 74.4% were female. Mean age was 41.6(17.3-83.0) years. 55(47%) underwent conservative management. 54(46.2%) underwent resection up front, and 8(14.8%) of these cases recurred. For the surgical cohort, median disease-free survival was 21.1(1.3-76.9) months. Of the 8 recurrences, 4 were treated with re-resection, 2 with radiation, and 2 with tamoxifen/NSAID. Three recurrences were ultimately deemed unresectable, and 4 were disease-free after repeat surgery. 4 patients received three or more interventions after first recurrence. Of the 55 patients treated conservatively, 24(43.6%) were deemed to have progressed based on imaging or symptoms. Median progression-free survival was 10.5(2.4-93.5) months. 10 patients had surgery after progression, 9 underwent definitive radiation, 3 started chemotherapy, 1 continued observation and 1 was lost to follow-up. 15/24(63%) had stable disease after the first intervention. Conclusions: Conservative management is successful in approximately 56.4% of desmoid tumors, and a further 27.3% are rendered stable or disease-free by the first aggressive treatment thereafter, for a total of 83.7%. Surgery has a favourable recurrence rate (14.8%) in this series, but some recurrences are associated with significant morbidity. Treatment should be tailored to individual patients in a multidisciplinary setting. A trial of observation to determine biology appears warranted in all patients.

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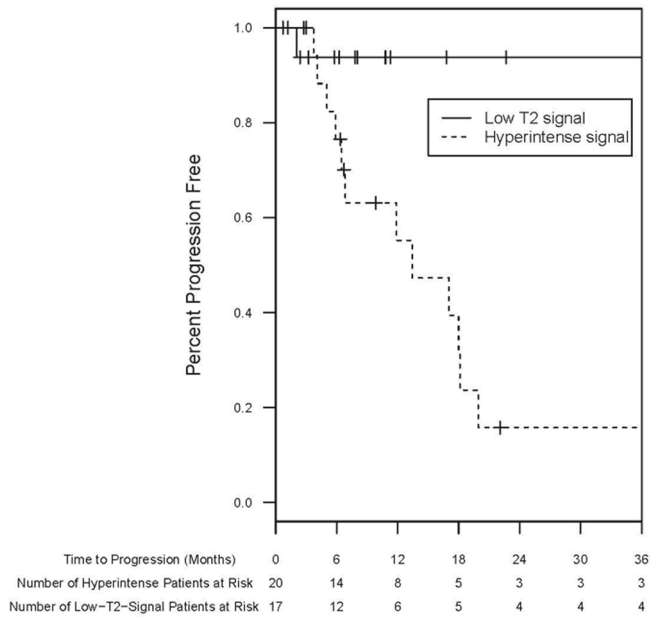
Hyperintense T2 MRI Signal Associates with Desmoid Progression During Active Observation M.R. Cassidy,[1]* R. Lefkowitz,[2] N. Long,[2] L. Qin,[2] M. Hameed,[2] S. Singer,[1] A. Crago.[1] *1. Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Desmoids can be locally aggressive, remain stable, or regress spontaneously during observation. Clinicopathologic models do not reliably

predict desmoid growth. We sought to identify MRI characteristics associated with progression. Methods: Desmoid patients undergoing serial MRIs with T2 sequences during active observation were identified retrospectively from an institutional database (2007-15). Tumor size and percent baseline tumor volume (BTV) showing hyperintense T2 signal (≥90 vs <90%) were determined independently by two radiologists for test and validation analyses. Progression was defined using RECIST, progression free survival (PFS) using Kaplan-Meier analysis, and correlation using Pearson's method. Results: 37 of 89 desmoids managed with observation had imaging available for analysis. Median age of this subset was 35yo (range 8-69), 40% of tumors were abdominal wall lesions, and median tumor size was 4.7cm (range 1.2-9.1). Age (p=0.24), tumor site (abdominal wall vs other; p=0.45) and size (p=0.17) did not associate with PFS. The 1-year PFS for 20 desmoid patients with hyperintense T2 signal in ≥90% BTV was 55% (defined by first radiologist for test analysis) compared to 94% for 17 patients with <90% high T2 signal (Figure, 8mos median follow-up censored patients; HR=11.5, p=0.003). 1 of 17 patients (6%) with <90% high T2 signal vs 12 of 20 patients (60%) with baseline ≥90 hyperintense T2 signal progressed at median 13 mos. In patients with abdominal wall desmoids, 0 of 10 tumors with <90% high T2 signal but 4 of 5 (80%) with ≥90 hyperintense T2 signal progressed at median 9.4 mos (p=0.002). T2 signal intensity defined by a second radiologist correlated with results of the first (ρ=0.75); in this validation, all tumors with hyperintense T2 signal in ≥90% BTV had progressed 20 mos after initial diagnosis but median PFS was not reached in the cohort with <90% hyperintense T2 signal (HR=5.4, p=0.08). Conclusions: Hyperintense T2 signal (in ≥90% BTV) associates with desmoid progression during observation and may help select patients who benefit from early intervention. Based on these results a prospective trial with multiple blinded radiologists is planned.



Progression free survival in desmoid tumor patients with hyperintense T2 signal and low T2 signal.

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Early and Late Complications of Percutaneous Biopsy of Retroperitoneal Masses at Three Tertiary Sarcoma Centers

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Background: Percutaneous biopsy of a potentially malignant lesion of the retroperitoneum remains controversial due to a perceived risk of immediate complications and adverse oncologic outcomes, including needle tract seeding (NTS). Purpose: To evaluate the incidence of 1) early complications and 2) NTS in patients who undergo percutaneous biopsy of a retroperitoneal (RP) mass. Methods: Consecutive patients who underwent percutaneous core needle biopsy for an RP mass were identified from a prospective database at 3 tertiary centres: 1) Mount Sinai Hospital/Princess Margaret Hospital (MSH/PMH), Toronto, 2) The Ottawa Hospital (TOH), and Istituto Nazionale dei Tumori (INTM), Milan. Early complications including bleeding, pain, infection and injury to other organs were recorded. Instances of NTS were identified from long term follow-up including physical examination and cross sectional imaging. Results: From 2009 – 2015, 298 percutaneous core needle biopsies of an RP mass were performed on patients managed at MSH/PMH or TOH. Of these, 7 (2.3%) resulted in minor bleeding with no transfusions required, 3 (1%) in significant pain managed effectively with acetaminophen and/or NSAIDS, and 1 (0.3%) in an unplanned admission to hospital for observation X 24h. There were no documented infections or injuries to other organs. From 1996 – 2013, 435 patients underwent resection of a retroperitoneal sarcoma at MSH/PMH or INTM following percutaneous core needle biopsy. At median follow-up of 50 months, 2 patients (0.46%) had developed sarcoma recurrence in the presumed biopsy tract. Conclusion: This large multi-institutional experience demonstrates that percutaneous core biopsy of an RP mass is associated with very few and very minor complications. The risk of needle tract seeding is < 0.5%. Coaxial sheathed biopsy needles are designed to minimize contamination of adjacent tissues and should be routinely employed.

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Nodal Status, Not Tumor Response to Neoadjuvant Radiation, Determines Survival for Patients with Esophageal Cancer

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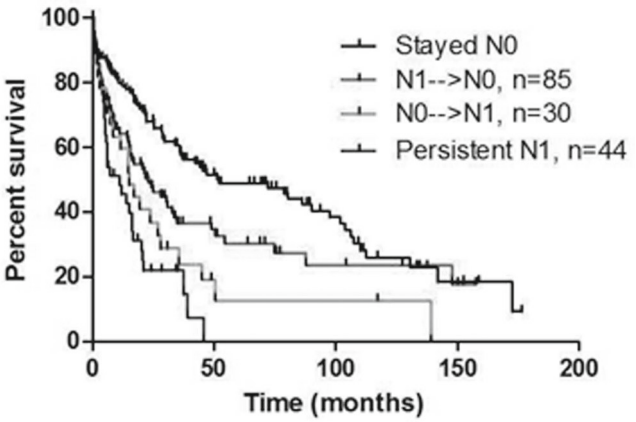
Introduction: The CROSS trial established the role of neoadjuvant radiation in the treatment of esophageal adenocarcinoma (EAC). While response to radiation is an important factor in predicting long-term outcomes, the vast majority of patients succumb to systemic disease. The purpose of this study is to assess predictors of survival in patients with EAC following radiation therapy. Methods: All patients who underwent resection after radiation therapy for EAC at a single institution were retrospectively identified from January 2004 to December 2014. Patients who died within 30 days of surgery were excluded. Cox-proportional hazard analyses were performed to identify clinico-pathological factors associated with survival after surgery. Results: In the time period, 334 patients underwent esophagectomy for EAC. In multivariable analysis age (P<0.0001), hospital length of stay (P=0.021), serum albumin (P=0.024), serum hemoglobin (P=0.018), and initial EUS N-stage (P=0.029) were predictive of survival after resection. The presence of a pathologic complete (pCR) response did not correlate to improved survival (P=0.291). There was no difference in outcome based on pathologic response to radiation (pCR vs. residual disease, median survival 44.2 vs. 37.2 months, P=0.750). Pre-treatment N0 patients had better survival than N1 patients (median survival 37.2 vs. 16.3 months, P<0.0001). Patients who remained N0 after radiation had much better outcomes (see Figure) than those that either demonstrated N1 disease in the resection specimen after radiation or were initially staged as N1 (stayed N0, median survival 52.0 months; N1→N0, median survival 22.9 months; N0→N1, median survival 15.3 months; persistent N1, median survival 11.4 months; P<0.0001). Conclusions: Pathologic response to radiation does not predict outcomes for patients with EAC. Patients with node positive EAC have poor outcomes even after neoadjuvant radiation therapy. These patients are at an increased risk of distant disease and should be offered additional systemic therapies prior to surgical resection.



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Predicting Factors for Complete Pathological Response After Neoadjuvant Therapy for Esophageal Cancer O. Zlotnik,* S. Morgenstern, N. Menasherov, V. Bard, Y. Kundel, L. Domachevsky, H. Bernstine, B. Brenner, H. Kashtan. *Rabin Medical Center, Petach-Tiqva, Israel.*

Background: Complete pathological response (pCR) to neoadjuvant treatment for esophageal cancer is a significant prognostic factor. We evaluated possible predictive factors for such pCR. Methods: All esophageal cancer patients that were operated at Rabin Medical Center between 2010-2016 were evaluated. All patients had PET-CT before and after neoadjuvant therapy and were categorized as complete metabolic response, partial response or no response. TRG scoring (American College of Pathologists) was used to compare patients with poor pathological response (TRG-3) and patients with complete pathological response (TRG-0) after neoadjuvant treatment. All pathological specimens were reassessed by a single pathologist. Results: One-hundred and twenty-three patients underwent neoadjuvant therapy followed by esophagectomy. Thirty-six patients had pCR (TRG-0) and 42 patients had poor pathological response (TRG-3). Seventeen of 25 patients (68%) with squamous cell carcinoma had a pCR, compared with 17/52 (32%) of patients with adenocarcinoma (P=0.06). None of the 10 patients with signet ring carcinoma had pCR (P=0.02). Eighteen of 26 patients (69.2%) with complete metabolic response on PET-CT had pCR, compared with 2/10 (20%) patients with no metabolic response. (P=0.014). Thirty-two of 49 patients (65.3%) who were treated with neoadjuvant chemoradiation had a pCR compared with 2/28 (7.1%) patients who were treated with neoadjuvant chemotherapy alone (p<0.0001). Barrett`s esophagus, preoperative T stage and N stage were not statistically significant predictive factors for pCR. Multivariate analysis demonstrated that the type of neoadjuvant therapy (chemoradiation vs chemotherapy alone) was the most significant predictive factor for pCR. Gender, histologic type, signet ring pathology and metabolic response (per PET-CT) were also predictive factors for response. Conclusions: Type of neo-adjuvant treatment is the most important predictive factor for pCR after neoadjuvant therapy for cancer of the esophagus. Other predictive factors include histology of the tumor and complete metabolic response on PET CT

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The Effect of Neoadjuvant Chemotherapy on Surgically Induced Global Gene Expression Change C.J. Allen,* A. Griswold, K. Rao, C. Schulman, D. Sleeman, J. Levi, V. Dudeja, K. Proctor, N. Merchant, A.S. Livingstone. *Surgery, University of Miami Miller School of Medicine, Miami, FL.*

Introduction: We recently reported that surgically induced gene expression change reflecting impaired adaptive immunity was associated with post-operative infection. The effects of pre-operative chemotherapy on this global genomic response to surgical injury is unknown. We test the hypothesis that neoadjuvant chemotherapy alters the pattern of gene expression change following major cancer surgery. Methods: From 2/2014 to 3/2015, a prospective observational study was performed. Blood samples were obtained from patients immediately before and within 24 hours after pancreaticoduodenectomy, esophagectomy, or pancreatectomy. Global gene expression (RNA) was assayed in whole blood. A >2 fold-change with a p<0.05 by ANOVA was considered differentially expressed. Hierarchical clustering and gene pathways of differentially expressed genes were evaluated. Within-patient gene expression fold-change was calculated. Outcomes included post-operative infection (i.e. intra-abdominal, surgical-site, pneumonia). Those who underwent neoadjuvant chemotherapy were compared to those who underwent upfront surgery. Results: 36 patients were analyzed (Table 1). Of 48,226 genes assessed, 441 were differentially expressed following surgery. Hierarchical clustering predicted pre- and post-operative status. Of those genes differentially expressed, 249 (56%) were upregulated and involved pathways of innate immunity, while 192 (44%) were downregulated and involved pathways of adaptive immunity. There was a positive association of gene expression fold-change with post-operative infection (3.66±0.67 vs 2.75±0.74; p=0.002). Rates of infection were similar between groups of with and without neoadjuvant therapy (24% vs 27%; p=1.000). There was no association of neoadjuvant chemotherapy on gene expression change (3.13±0.82 vs 2.87±0.80; p=0.361). Conclusions: Cancer surgery induces a quantifiable gene expression pattern of change that is associated with post-operative complication. There is no observable effect of neoadjuvant chemotherapy on this surgically induced gene expression change or on the incidence of infectious complications.

Patient/disease, operative, and outcome characteristics (n=36)

Age, years		66±10
Procedure	Pancreaticoduodenectomy	20(56%)
	Transhiatal Esophagectomy	14(39%)
	Partial Pancreatectomy	2(6%)
Histology	Adenocarcinoma	34(94%)
	Squamous Cell Carcinoma	1(3%)
	Lymphoma	1(3%)
Neoadjuvant chemotherapy		15(42%)
Length of surgery, hours		5.3±2.1
Estimated blood loss, mL		375(200-600)
Within-patient gene expression fold-change		2.97±0.81
Post-operative infection		9(25%)
Venous thromboembolism		3(8%)
Length of stay, days		9(7-11)
In-hospital mortality		1(3%)
18-month disease-free survival		20(56%)

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Histopathological Study of Esophageal Resected Specimens in Clinical Complete Responders (cCR) After Definitive Chemoradiation (dCRT) in Locally Advanced Esophageal Squamous Cell Cancer (ESCC) C. Tharavej,* K. Kittisin, S. Udomsaweangsup. *Surgery, Chulalongkorn University, Bangkok, Thailand.*

"Watch and wait" strategy following dCRT has been recommended in cCR who have no residual cancer cell identification. However, local recurrent rate is high, and when detected is usually too late for salvage esophagectomy. We hypothesized that significant number of cCR with false negative test for residual cancer after dCRT may have occult microresidual disease. The aim of this study was to investigate the pathological response in esophageal resected specimens of locally advanced ESCC who underwent planned esophagectomy after dCRT. Methods Patients who had locally advanced resectable ESCC (T3-4/N0-1/M0) were included. All had feeding jejunostomy before having concurrent 2 cycles of cis-platin and 5-FU with 60 Gy intensity-modulated radiation therapy (IMRT). Patients underwent re-staging studies including EGD with biopsies, CT and some had PET/CT at 3 months after complete dCRT. cCR was defined when negative EGD with biopsies and no disease progression on CT or PET/CT. All operable and physically fit patients underwent planned tranthoracic esophagectomy with 2 field lymphadenectomy at 4 months after dCRT. Results Seventy-two patients had dCRT. Of 72 patients, 51(71%) were cCR, 9 had local residual tumor only, 11 had distant metastases and 1 died from toxicity of dCRT. One cCR refused surgery and 6 with local residual disease were unfit for salvage surgery. Fifty cCR and 3 local recurrence underwent esophagectomy. There was 1(1.9%) operative mortality and overall 5-year survival was 31%. Of 50 cCR, 22(44%) had pCR, 18 were tumor regression grade (TRG) 2 and 10 were TRG3/4. Prevalence of ypT0N1 was high (16%). In 28 cCR with non-pCR, only 32% of viable tumor cell presented in mucosal layer. Conclusions In locally advanced ESCC treated with dCRT, occult microresidual disease that left undetected was presented in esophageal wall or surrounding lymph node in > 50%. Moreover, only one third of tumor

cell was presented in mucosal layer. Intensive surveillance with esophagoscopy and biopsies may not be effective after dCRT. Planned esophagectomy should be an optional in fit patient.

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Comparison of Laparoscopic Proximal Gastrectomy with Double Tract Reconstruction and Laparoscopic Total Gastrectomy for Proximal Early Gastric Cancer D. Park,* D. Jung, Y. Lee, D. Kim, Y. Park, S. Ahn, H. Kim. *Surgery, Seoul National University Bundang Hospital, Seongnam-si, Korea (the Republic of).*

Introduction: Laparoscopic proximal gastrectomy (LPG) with double tract reconstruction (DTR) is known to reduce reflux symptoms, which is a major concern after proximal gastrectomy. The aim of this study is to compare retrospectively the clinical outcomes of patients undergoing LPG with DTR with those treated by laparoscopic total gastrectomy (LTG). Methods: Ninety-two and 156 patients undergoing LPG with DTR and LTG for proximal stage I gastric cancer between June 2003 and April 2015 at Seoul National University Bundang Hospital were retrospectively analyzed for short- and long-term clinical outcomes. Results: There were no significant differences in the demographics, T-stage, N-stage, and complications between two groups. The LPG with DTR group had a shorter operative time and lower estimated blood loss than the LTG group (198.3 versus 225.4 min, $P < 0.001$; and 84.7 versus 128.3 mL, $P = 0.001$). The incidence of reflux symptoms ≥ Visick grade II did not significantly differ between the groups during a mean follow-up period of 37.2 months (2.0 vs. 2.5%, $P = 0.999$). The hemoglobin changes were significantly lower in the LPG with DTR group compared to those in the LTG group in the first and second postoperative years (5.03 versus 9.18%, $P = 0.004$ and 3.45 versus 8.30%, $P = 0.002$, respectively), as was the mean amount of vitamin B12 supplements 2 years after operation (0.1 mg versus 3.1 mg, $P < 0.001$). The overall 5-year survival rates were 96.1% and 95.9% for the LPG with DTR and LTG groups, respectively ($p = 0.575$). Conclusions: LPG with DTR maintained comparable oncological safety and anastomosis-related late complications compared to LTG and is preferred over LTG in terms of preventing postoperative anemia and vitamin B12 deficiency.

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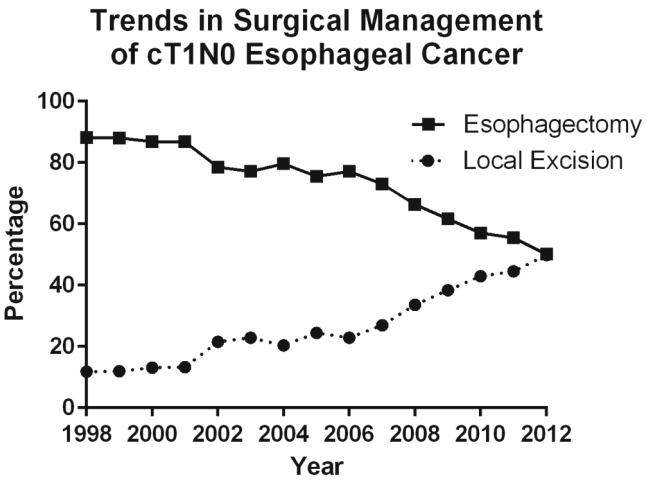
National Trends in Local Excision and Esophagectomy for cT1N0 Esophageal Cancer E.C. Sturm,* W. Zahnd, J. Mellinger, S. Ganai. *General Surgery, Southern Illinois University School of Medicine, Springfield, IL.*

Introduction: Esophageal cancer management has evolved due to improvements in staging and treatment strategies. Endoscopic local excision presents an attractive option for definitive management of T1 cancers, avoiding the morbidity of esophagectomy. We hypothesized that for cT1N0 cancers, patients who underwent local excision would have lower survival compared to esophagectomy due to potential discordant staging. Methods: The National Cancer Database was queried for esophageal squamous cell carcinoma (SCC) and adenocarcinoma (AC) with AJCC T1N0 clinical stage who underwent local excision (n=1625) or esophagectomy (n=3255) between 1998 and 2012. Chi-square analysis was used to compare demographic and clinical characteristics by procedure. Chi-square trend analysis was performed to assess trends in procedure type over time. Cox Regression analysis was performed to assess survival by procedure controlling for demographic and clinical characteristics. Results: Between 1998 and 2012, the proportion of patients who underwent local excision increased from 12% to 50% for all patients (Figure; $p<0.001$); from 17% to 40% for SCC patients ($p<0.001$); and from 9% to 51% for AC patients ($p<0.001$). Surgical procedure varied significantly by demographic, socioeconomic status, facility, and tumor-related factors. 65% of cT1N0 cancers had concordant clinical and pathological staging after esophagectomy, with 11% having positive nodal disease; 44% were concordant after local excision. While no significant difference was seen in unadjusted survival, adjusted Cox Regression analysis indicated worse survival after esophagectomy compared to local excision for all cases (HR 1.67; 95% CI, 1.40-2.00) and for ACs with concordant staging (HR 1.54; 95% CI, 1.11-2.14). Conclusions: Local excision for cT1N0 esophageal cancer has increased over time. Staging concordance for esophagectomy is seen in two-thirds of cases. Contrary to our hypothesis, patients undergoing local excision for T1N0 cancers have better overall survival than those undergoing esophagectomy, which may reflect early differences in mortality and/or selection bias. As this study was unable to distinguish T1a from T1b, further analysis is warranted.



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Gastrointestinal Stromal Tumors: Immune Protein Expression and Clinical Outcomes A.M. Blakely, W. Young,* A. Matoso, T.J. Miner. *Rhode Island Hospital / Brown University, Providence, RI.*

Introduction: The immune microenvironment is emerging as an important prognostic factor with potential therapeutic targets for various malignancies. Although programmed death-ligand 1 (PD-L1) and indoleamine 2,3-dioxygenase (IDO) have been studied in some tumor types, significance of their expression in gastrointestinal stromal tumors (GISTs) is largely unknown. Methods: Tissue microarrays at an academic tertiary care center were constructed from pathology files from 1996 to 2016. Immunohistochemistry for PD-L1 and IDO was performed and correlated with tumor size, mitoses, and clinical outcomes. Tumor infiltrating lymphocytes (TILs) were counted using image analysis software. Results: 131 GISTs were analyzed. Median patient age was 64 years (range 30-89); 51.1% were male. Tumor location included 89 stomach (67.9%), 34 small bowel (26.0%), 4 colorectal (3.1%), and 4 other (3.1%). Median follow-up was 58 months. Mean tumor size was 5.6±4.5cm, range 0.5 to 24; mean mitoses were 7.2/50HPF. 19 (14.5%) metastasized to mesentery (n=8), liver (n=6), and elsewhere (n=5). Mean survival was 61 months (range 7-127); 5 patients died of disease (3.8%). PD-L1 immunostain was positive in 89 (67.9%), including 11 of 19 (57.9%) malignant and 78 of 112 (69.6%) benign tumors ($p=0.4$). PD-L1 positive tumors were larger (6.3±4.4 vs. 4.4±3.4 cm; $p=0.02$) and had more mitoses/50HPF (8.9±5.4 vs. 3.9±3.5; $p=0.006$) than PD-L1 negative tumors. IDO immunostain was positive in 116 (88.5%), including 14 of 19 (73.7%) malignant and 102 of 112 (91.1%) benign tumors ($p=0.07$). There was no significant difference in size or mitotic count between IDO positive and negative tumors. Mean number of CD8-positive TILs was 168±35/mm2 and mean number of PD-L1 positive TILs was 147±28/mm2 in PD-L1 positive tumors. PD-L1 positive tumors had significantly more TILs than PD-L1 negative tumors (113±21 vs. 104±18; $p<0.001$). Conclusions: The majority of GISTs express PD-L1 and IDO. Expression of PD-L1 was associated with increased tumor size and higher mitotic activity. PD-L1 and IDO could play a significant role in the tumor biology of GISTs; immunotherapy targeting one or both may provide novel treatment options.

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TP53 Mutation Rates are Significantly Elevated in African American Patients with Gastric Cancer E. van Beek,* J.M. Hernandez, D. Goldman, T. Kim, L. Tang, J.F. Hechtman, J. Zheng, M. Capanu, D.B. Solit, Y.Y. Janjigian, V.E. Strong. *Memorial Sloan Kettering Cancer Center, New York City, NY.*

Background: Gastric cancer is a heterogenous disease that results from complex interactions between environmental and genetic factors, the latter of which may contribute to the disparate outcomes observed between eastern and western populations. We therefore sought to determine if genomic differences exist in a diverse population of patients treated a single institution by evaluating tumor mutational profiles stratified by race. Methods: All patients with gastric adenocarcinoma (GEJ excluded) who underwent targeted next-generation sequencing of cancer genes by Memorial Sloan Kettering-Integrated Mutation

Profiling of Actionable Cancer Targets (MSK-IMPACT) platform were identified. Silent mutations were excluded. Patient race was categorized as Asian, Black, Hispanic or White. Fisher's exact test was used to examine differences in mutation rates between racial designations for the most common mutations encountered. P-values were adjusted using the False Discovery Rate method. Results: One hundred nineteen patients with 595 mutations were included. The alterations in DNA identified included missense mutations (66%), frame shift deletions (13%) and nonsense mutations (9%). The most frequently mutated genes identified included ARID1A, CDH1, ERBB3, KRAS, PIK3CA, and TP53. Of these, TP53 was the most frequently mutated gene (50%), affecting 60 patients. The proportion of patients with TP53 mutations was significant different between the races. TP53 mutations were present in 89% (16/17) of Black patients, 56% (10/18) of Asian patients, 43% (9/21) of Hispanic patients and 40% (25/62) White patients. Conclusions: Our study is the first to evaluate tumor genomic differences in a diverse population of patients with gastric cancer treated at a single center. In doing so, we identified significantly higher rates of TP53 mutations among African Americans. Further interrogation, including impact upon clinical end points, is warranted.

		Asian	Black	Hispanic	White	Unadjusted p-value	Adjusted p-value
ARID1A	Yes	3 (16.7)	1 (5.6)	5 (23.8)	7 (11.3)	0.36	0.54
	No	15 (83.3)	17 (94.4)	16 (76.2)	55 (88.7)		
CDH1	Yes	3 (16.7)	2 (11.1)	1 (4.8)	11 (17.7)	0.53	0.61
	No	15 (83.3)	16 (88.9)	20 (95.2)	51 (82.3)		
ERBB3	Yes	3 (16.7)	2 (11.1)	1 (4.8)	5 (8.1)	0.61	0.61
	No	15 (83.3)	16 (88.9)	20 (95.2)	57 (91.9)		
KRAS	Yes	0 (0)	0 (0)	2 (9.5)	8 (12.9)	0.22	0.54
	No	18 (100)	18 (100)	19 (90.5)	54 (87.1)		
PIK3CA	Yes	1 (5.6)	1 (5.6)	4 (19)	4 (6.5)	0.31	0.54
	No	17 (94.4)	17 (94.4)	17 (81)	58 (93.5)		
TP53	Yes	10 (55.6)	16 (88.9)	9 (42.9)	25 (40.3)	0.002	0.012
	No	8 (44.4)	2 (11.1)	12 (57.1)	37 (59.7)		

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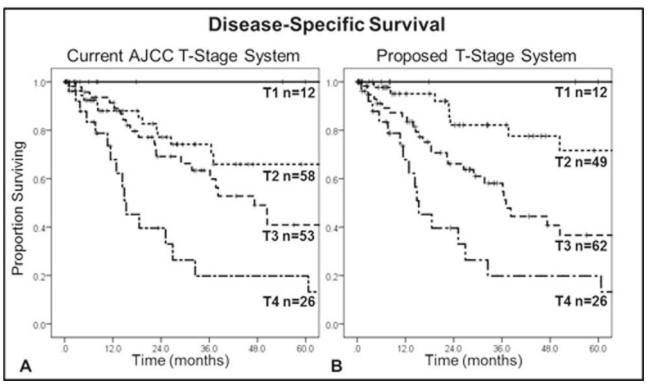
A Novel T-Stage Classification System for Adrenocortical Carcinoma: Proposal from the U.S. Adrenocortical Carcinoma Study Group C.E. Poorman,[1] C.G. Ethun,[1]* L.M. Postlewait,[1] T.B. Tran,[2] J.D. Prescott,[3] T.M. Pawlik,[3] T.S. Wang,[4] J. Glenn,[4] I. Hatzaras,[5] R. Shenoy,[5] J.E. Phay,[6] K. Keplinger,[6] R. Fields,[7] L.X. Jin,[7] S.M. Weber,[8] A. Salem,[8] J.K. Sicklick,[9] S. Gad,[9] A. Yopp,[10] Q. Duh,[11] N. Seiser,[11] C.C. Solorzano,[12] C.M. Kiernan,[12] K. Votanopoulos,[13] G. Poultsides,[2] S.K. Maithel.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University School of Medicine, Stanford, CA; 3. Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; 4. Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 5. Department of Surgery, New York University School of Medicine, New York, NY; 6. Department of Surgery, The Ohio State University, Columbus, OH; 7. Department of Surgery, Washington University School of Medicine, St. Louis, MO; 8. Department of General Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 9. Department of Surgery, University of California San Diego, San Diego, CA; 10. Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 11. Department of Surgery, University of California San Francisco, San Francisco, CA; 12. Department of Surgery, Vanderbilt University, Nashville, TN; 13. Department of Surgery, Wake Forest School of Medicine, Winston-Salem, NC.*

Background: The 7th AJCC T-stage classification system for adrenocortical carcinoma (ACC), based on size and extra-adrenal invasion, does not adequately stratify patients by survival. Lymphovascular invasion (LVI) is a known poor prognostic factor. We propose a novel T-stage system that incorporates LVI to better risk-stratify patients undergoing resection for ACC. Methods: Patients undergoing curative-intent resections for ACC from 1993-2014 at 13 institutions comprising the US ACC Study Group were included. Primary outcome was disease-specific survival (DSS). Results: Of 265 patients with ACC, 149 had complete data for analysis. The current T-stage system failed to differentiate patients with T2 vs T3 disease (p=0.10; Fig 1A). Presence of LVI was associated with worse DSS compared to no LVI (36 vs. 168mos; p=0.001). After accounting for the individual components of the current T-stage system (size and extra-adrenal invasion), LVI persisted as a poor prognostic factor on multivariable analysis (HR 2.14, 95%CI 1.05-4.38, p=0.04). LVI positivity further stratified patients with T2 and T3 disease, (T2: 37mos vs median not reached; T3: 36 vs 96mos; p=0.03), but did not influence survival in patients with T1 or T4 disease. By incorporating LVI, a new T-stage classification system was created: [T1: <5cm, (-)local invasion, (+/-)LVI; T2: >5cm, (-)local invasion, (-)LVI OR any size, (+)local invasion, (-)LVI; T3: >5cm, (-)local invasion, (+)LVI OR any size, (+)local invasion, (+)LVI; T4: any size, (+)adjacent organ invasion, (+/-)LVI]. Each progressive new T-stage group was associated with worse median DSS (T1: 167mos; T2: 96mos; T3: 37mos; T4: 15mos; p<0.001; Fig 1B). Conclusion: The current AJCC T-stage system for ACC does not adequately stratify patients by survival, particularly for T2 and T3 disease. The proposed T-stage classification system, which incorporates lymphovascular invasion, better differentiates T2 and T3 disease and accurately stratifies patients by disease-specific survival. If externally validated, this novel T-stage classification should be considered for future AJCC staging systems.



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Clinical Risk Score for Malignancy in Surgical Patients with Indeterminate Bethesda III and IV Thyroid Nodules J.C. Farra,* D. Yakoub, G.A. Rubio, W. Zhao, K. Tulay, J.I. Lew. *Surgery, University of Miami, Miami, FL.*

Introduction: Surgical management of indeterminate Bethesda III and IV thyroid nodules remains a clinical dilemma. Clinical factors used in a sum score for evaluation of these thyroid nodules may predict underlying malignancy. This study examines the sum of selected demographic and clinical factors in predicting malignancy for patients with indeterminate thyroid cytology, which may assist the surgeon in the clinic setting to determine extent of thyroidectomy. Methods: A retrospective review of prospectively collected data of surgical patients from a single tertiary medical center was performed. Only patients with a dominant thyroid nodule and initial indeterminate or Bethesda III/IV cytology by FNA were analyzed. Logistic regression models were fitted to identify significance of demographics, preoperative TSH levels, and ultrasound features for prediction of thyroid cancer. Results: Of 595 patients, 152 (26%) had indeterminate thyroid nodules by FNA. Of this subgroup, 67 patients (44%) had thyroid cancer on final pathology. An aggregated sum score was calculated based on weighted clinical factors: age <45, female sex, White, Hispanic, Asian and other race/ethnicity, nodule hypoechoechogenicity, and preoperative TSH level ≥ 1. The higher the sum score, the higher risk of thyroid cancer with each value increasing the risk by 1.08 times (95%CI: 1.02- 1.14, p<0.001). For every five points increase in a patient's weighted sum score, the odds ratio of having thyroid cancer was increased by 1.46 (95% CI: 1.11-1.92, p<0.01). Additionally, patients with a weighted sum score ≥8 were 3.37 (95%CI: 1.69-6.71, p<0.01) times more likely to have thyroid cancer compared to patients with a score <8. A score of 1 corresponded to a malignancy risk of 27%, whereas a score of 20 corresponded to a malignancy risk of 62%. Conclusions: In patients with indeterminate thyroid nodules, a sum score based on the combination of age, sex, race/ethnicity, ultrasound features, and preoperative TSH significantly predicts thyroid malignancy. This clinical risk score, therefore, serves as a useful adjunct in helping surgeons determine the extent of thyroidectomy in these patients.

Logistic regression: effect of selected predictors on thyroid cancer (reduced model)

		N = 595 (All patients)				N = 152 (Indeterminate patients)				
		Univariate		Multivariate		Univariate		Multivariate		
Variable	Category	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	Coefficient	OR (95%CI)	P
Sex	Female vs. Male	0.56 (0.35, 0.89)	0.014	0.58 (0.35, 0.95)	0.032	1.04 (0.46, 2.32)	0.927	0.0827	1.09 (0.46, 2.55)	0.849
Race	Non-Black vs. Black	3.30 (2.03, 5.37)	<001	2.61 (1.56, 4.36)	<001	1.69 (0.64, 4.46)	0.289	0.2756	1.32 (0.48, 3.61)	0.592
Age at operation (yrs)	< 45 vs. ≥ 45	1.42 (1.02, 1.97)	0.038	1.44 (1.01, 2.08)	0.047	1.40 (0.73, 2.70)	0.316	0.4339	1.54 (0.77, 3.09)	0.220
Pre operation TSH	≥1.0 vs. <1	1.95 (1.40, 2.72)	<001	1.89 (1.31, 2.71)	0.001	1.74 (0.85, 3.56)	0.130	0.6346	1.89 (0.88, 4.05)	0.104
US Dominant Nodule Echogenicity	Hypoechoic vs Iso / hyperechoic	3.76 (2.65, 5.32)	<001	3.21 (2.24, 4.61)	0.001	2.32 (1.19, 4.55)	0.014	0.8475	2.33 (1.17, 4.65)	0.016
Indeterminate FNA results	No vs. Yes	1.51 (1.05, 2.19)	0.028	1.73 (1.16, 2.60)	0.008					

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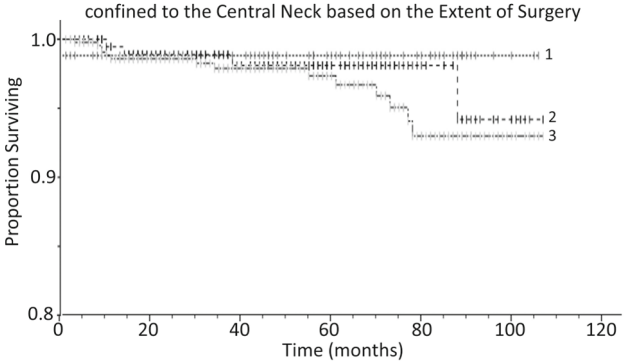
Survival in Patients with Medullary Thyroid Cancer After Less than Recommended Surgery R.W. Randle,* M.F. Bates, D.F. Schneider, R.S. Sippel, S.C. Pitt. *Surgery, University of Wisconsin-Madison, Madison, WI.*

Introduction: For patients diagnosed with Medullary Thyroid Cancer (MTC), total thyroidectomy with bilateral central neck dissection is the recommended procedure. However, many patients are diagnosed after less extensive resections for benign disease or indeterminate nodules. Therefore, we aimed to evaluate the disease specific survival (DSS) of patients with MTC confined to the central neck based on the extent of the initial surgery. Methods: We performed a retrospective review of patients with MTC using the SEER registry from 2004-2012. We excluded patients with lateral nodal involvement (N1b) or metastatic disease and compared DSS based on the extent of initial resection. Results: The final cohort (n=766) included 85 (11%) less than total thyroidectomies (TT), 212 (28%) TT alone, and 469 (61%) TT with lymph node excision. These three groups were similar in gender distribution (p=0.32) and mean tumor size (2.2cm for < TT, 1.9 for TT alone, and 2.2 for TT with nodes, p=0.13). Patients receiving a TT with nodal excision were slightly younger (mean age 56y for < TT, 56 for TT alone, and 51 for TT with nodes, p<0.001) and more likely to have multifocal tumors (8% < TT, 22% TT alone, and 27% TT with nodes, p<0.001) and extrathyroidal extension (1% < TT, 4% TT alone, and 9% TT with nodes, p=0.005). Despite differences in the extent of initial surgery, DSS was similar between groups (Figure). After controlling for significant predictors of DSS including age, tumor size, and extrathyroidal extension, the extent of the initial surgical resection did not predict survival (HR 0.28 for < TT, 95% CI 0.26-3.11 and HR 0.62 for TT alone, 95% CI 0.17-2.22 compared to TT with nodes, p=NS for all). Conclusion: The extent of the initial resection does not appear to significantly change DSS in patients with MTC confined to the central neck. While total thyroidectomy with bilateral central neck dissection remains the most appropriate initial operation, these data support surveillance of patients with incidental, sporadic MTC diagnosed after less extensive resections.

Figure: Disease Specific Survival for Patients with Medullary Thyroid Cancer confined to the Central Neck based on the Extent of Surgery



	No. of Patients	5 Year Survival (%)	% Surviving at Last Follow-up	P
1. Less Than Total Thyroidectomy	85	98.8	98.8	0.47
2. Total Thyroidectomy Alone	212	98.1	94.2	
3. Total Thyroidectomy with Nodes	469	97.3	93.0	

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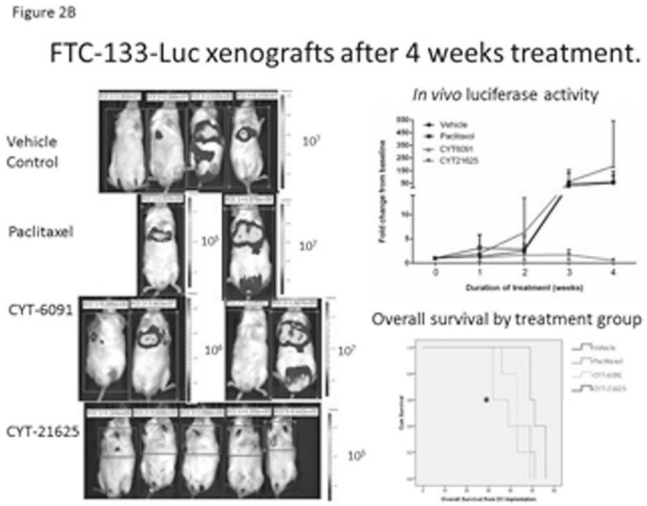
A Novel Targeted Nanomedicine is Effective in Transgenic and Metastatic Mice Models of Endocrine Cancers N. Nilubol,[1]* Z. Yuan,[3] G. Paciotti,[2] L. Tamarkin,[2] C. Sanchez,[3] K. Gaskins,[1] E. Freedman,[1] S. Cao,[4] J. Zhao,[4] D.G. Kingston,[4] S.K. Libutti,[3] E. Kebebew.[1] *1. Endocrine Oncology, National Cancer Institute, Bethesdas, MD; 2. CytImmune Sciences, Rockville, MD; 3. Albert Einstein College of Medicine, Bronx, NY; 4. Department of Chemistry and the Virginia Tech Center for Drug Discovery, Blackburg, VA.*

Introduction Nanomedicine for cancer therapy is actively being evaluated in a variety of malignancies in preclinical studies and some have been translated into clinical trials. CYT-21625 is the first-in-class gold nanomedicine that simultaneously delivers recombinant human tumor necrosis factor (rhTNF) and a paclitaxel prodrug. In this study, we evaluated the efficacy and toxicity, and mechanism of action of CYT-21265 in transgenic and metastatic mice models of endocrine cancers Methods Mice with metastatic poorly differentiated thyroid cancer (PDTC) and anaplastic thyroid cancer (ATC), and MEN1 conditional knock-out mice that develop pancreatic neuroendocrine tumors (PNETs) were treated with CYT-21625, gold nanoparticles with rhTNF only (CYT-6091), paclitaxel, and vehicle control to assess the anticancer activity of CYT-21625. The tumor selectivity was assessed using CT, MRI, and 18F-FDG PET scans in mice with PNETs. Results Mice with metastatic ATC xenograft that were treated with CYT-21625 had a significantly lower tumor burden compared to the other groups (P<0.01). Mice with metastatic PDTC xenograft had a longer overall survival than mice in vehicle and paclitaxel groups (P=0.01) and had lower tumor burden compared to other groups (p=0.03). Treatment with CYT-21625 resulted in loss of CD34 expression in intratumoral vasculature, decreased proliferating cell nuclear antigen staining, and increased cleaved caspase-3. Intratumoral vascular leakage demonstrated by MRI and immunofluorescence occurred only in mice with PNET and ATC treated with CYT-6091 and CYT-21625. CT and 18F-FDG PET showed deposit of CYT-6091 and CYT-21625 in PNETs. Mice with insulin secreting PNETs had a significant decrease in their elevated serum insulin levels compared to other groups. There were no toxicities observed in mice treated with CYT-21625. Conclusion CYT-21625 is effective in mice with ATC and PNETs. Thus, it should be studied in patients with advanced PNETs, PDTC and ATC.



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Immune Checkpoint Inhibitor Therapy as a Novel and Effective Therapy for Aggressive Cutaneous Squamous Cell Carcinoma

G. Beasley,[2]* J. Kurtz,[1] J.H. Howard,[2] A. Terando,[2] D. Agnese,[2] L. David,[2] T. Olencki.[2] *1. Doctors Hospital, Columbus, OH; 2. Ohio State University, Columbus, OH.*

Background: Patients with metastatic or locally aggressive cutaneous squamous cell carcinoma (SCC) have historically had limited and non-effective treatment options. While surgery remains the mainstay of treatment, resection can be disfiguring and technically not feasible for larger lesions. As such, we sought to examine the outcomes of patients with SCC treated with Nivolumab, an anti-programmed cell death protein 1 (PD-1) inhibitor. Methods: Eleven patients with SCC who were treated with Nivolumab for metastatic or locally advanced cutaneous SCC from March 2015 to present were identified and reviewed. Results: Three patients had metastatic disease and 8 patients had locally advanced disease. All patients had undergone at least 1 surgery; 7 patients also had been treated with radiation. Five patients had failed other systemic treatments and 1 patient had CLL. Of the 11 patients treated, 10 had dramatic responses with improvement in clinical symptoms and impressive tumor reduction (Figure 1). Objectively, 3 patients had a complete response, 7 patients had a partial response, and 1 patient had progression of disease. An 88-year-old patient died from an ischemic cerebrovascular incident possibly related to treatment. Therapy was otherwise well tolerated and 7 patients currently continue on therapy. Nine patients continue to have stable or no new disease at a median time of 22 months from the initiation of treatment. Conclusion: PD-1 blocking agents may provide clinically meaningful therapeutic results for patients with aggressive cutaneous SCC who are not surgical candidates.

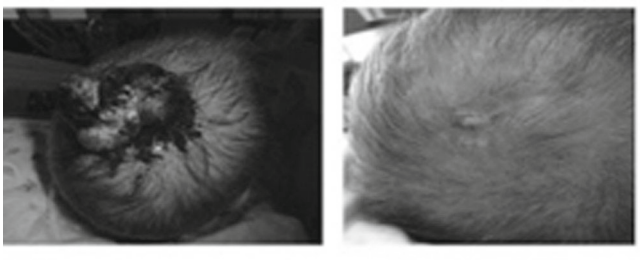

Figure 1: Aggressive squamous cell before (left) and after (right) treatment with anti-PD1 therapy

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Granular Cell Tumor Experience at a Dedicated Cancer Center

A. Moten,[1]* S. Movva,[2] M. von Mehren,[2] N.F. Esnaola,[2] S.S. Reddy,[2] J.M. Farma.[2] *1. Surgery, Temple University Hospital, Philadelphia, PA; 2. Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Granular cell tumors (GCT) are rare lesions that can occur in almost any location in the body. Although multiple case reports have been published, there have been very few large-scale studies on GCT. Aim: The aim of this study was to define patient characteristics, treatment patterns and outcomes of patients with GCT. Methods: An IRB-approved retrospective chart review was performed of patients with GCT treated at a comprehensive cancer center. Descriptive statistics and bivariate/multivariate regressions were performed; survival rates were analyzed. Results: Fifty patients were treated for GCT between 1992 and 2015. Mean age was 47.8 years; 62% were female and 64% were white. Females were more likely to be black than males (48.4% versus 10.5%, respectively; P=0.01). Mean tumor size was 1.57cm. The most frequent location of tumors was the gastrointestinal (GI) tract (n=30; 60%), followed by skin/subcutaneous tissue (n=19; 38%), then respiratory tract (n=1; 2%). Tumors of the GI tract occurred in the oral cavity (n=9), esophagus (n=16), stomach (n=1), colon (n=3) and anal canal (n=1). Most patients (68%) underwent primary excision or endoscopic removal of their tumors without undergoing prior biopsy. Adjuvant chemotherapy was rare (2%). Three patients (6%) had multifocal tumors; they were more likely to experience recurrence than patients with solitary tumors (33.3% versus 10.6%, respectively; P=0.05). Six patients (12.0%) experienced recurrence, with a median time to recurrence of 13.5 months. Of those with recurrent tumors, 66.7% underwent repeat surgery. Overall 5-year survival was 89.4%. There was no increased risk of death based on gender, race, tumor location, or recurrence status. One patient with multifocal disease underwent next generation sequencing identifying a KIT, PRKAR1A and TSC2 mutation. Conclusion: Patients with GCT treated with excision alone fair well without adjuvant treatment, regardless of whether recurrence occurs. However, patients with multifocal tumors are more likely to experience recurrence and should be closely monitored. Further research, including molecular profiling, may provide further insight into these rare tumors.

Patient demographics

	All, n (%)	Male, n (%)	Female, n (%)	P-value
Total	50 (100.0)	19 (38.0)	31 (62.0)	
Mean age (years)	47.8	51.8	45.3	
Age (years)				0.06
<40	13 (26.0)	3 (15.8)	10 (32.3)	
40-49	16 (32.0)	5 (26.3)	11 (35.5)	
50-59	10 (20.0)	6 (31.6)	4 (12.9)	
60-69	8 (16.0)	2 (10.5)	6 (19.4)	
≥70	3 (6.0)	3 (15.8)	0	
Race				0.01
White	32 (64.0)	16 (84.2)	16 (51.6)	
Black	17 (34.0)	2 (10.5)	15 (48.4)	
Unknown	1 (2.0)	1 (5.3)	0	
Comorbidities				0.70
No	11 (22.0)	3 (15.8)	8 (25.8)	
Yes	32 (64.0)	13 (68.4)	19 (61.3)	
Unknown	7 (14.0)	3 (15.8)	4 (12.9)	
Cancer history				0.30
No	28 (56.0)	8 (42.1)	20 (64.5)	
Yes	16 (32.0)	8 (42.1)	8 (25.8)	
Unknown	6 (12.0)	3 (15.8)	3 (9.7)	

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National Disparities in Stage-Appropriate Therapy for Resectable Non-Small Cell Lung Cancer: Opportunities for Intervention

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Introduction: Stage I-II non-small cell lung cancer (NSCLC) ideally should be resected in all medically operable patients. However, a significant proportion of patients never receive curative-intent surgery in the United States. The primary aims of this study were to analyze national trends in the proportion of patients who undergo surgery for early stage NSCLC and to identify modifiable factors associated with disparities in receiving optimal therapy. Methods: Using the National Cancer Data Base, all patients with clinical stage I-II NSCLC diagnosed 2004-2013 were analyzed. Clinico-pathologic and

demographic variables were analyzed in a multivariate model to identify predictors of resection and to analyze the impact of surgery on overall survival (OS). Results: Of 310,837 Stage I-II NSCLC patients, 188,618 (60.7%) underwent resection. Failure to resect was independently associated with reduced median OS (19.9 vs. 71.4 mo, HR 2.58, p<0.001). The median age of resected patients was 69.0 vs. 74.0 years for unresected patients (p<0.001). In multivariate analysis, non-modifiable independent predictors of not receiving surgery included black race (OR-1.44 vs. white), male gender (OR-1.19), older age (OR-1.07), residing in areas with median income <$38,000 (OR-1.05), areas with <21% high school degrees (OR-1.04), and metro areas with population <1 million (OR-1.20) (all p<0.002). Risk factors which could be targeted for earlier diagnosis and improved access included larger tumor size (OR-1.13), no insurance or non-private insurance (OR-2.07 private vs. none), and non-academic treatment facility (OR-1.17) (all p<0.001). Conclusions: Almost 40% of patients with resectable NSCLC fail to undergo surgery, which is the key determinant of OS besides clinical stage. Mitigating disparities in national resection rates for Stage I-II NSCLC requires improved outreach efforts in low-income/low-education counties, targeted screening programs to find earlier-stage tumors, and open access to surgical consultations at academic safety-net hospitals less likely to deny operations for patients at risk for not receiving surgery.

Factors associated with no resection in stage I-II non-small cell lung cancer		Odds Ratio *
Black race (vs. white)		1.44 (1.39 - 1.48)
Male		1.19 (1.12 - 1.27)
Older age		1.07 (1.07 - 1.07)
County with median income <$38,000		1.05 (1.02 - 1.08)
County <21% high school degrees		1.04 (1.02 - 1.07)
Population < 1 million		1.20 (1.17 - 1.22)
Potentially modifiable factors	Larger tumor size	1.13 (1.11 - 1.15)
	No or non-private insurance	2.07 (1.93 - 2.22)
	Non-academic facility	1.17 (1.13 - 1.20)

*all p<0.002

Among the independent risk factors significantly associated with no resection for stage I-II non-small cell lung cancer are some potentially modifiable targets to reduce disparities in national resection rates (p<0.002).

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External Validation of a Survival Nomogram for Non-Small Cell Lung Cancer Using the National Cancer Data Base K. Young,* E. Efiong, J. Dove, J. Blansfield, M. Hunsinger, J. Wild, M. Shabahang, M. Facktor. *Gesinger Medical Center, Danville, PA.*

Introduction With the rising interest in personalized medicine, survival nomograms have sparked clinical interest because they offer individualized predictions using a more diverse set of factors than traditional staging, including the American Joint Committee on Cancer's Tumor Node Metastasis (AJCC TNM) system. A nomogram predicting overall survival (OS) for resected, non-metastatic non-small cell lung cancer (NSCLC) has been previously derived from Asian patients. The present study aims to determine the predictive capability of this nomogram in the United States (US) using the National Cancer Data Base (NCDB). Methods This was a retrospective review of adults with resected, non-metastatic NSCLC entered into the NCDB between 2004 and 2012. Concordance indices and calibration plots were used to analyze discrimination and calibration, respectively. Multivariate analysis was also used. Results A total of 57,313 patients were included. The predominant histologies were adenocarcinoma (48.2%) and squamous cell carcinoma (31.3%). Patients were diagnosed with Stage I-A (38.3%), Stage I-B (22.7%), Stage II-A (14.2%), Stage II-B (11.5%) and Stage III-A (13.3%). Median OS was 74 months. OS rates (1-, 3- and 5-year) were 89.8% (95% Confidence Interval [CI], 89.5-90.0%), 71.1% (95% CI, 70.7-71.6%) and 55.7% (95% CI, 54.7-56.6%), respectively. The nomogram's concordance index (C-index) was 0.804 (95% CI, 0.792-0.817). AJCC TNM staging demonstrated higher discrimination (C-index: 0.833; 95% CI, 0.821-0.840). Conclusion The nomogram's individualized estimates accurately predicted survival in this patient collective, demonstrating a higher level of discrimination in this population than in the developer's cohorts. However, the generalized survival estimates provided by traditional staging demonstrated better predictive capability. Therefore, AJCC TNM staging should remain the gold standard for the prognostication of resected NSCLC in the US.

ABSTRACTS

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V1

Solo Single Port Laparoscopic Pedicled Omental Harvest for Immediate Breast Reconstruction S. Ahn,* D. Park, H. Kim. *Department of Sugery, Seoul National University Bundang Hospital, Seongnam, Korea (the Republic of).*

Background: Breast cancer surgery and accompanying reconstruction have been diversitified. We describe our technique of immediate breast reconstruction by using single port harvested omental flap (SHOF). Methods: During a 12-month period, 26 immediate breast reconstruction with SHOF were performed. For SHOF, only one 2~2.5cm transumbilical incision was used under lithotomy position. Solo single port total omentectomy was performed with ligation of left gastroepiploic vessels and arcade of gastroepiploic arcade was dissected from the stomach up to the distal antrum or intrapyloric vessels, and right gastroepiploic vessels was the main blood supplier for omental flap. Dissected omentum was carefully harvested on mastectomy site with no fixation suture through two finger's width subxyphoid tunneling. Results: The mean BMI was 21.8 ± 2.6. The mean total operation time and SHOF operation time were 204.9 ± 29.7 and 56.3 ± 8.7 minutes, respectively. There was no technical failure and adverse event in SHOF. The mean specimen weight was 169.9 ± 48.9 g. Morbidity included 1 minor skin ischemia (3.8%) of the SHOF. There was no complication related to SHOF. Cosmetic results were mostly satisfactory, especially in the umbilical scar. The mean postoperative hospital stay was 8.2 ± 4.4 (4~22) days. Conclusion: In spite of a limit of case number, SHOF for immediate breast reconstruction is technically feasible and safe. The use of single port can maximize cosmetic result comparing with multiport laparoscopic omental harvest.

V2

Robotic-Assisted Total Pelvic Exenteration for Recurrent Cervical Cancer in a Jehovah's Witness I.T. Konstantinidis,* F. Tozzi, C. Lau, M. Wakabayashi, K. Chan, B. Lee. *Surgical Oncology, City of Hope Medical Center, Duarte, CA.*

Introduction: Robotic assisted total pelvic exenteration (TPE) can offer a minimally invasive approach to a major multi-organ operation. In this video, we summarize a stepwise approach of robotic TPE for recurrent cervical cancer. Methods: The patient is a 70 year old female with a history of cervical cancer post chemoradiation and radical hysterectomy. She experienced local recurrence at the vaginal cuff involving the rectum and bladder. She is a Jehovah's witness and refused administration of blood products. We offered her robotic assisted TPE. The patient was placed in lithotomy position. A total of 6 robotic ports were used and the da Vinci Si robotic system was docked between the legs. We proceeded as follows: 1) The abdomen and pelvis were thoroughly explored for evidence of metastatic disease 2) The pelvic sidewalls were mobilized and bilateral ureters identified 3) The mesorectal plane was dissected to the level of the levators 4) The lateral and anterior pelvic structures were completely mobilized. Parametrial tissues were mobilized to the pelvic wall 5) The bladder was separated from the pubis symphysis, the space of Retzius entered and the bladder and proximal urethra freed 6) A perineal incision was made around the vagina, perineal body and anus which were excised 7) An Alloderm mesh secured the pelvic floor. An omental J flap was mobilized 8) Mini laparotomy was required for retrieval. An ileal conduit and a permanent end colostomy were constructed Final pathology was consistent with recurrent cervical squamous cell carcinoma invading into vaginal, bladder and rectal walls. Surgical margins and 0/4 lymph nodes were negative for carcinoma. Conclusion: Robotic assisted total pelvic exenteration is technically feasible in a Jehovah's witness under a multidisciplinary surgical team even in the setting of prior radical hysterectomy and irradiated tissue.

V3

Cortical-Sparing Posterior Retroperitoneoscopic Adrenalectomy for Hereditary Pheochromocytoma M.E. Egger,* N.D. Perrier. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Certain hereditary syndromes such as multiple endocrine neoplasia type 2 (MEN2) and von Hippel-Lindau syndrome (VHL) are associated with increased risk of pheochromocytoma. Treatment of unilateral disease must take into account the risk of future development of a second pheochromocytoma on the contralateral side, especially in young, otherwise healthy patients. Methods: The case of a 19 year gentleman with VHL and multifocal, unilateral pheochromocytoma is reviewed. Results: The patient's imaging revealed two adrenal nodules consistent with pheochromocytoma in the setting of elevated normetanephrine levels. The nodules were isolated to the inferior pole of the right adrenal gland. The remaining superior pole on the right and the contralateral adrenal were normal in appearance. A unilateral, cortical-sparing posterior retroperitoneoscopic approach was chosen. The video outlines the steps of developing a working space while identifying the relevant landmarks for right adrenalectomy. The right adrenal vein was identified and divided. A cortical-sparing adrenalectomy was performed, sparing the superior portion of the right gland, which appeared normal on intra-operative assessment. Conclusions: The cortical-sparing posterior retroperitoneoscopic adrenalectomy is a useful technique to treat young patients with VHL or MEN2-associated unilateral pheochromocytoma.

V4

Robotic Posterior Retroperitoneal Adrenalectomy with Indocyanine Green (ICG) Fluorescence H. Takahashi,* E. Berber. *General Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Introduction Although laparoscopic posterior retroperitoneal (PR) adrenalectomy avoids intra-abdominal dissection and provides a direct access to the adrenal, instrument collision and suboptimal ergonomics could be an issue in some patients. While robotic instrumentation might overcome these limitations, the lack of tactile feedback is a drawback of this technology. We have previously reported that indocyanine green (ICG) with fluorescent imaging might facilitate this procedure by creating a contrast between fluorescent adrenal gland and hypofluorescent retroperitoneal tissues. We present a video demonstrating our technique of ICG –assisted robotic PR adrenalectomy. Patient and Methods The patient is a 41-year-old female with history of hypertension and borderline diabetes, who has had facial swelling, easy bruising and irregular periods for the last 3-4 years. She has developed anxiety and hirsutism over the last couple of months. Her biochemical work up showed normal serum cortisol, suppressed ACTH and elevated 24-hour urine cortisol levels. CT scan of the abdomen revealed 3.1 x 2.1 cm right adrenal mass. With a diagnosis of Cushing's syndrome, she was consented for a robotic right PR adrenalectomy with ICG imaging. Results The operation was performed under general anesthesia and in prone position. Using one 12mm trocar for the camera, two 8 mm trocars with the robot and one 5 mm trocar for the 1st assistant, right PR adrenalectomy was performed under ICG-fluorescence guidance. The procedure took 2hours 24 minutes and estimated blood loss (EBL) was 10mL. Postoperative course was uneventful and the patient was discharged on the postoperative day #1 on oral hydrocortisone (30mg in the morning and 20mg at bedtime). Final pathology demonstrated adrenocortical adenoma without malignancy. Conclusion This video demonstrates a safe technique for performing robotic PR adrenalectomy for an adrenocortical adenoma producing cortisol. It also depicts how ICG could be used to guide the dissection.

V5

Robot-Assisted Total Gastrectomy with Extended D2 Lymphadenectomy After Neoadjuvant Chemotherapy: The Approach to Aberrant Vasculature C.E. Barrows,* A. Ore, J. Critchlow, A. Moser. *Beth Israel Deaconess Medical Center, Boston, MA.*

Introduction: Outcomes of minimally-invasive gastrectomy are comparable to open in early stage gastric cancer. Given emerging evidence favoring combined modality therapy for high-risk gastric cancer, we implemented robot-assisted minimally-invasive gastrectomy with extended D2 lymphadenectomy after neoadjuvant treatment. This video highlights our approach in a technically complex case with aberrant vascular anatomy. Methods: A 69 year-old female completed all intended cycles of neoadjuvant chemotherapy for T3Nx gastric adenocarcinoma of the lesser curvature. The operative technique is a hybrid laparoscopic/robotic approach. Following exploratory laparoscopy, the right gastric artery was divided at its origin and the proximal duodenum (D1) mobilized from the pancreatic head and divided. The right gastroepiploic pedicle was divided at its origin, and the omentum was resected with the specimen. The short gastric vessels were divided. A 50cm Roux en Y was created laparoscopically, and the robot was docked to perform the extended lymphadenectomy and divide the esophagus. Thorough en-bloc resection of peri-portal, celiac, common hepatic, left gastric, and crural, and peripancreatic lymph nodes was performed. A large replaced left hepatic artery was identified, skeletonized, and meticulously preserved during ligation of left

gastric branches. Upper endoscopy localized the lesion at 6cm from the GE junction. The phrenoesophageal membrane was opened, and the esophagus was divided. Frozen section examination of the proximal and distal margins was negative. End-to-side robotic intracorporeal esophagojejunostomy was created with 4-0 running V-lock suture, and a drain was placed. Results: The post operative course was uneventful, with negative barium swallow on post operative day 5. Final pathology revealed T2 moderately differentiated intestinal type adenocarcinoma, negative margins, and 1 of 42 lymph nodes positive for malignancy after 100 cc blood loss. Conclusion: Total gastrectomy with extended vascular dissection and lymphadenectomy is safe and feasible for advanced gastric cancer after neoadjuvant therapy using a robot-assisted approach.

V6

Robotic Technology Facilitates Minimally Invasive Radical Gastrectomy in Patients with Elevated Body Mass Index T. Kim,* R.P. Merkow, V.E. Strong. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: Prospective studies have shown superior short-term and equivalent long-term outcomes of minimally invasive compared with open radical gastrectomy in patients with resectable gastric adenocarcinoma. However, the rarity of presentation and high prevalence of obesity pose challenges for Western surgeons to learn and master the technique. Based on our experience at a high-volume gastric cancer center, we present a video that demonstrates the operative approach and highlights the technical issues encountered in obese patients, which can be partly alleviated by robotic technology. METHODS: Patients undergoing robotic-assisted gastrectomy with curative intent for histologically-confirmed gastric adenocarcinoma were included based on low versus high body mass index (BMI). Distal gastrectomy with D2 lymphadenectomy was performed using the da Vinci Xi® system (Intuitive Surgical). Regional lymph node imaging was performed using indocyanine green (ICG) injection with near-infrared fluorescence imaging (NIFI, SPY Imaging, Novadaq) incorporated into the robotic platform (Firefly Fluorescence Imaging Scope, Intuitive Surgical). RESULTS: Optimal room and port arrangement are reviewed. The major steps of the operation are presented, including: 1) entry into the lesser sac; 2) gastroepiploic vessel ligation and node harvest; 3) right gastric vessel ligation and node harvest; 4) distal transection of the duodenum; 5) left gastric vessel ligation and harvest of nodes along the lesser curvature, common hepatic, celiac, and left gastric arteries; 6) proximal transection of the stomach with attention to tumor location (confirmed endoscopically and marked with external stitch); 7) specimen extraction via enlarged umbilical port site; 8) Billroth II reconstruction. The video contrasts visualization in a thin versus obese patient, with or without NIFI. CONCLUSIONS: Intra-abdominal adiposity increases the technical difficulty of radical gastrectomy. The video herein demonstrates a systematic operative approach and the ability of robotic and ICG/NIFI technology to enhance lymph node visualization and regional lymphadenectomy in this setting.

V7

Totally Laparoscopic Left Hepatectomy for Hepatocellular Carcinoma G. Eeson,[2] C.H. Law,[1] J. Hallet.[1]* *1. Sugery, University of Toronto, Toronto, ON, Canada; 2. Kelowna General Hospital, Kelowna, BC, Canada.*

Introduction: Laparoscopic surgery is now established as standard of care for a variety of abdominal malignancies. However, the uptake of the laparoscopic approach has been slower for liver resection. Methods: This video details the steps to laparoscopic left hepatectomy. Results: We focus on the case of a 46 year old patient diagnosed with a new liver nodule on the background of chronic hepatitis B. Imaging characteristic were consistent with hepatocellulary carcinoma. A laparoscopic anatomic left hepatectomy was proposed to minimize the invasiveness of the procedure and enhance recovery. The video begins with presentation of the patient and ports positioning. The portal inflow is dissected at the base of the umbilical fissure. The hepatic arteries to segments 4 and 2/3 and the left portal vein are dissected circumferentially and divided. A choelcystectomy is performed and the gallbladder fundus is left attached to be used for manipulation of the left liver lobe. The left triangular and coronary ligaments as well as the ligamentum venosum are divided. The parenchyma is transected using a combination of crush-clamp technique and bipolar energy device. Parenchymal hemostasis techniques are presented. The left bile duct is identified in its intra-hepatic portion, dissected, and divided. Management of left hepatic vein bleeding due to stapling device misfire is demonstrated step by step. The specimen is extracted through a pfannenstiel incision. Operative time was 240 minutes and estimated blood loss 200 mL. The patient experienced an uneventful post-operative course. Final pathology revealed an angiomyolipoma with epithelioid features. Conclusion: Laparoscopic liver surgery presents opportunities to reduce blood loss, decrease morbidity, and enhance recovery. We herein illustrate the steps for laparoscopic left hepatectomy, including laparoscopic management of hepatic vein bleeding. This video provides a systematic and detailed approach to laparoscopic liver resection to contribute to better understanding and spread of the technique.

V8

Laparoscopic Management of Gallbladder Cancer: A Stepwise Approach S. Yamashita, E. Loyer, Y. Chun, J.E. Lee, J. Vauthey, C. Conrad.* *Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.*

Abstract Background: In the era of laparoscopic cholecystectomy incidentally discovered gallbladder cancers (IGBC) has become a common clinical presentation. Although oncologic safety of laparoscopic treatment for selected patients with GBC has been demonstrated, a laparoscopic approach for IGBC remains uncommonly practiced due to the technical challenge of the frequently re-operative cases. Patient: A 75-year-old man underwent laparoscopic cholecystectomy for the diagnosis of chronic cholecystitis and sludge at an outside institution and pathology revealed a T3 gallbladder carcinoma with positive margin at the cystic duct stump. Restaging computed tomography at time of referral showed findings in the hepatoduoenal ligament and gallbladder fossa concerning for residual tumor versus postoperative inflammation. Following 4 cycles of gemcitabine and cisplatin, restaging revealed interval resolution of the postoperative change, continued low tumor marker CA19-9 and no evidence of metastatic disease. Technique: With the patient in French position, significant adhesions around the hepatoduodenal ligament had to be dissected. Lymph node stations 12 and 16 were removed following a Kocher maneuver and hepatoduodenal ligament lymphadenectomy, preserving an accessory right hepatic artery. The cystic duct stump was removed at the level of the confluence with the common bile duct. The resulting defect was reconstructed with interrupted sutures. Using intraoperative ultrasonography (IOUS) guidance, an anatomical resection of segments 5/4b was performed. An alternative approach is a laparoscopic Glissonian approach that can facilitate a safe anatomical resection. An air cholangiogram detected no bile leak and confirmed biliary patency. Postoperative recovery was uneventful and pathology showed residual adenocarcinoma in segments 4b/5 with 50% tumor viability and negative margins. Conclusion: As laparoscopic management of IGBC is a challenging re-operative case, a systematic approach using accurate preoperative anatomical assessment, meticulous IOUS-guided surgery, and air cholangiogram is recommended to minimize the morbidity of this operation.

EHV1

Oncoplastic Surgery Post-central Mastectomy
S. Rodriguez-Qizilbash,* R.J. Younan. *Department of Surgery, Centre Hospitalier Universitaire de Montréal, Montréal, QC, Canada.*

A 48-year-old woman with Paget's disease and a retro-areolar in situ carcinoma undergoes a central mastectomy. This video presents the immediate post-central mastectomy oncoplastic reconstruction performed by a surgical oncologist for a central breast tissue deficit. The technique involves undermining the breast tissue over the muscle fascia. Then, the remaining gland is closed using 5 different layers of purse string suture, starting from posterior to anterior. The resulting breast no longer has a central deficit and has achieved an optimal esthetic result.

EHV2

Minimally Invasive Ivor Lewis Esophagogastrectomy with Side-to-Side Anastomosis R. Shah,[1]* K. Ben-David,[2] S. Hochwald,[1] M. Kukar.[1] *1. Roswell Park Cancer Institute, Buffalo, NY; 2. Mount Sinai Medical Center, Miami Beach, FL.*

Introduction Minimally invasive esophagectomy has shown to improve functional outcomes without compromising oncologic principles. Existing techniques utilizing end to end anastomosis have demonstrated high stricture rates. Here, we present our technique for a 6 cm side to side stapled intrathoracic anastomosis. Technique Our patient is a 60-year-old man who

presented with a four month history of dysphagia and weight loss. He underwent an upper endoscopy which revealed an ulceroproliferative lesion in the distal esophagus with biopsy proven adenocarcinoma. Staging CT and PET scan exhibited hypermetabolic lymph nodes along the left gastric artery and redemonstrated the mass in the distal esophagus with no evidence of distant metastatic disease. The surgery commenced in the abdomen with 4 ports as depicted. Following a diagnostic laparoscopy, initial steps of the procedure included mobilization of the stomach with care to preserve the right gastroepiploic vessels. Dissection of the left gastric lymph nodes is demonstrated with complete skeletonization of the vessels prior to division. Mobilization of the distal esophagus was completed, the gastric conduit was fashioned and a 16 French feeding jejunostomy placed. The patient was placed in the left lateral decubitus position. Utilizing 5 ports as shown, the esophagus was completely mobilized and transected above the level of the azygos vein. A 6 cm side-to-side stapled anastomosis was performed and the anastomosis was inspected endoscopically, and a negative leak test confirmed. This patient had an uneventful post-operative course and was discharged on POD 7 on a full liquid diet. Final pathology showed a complete pathologic response, ypT0 N0 (0/29) with all negative margins. The patient was seen in follow-up 2 weeks later and was doing well and advanced to a regular diet. Conclusion We have recently published our experience with over 300 minimally invasive esopahgectomies with stapled side to side anastomosis. 60 patients had an intrathoracic anastomosis and 1 patient developed an anastomotic leak that was managed by endoscopic stent placement. Symptomatic anastomotic stricture rate for the entire cohort, requiring dilation was 4.1%.

EHV3

Laparoscopic Partial Splenectomy for Unknown Primary Cancer: A Stepwise Approach E.P. Vega, S. Yamashita, J. Fleming, J. Vauthey, J.E. Lee, C. Conrad.* *UT MD Anderson Cancer Center, Houston, TX.*

Background: Laparoscopic partial splenectomy (LPS) for focal splenic lesions is technically demanding and carries risk of hemorrhage. Nevertheless, it can be a valuable option, particularly for children and adults in whom attempt at preservation of splenic immunologic function outweighs risk associated with organ preservation. Patient: A 58-year-old man was diagnosed with a focal splenic lesion at the upper splenic pole on surveillance imaging following axillary lymph node metastasis for cancer of unknown primary origin (CUP). After an interval of 8 months, repeat FDG-PET showed increase in size and PET-avidity without any evidence of new lesions. Due to isolated site and history of CUP, the patient was considered for a LPS. Technique: With the patient in reversed modified French position, the upper pole splenic vessels were controlled and a well-defined area of ischemia encompassing the lesion identified. Under intermittent inflow occlusion and ultrasonography guidance, the parenchymal transection was performed. Total operative time was 180 min., estimated blood loss was 175cc, the patient was discharged on postoperative day 2, and final pathology confirmed an Epstein-Barr virus associated inflammatory pseudotumor. Conclusion: Safe LPS requires systematic pre-operative assessment of hilar vascular anatomy and a stepwise approach to controlling the vessels intra-operatively. Anatomic parenchymal transection and intermitted vascular isolation for lesions close to the demarcation zone minimizes blood loss. Risk/benefit stratification of LPS may be beneficial in select patients only. Whether in patients with CUP LPS may aid in preserving innate and adaptive immunity with potential clinical, including oncologic, benefits will require further investigations.

EHV4

Robotic Distal Subtotal Gastrectomy with D2 Lymphadenectomy for Advanced Gastric Cancer Y. Woo, J. Desiderio,* Y. Fong. *Surgery, City of Hope National Cancer Center, Duarte, CA.*

Introduction The robotic approach for technically demanding cancer operations, such as radical surgery for advanced gastric cancer, has been standardized to facilitate minimally invasive surgery. Case presentation A 39-year-old woman with biopsy proven gastric adenocarcinoma was staged cT3N1M0. After discussion of treatment options including upfront surgery followed by adjuvant treatment versus neoadjuvant treatment followed by surgery, the patient underwent a robotic distal subtotal gastrectomy with D2 lymphadenectomy. Procedure Four 8mm robotic trocars and one 15mm assist trocar were placed. The daVinci Xi System's Cart was brought in from the patient's left side and docked. The instruments were inserted into the robotic arms (Arm1 Cadiere; Arm2 Harmonic; Arm3 Camera; Arm4 Maryland). The gastrocolic ligament was divided proximally to identify and divide the left gastroepiploic vessels (LNS#4sp). Then, the greater curvature was cleared of LNS#4d. The division continued distally to the base of the right gastroepiploic vein. The right gastroepiploic artery was divided at its origin (LNS#6). The duodenum was sectioned. The base of the right gastric artery was identified and divided (LNS#5). The soft tissue anterior to and medial to the portal vein along the proper hepatic artery was cleared (LNS#12a), as well as along the common hepatic artery (LNS#8a) up to the celiac axis. The left gastric vein was divided, offering access to LNS#9. The base of the left gastric artery was identified and divided (LNS#7). The nodes along the proximal part of the splenic artery (LNS#11p) were cleared. The soft tissue along the esophageal crus and the lesser curvature was dissected (LNS#1#3). The proximal stomach was resected. A loop of small bowel was identified and a side-to-side anastomosis was created. Patient followed an ERAS protocol and was discharged on fourth postoperative day. Final pathology revealed a pT3N2 poorly differentiated adenocarcinoma with 73 nodes examined. Conclusion The robotic system can enhance a minimally invasive oncological dissection, allowing a complete removal of the soft tissue around major vessels, considered the most challenging step for a complete D2 gastrectomy.

EHV5

Laparoscopic Proximal Gastrectomy for Gastric Adenocarcinoma E. Gabriel,* M. Kukar, S. Hochwald. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction For carcinoma of the proximal stomach, a proximal gastrectomy is a preferable option for patients with multiple comorbidities who are not able to tolerate the larger procedure of a total gastrectomy. A laparoscopic approach offers the potential of less postoperative discomfort and complications yet achieves the goals of a margin negative resection and aggressive lymphadenectomy. Methods This video demonstrates the key steps of a laparoscopic proximal gastrectomy. Results We present a case of a 74-year-old man with multiple comorbidities who presented with a bleeding gastric adenocarcinoma that required embolization. This was staged by EUS to be T2N0. CT scan was negative for regional/distant disease. Four 5 mm ports and one 12 mm port were utilized. Following a diagnostic laparoscopy, complete mobilization of the stomach was performed preserving the right gastroepiploic vessels. Dissection of perigastric lymph nodes and stations 7-9 were included. Tumor location was confirmed endoscopically, and the stomach was transected across the body removing the tumor with a wide distal margin. Mobilization of the distal esophagus/GEJ was completed. The distal esophagus was transected, and the specimen was removed through a 4 cm left upper quadrant incision. The anastomosis was performed with a 25 mm Orville EEA stapler to create an end-to-side esophagogastrostomy. The anvil was passed transorally and positioned out of the end of the esophagus. The proximal end of the remnant gastric staple line was opened in order to pass the stapler. After completion of the anastomosis, the gastrotomy was closed with a linear stapler. The patient tolerated the procedure well. He was discharged on POD 6 on a full liquid diet after an uneventful course. Final pathology was T1b N0 (0/17) with 4 cm and 1.5 cm gastric and esophageal margins, respectively. Conclusions Appropriate oncologic resection for carcinomas of the proximal stomach can be achieved through a minimally invasive approach. In our current series of 5 patients who have undergone laparoscopic proximal gastrectomy, each with multiple comorbidities, there have been adequate oncologic and functional results with no significant early postoperative complications.

ABSTRACTS

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PT1

The Impact of Preoperative Breast MRI on Surgical Management of Women with Newly Diagnosed DCIS J. Smith,[1]* S.C. Partridge,[2] K.E. Adrienne,[2] S. Peacock,[3] S.H. Javid,[4] J.N. Kim,[5] C.D. Lehman,[6] J.M. Lee,[2] H. Rahbar.[2] *1. Department of Radiology, University of Washington School of Medicine, Seattle, WA; 2. Department of Radiology, University of Washington School of Medicine and Seattle Cancer Care Alliance, Seattle, WA; 3. Department of General Internal Medicine, University of Washington School of Medicine, Seattle, WA; 4. Department of Surgery, University of Washington School of Medicine and Seattle Cancer Care Alliance, Seattle, WA; 5. Department of Radiation Oncology, University of Washington School of Medicine and Seattle Cancer Care Alliance, Seattle, WA; 6. Department of Radiology, Massachusetts General Hospital, Boston, MA.*

Introduction: Preoperative breast MRI (pMRI) is the most sensitive modality for determining extent of ductal carcinoma in situ (DCIS). However, its impact on surgical management is less clear, and there is concern that pMRI is contributing to rising mastectomy rates. Accordingly, we sought to evaluate the impact of pMRI on the number and type of surgeries as well as breast conservation surgery (BCS) success rates for DCIS treatment at a center where pMRI is routinely obtained. Methods: After IRB approval, we identified all women without a personal history of ipsilateral breast cancer who were diagnosed with pure DCIS (no associated invasive disease) on core needle biopsy (CNB) between 2004-2013 and underwent surgical management within 180 days of CNB date. Number and type of surgeries as well as time from CNB diagnosis to first surgery were obtained for each subject from our MRI database. Patient features, including age, family history, BRCA status, breast density, and DCIS pathology subtype, were extracted from the electronic medical record. These variables were compared between the pMRI and no pMRI groups using Wilcoxon signed-rank or chi-squared test. Results: 388 women (342 pMRI, 46 no pMRI) with CNB-diagnosed DCIS were included. Women who received pMRI underwent fewer mean total surgeries than women who did not have pMRI (1.21 vs. 1.41, p=0.01). This benefit persisted among the 252 women in whom BCS was attempted (pMRI mean=1.32, n=219 vs. no pMRI mean=1.60, n=33; p=0.03). In those who had successful BCS (final surgery not mastectomy), women with pMRI underwent fewer surgeries (mean=1.20 vs. 1.40, p=0.03) and were more likely to undergo a single successful BCS (72% vs. 55% success rate, p=0.03) than women who did not have pMRI. There were no significant differences in mastectomy rate or time from CNB diagnosis to first surgery among the groups (p>0.05). Furthermore, the groups did not differ in age, family history, BRCA status, and DCIS subtype (grade, necrosis, hormone receptor) (p>0.05). Conclusion: pMRI may improve the surgical management of DCIS, leading to fewer operations and better BCS success rates without more mastectomies or delays in surgical treatment.

	Pre-op MRI	No MRI	P-Value
Age (Mean)	55.6	54.0	0.37
Pre-Menopause	122/342 (36%)	22/46 (48%)	0.20
Family history	151/342 (44%)	18/46 (39%)	0.60
Dense breasts	230/342 (67%)	30/46 (65%)	0.87
Index DCIS ER positive	273/342 (80%)	32/46 (70%)	1.0
Index DCIS Necrosis present	282/342 (82%)	35/46 (76%)	1.0
Index DCIS Grade			0.28
Low	35/342 (10%)	6/46 (13%)	
Intermediate	128/342 (37%)	16/46 (35%)	
High	179/342 (52%)	23/46 (50%)	
Days to surgery	55.2	52.7	0.66
Average number of surgeries	1.21	1.43	0.01
Average number of surgeries when 1st attempted BCS	1.32	1.60	0.03
Average number of surgeries of those with successful BCS	1.20	1.40	0.03
BCS successful on 1st attempt	139/193 (72%)	14/26 (55%)	0.03
Mastectomies	149/342 (44%)	20/46 (44%)	1.0

PT2

Surgery and Survival in Patients with Stage IV Breast Cancer C. Arciero,* Y. Liu, T. Gillespie, P. Subhedar. *Surgery, Emory University School of Medicine, Atlanta, GA.*

Background: In an era of increasingly effective chemotherapy and targeted agents, the role that surgery plays in the overall survival of patients with Stage IV breast cancer continues to be questioned. Methods: An examination of the NCDB database from 2003-2011 was undertaken to examine factors related to the utilization of surgery and with overall survival in patients with Stage IV disease. Univariate and multivariable analyses were conducted to determine patient and treatment factors related to survival. Overall survival was estimated using the Kaplan-Meier method. Results: A total of 18,751 patients with Stage IV breast cancer were identified from from 2003 to 2011, with 11,429 meeting inclusion criteria. Surgical intervention (mastectomy or partial mastectomy) on the primary tumor occurred in 5,679 patients (49.7%), with likelihood of surgery decreasing throughout the study period (55.3% surgery 2003-2005; 40.1% surgery 2009-2011). Selection for surgical intervention was associated with small (T1), well/moderately differentiated tumors, fewer nodal metastases (N0/1), and were estrogen receptor positivity. Surgery remained independently associated with overall survival, but to a lesser extent than systemic therapy, estrogen receptor status, tumor grade and Charlson-Deyo score. The median survival was significantly improved in patients receiving surgical intervention (35 months versus 25.8 months, p<0.001). But, systemic therapy was noted to have a much larger impact on survival when comparing systemic therapy plus surgery (40.1 months), systemic therapy alone (30.4 months), surgery alone (9.7 months) and best supportive care (4.7 months) (p<0.001). Conclusions: Systemic therapy is associated with a much larger impact on survival in patients with Stage IV breast cancer compared with surgery. While surgery of the primary tumor may priovide a modest improvement in overall survival, this is likely related to selection bias based on tumor and patient factors.

PT3

Efficiency of Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography to Evaluate Neoadjuvant Chemotherapy in Breast Cancer T. Ishiba,[1]* T. Nakagawa,[2] G. Oda,[2] Y. Yamashita,[1] Y. Nakashima,[1] H. Baba,[1] N. Hoshino,[1] Y. Nishioka,[1] H. Uetake.[2] *1. Surgery, Soka Municipal Hospital, Soka, Japan; 2. Tokyo Medical and Dental University, Tokyo, Japan.*

Badkground: Neoadjuvant chemotherapy (NAC) has become a standard therapy for patients with advanced breast cancer. Fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) can evaluate metastases in the entire body simultaneously, and has several potential advantages over conventional imaging modalities. The purpose of this study was to evaluate whether FDG-PET/CT can determine NAC response and whether FDG-PET/CT can be a new prognostic marker. Methods: We imaged 83 breast cancer tumors with FDG-PET/CT, ultrasound (US), and magnetic resonance imaging (MRI) to evaluate NAC efficacy. As we previously analyzed 110 breast cancers with FDG PET/CT, we defined a threshold of >1.7 maximum standardized uptake value (SUVmax) as abnormal fluorodeoxyglucose (FDG) uptake. Results: After NAC, 16 (19.3 %) tumors had a complete response, 54 (65.1 %) had a partial response, 11 (13.3 %) showed stable disease, and 2 (2.4 %) showed progressive disease. One of the two patients with progressive disease had bone metastasis detected by FDG-PET/CT and was not operated on. Remote metastases were evident in 2.4 % of patients after NAC as determined by FDG-PET/CT. Overall, 17 patients had pathological complete response (pCR). The sensitivity of abnormal FDG uptake after NAC for non-pCR was 20.3 % and the specificity was 94.7 %. Patients with abnormal FDG uptake after NAC experienced significantly more recurrences (P = 0.004) and more of them died (P = 0.010). Moreover, the difference in diseasefree survival was more significant in the estrogen receptor (ER)-negative group. Conclusion: FDG-PET after NAC may be more effective for predicting prognosis than for evaluating treatment response. This tendency was particularly remarkable in ER-negative breast cancer tumors. FDG-PET/CT is useful for reevaluating surgical applicability after NAC.

PT4

Postoperative Extent of Disease Evaluation is Not Associated with Discovery of Distant Metastatic Disease in Patients Upstaged at Surgery T.N. Williams,* O. Debra, E. Pickholz, C. Weltz, H. Schmidt, E. Port. *Mount Sinai Icahn School of Medicine, New York, NY.*

Introduction: NCCN guidelines do not recommend extent of disease (EOD) screening in asymptomatic early stage breast cancer patients. However, patients discovered to have more advanced disease pathologically (larger tumors, positive lymph nodes) may be recommended for EOD evaluation post-operatively, raising concern for the value of having had surgery if evidence of stage IV disease is discovered. We investigated the yield of post-operative EOD evaluation in patients upstaged through surgery. Methods: retrospective review of a prospective database identified clinically and radiologically early stage,

node-negative patients who underwent surgery for breast cancer between 2010-2015. Those who were pathologically upstaged to stage II or higher were identified and EOD study results performed within 6 months after surgery were reviewed. Results: 98 upstaged patients were identified. Axillary lymph node metastasis was the reason for upstaging in all cases 98/98 (100%).(See Table). Post-operative EOD was performed in 53/98 (54%) patients undergoing a variety of different imaging modalities (see Table). Patients selected for EOD had a mean of 4.3 positive nodes, compared to 1.6 positive nodes in those not scanned, and patients were significantly more likely to undergo EOD if upstaged to stage III compared to stage II, (88% vs. 42%, p=0.0001). Suspicious findings generated further imaging studies in 12/53 (23%) of those scanned, and 1 underwent biopsy of a distant site, which was negative for malignancy. Conclusion: We did not identify any case where patients upstaged by pathology results from surgery led to the discovery of stage IV disease in the immediate post-operative period (thereby obviating the benefit of having undergone surgery). Asymptomatic breast cancer patients with clinical early stage disease may not require post-operative EOD despite discovery of more advanced stage disease pathologically.

Patient characteristics

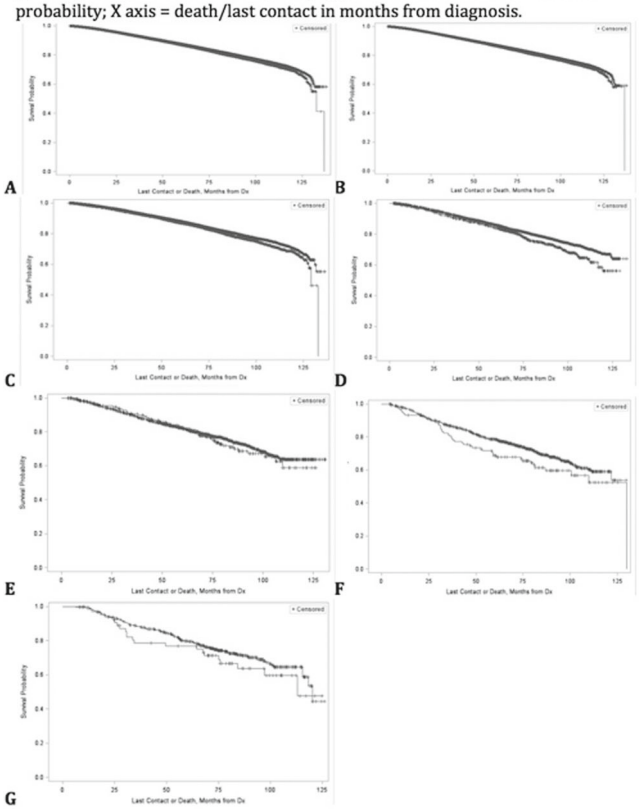
N= 98 patients	98
Mean age (range)	53 years old (31-82)
lumpectomy mastectomy	44/98 (45%) 54/98 (55%)
Mean tumor size (range)	1.9 cm (0.6-5.5cm)
Post-operative stage: 2A 2B 3A 3C	49/98 (50%) 24/98 (25%) 20/98 (20%) 5/98 (5%)
Mean # positive nodes in all patients (range)	3 (1-26)
Mean # positive nodes with EOD (range) Mean # positive nodes w/o EOD (range)	4.3 (1-26) 1.6 (1-5)
EOD imaging modality: PET CT/Bone scan CT only Bone scan only Abdominal U/S + bone scan	30/53 (56%) 18/53 (34%) 2/53 (4%) 2/53 (4%) 1/53 (2%)

PT5

Impact of Time to Surgery on Rural-Urban Disparities in Breast Cancer E.C. Buckley,* W. Zahnd, D. Rea, J. Mellinger, S. Ganai.
General surgery, SIU-SOM, Springfield, IL.

Introduction: Recent studies demonstrate time to surgery (TTS) influences breast cancer survival and that efforts to reduce TTS should be pursued to enhance survival. Rural patients experience barriers in access to care and may have treatment delays. We hypothesized that rural patients would have delayed TTS and decreased breast cancer survival compared to urban patients. Methods: We utilized data from the National Cancer Database to study 240,293 patients diagnosed with invasive, non-inflammatory, non-metastatic breast cancer who underwent surgery as initial treatment between 2003 and 2007, with follow-up available through 2012. Chi-square analysis and independent t-test were used to compare TTS by rural-urban status. Survival curves were constructed by time to surgery. Cox regression analysis was used to calculate hazard ratios (HR) and 95% confidence intervals (CI) controlling for demographic, clinical, and treatment characteristics. Results: Rural patients comprised 15% of the cohort and were poorer, had longer travel distance, were less educated, and were less often treated at an academic center than urban patients. Stage was similar between groups, with the majority having Stage I disease. In both groups, most patients had surgery within 30 days of diagnosis (74% rural and 68% urban). Mean TTS was 24±22 days for rural vs 27±26 days for urban patients. Significantly worse survival was noted in rural compared to urban patients in unadjusted analysis overall, and when stratified by TTS up to 90 days after diagnosis (Figure). No survival difference was seen when TTS exceeded 90 days. After adjusting for demographic, clinical and treatment characteristics, rural patients had improved survival compared to urban patients overall (HR 0.94; 95% CI 0.89-0.99), and when stratified by TTS within 30 days of diagnosis (HR 0.91; 95% CI 0.86-0.97). No survival difference was seen when TTS exceeded 31 days in the adjusted analysis. Conclusion: Time to breast surgery was longer for urban areas. Adjusted analysis refutes our hypothesis and demonstrates that rural patients have a 6% lower risk of death from breast cancer compared to urban patients after controlling for cofounders.

Figure: Survival probability of rural and urban breast cancer patients. **A** = overall (p <0.0001). **B** = within 30 Days of diagnosis (p<0.0001). **C** = between 31 and 60 days (p=0.002). **D** = between 61 and 90 days (p=0.002). **E** = between 91 and 120 days (p=0.57). **F** = between 121 and 180 days (p=0.08). **G** = 181 days or more (p=0.32). Red/lower line = rural; blue/upper line = urban. Y axis = survival probability; X axis = death/last contact in months from diagnosis.



PT6

Factors Associated with Lack of Tamoxifen Initiation in Young Women at High-risk for Breast Cancer N.N. Rizk,[1]* D. Dokic,[2] J. Kochkodan,[1] S. Estevez,[2] H. Singh,[1] M. Yanik,[1] J.S. Jeruss.[1]
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2. Northwestern University, Chicago, IL.

Background: Tamoxifen chemoprevention has the potential to significantly reduce the incidence of breast cancer. However, there are disparities in the implementation of tamoxifen, which is a teratogen, for young women at high-risk for developing this disease. To examine these disparities, we identified a cohort of young high-risk women and examined reasons for lack of treatment initiation. We hypothesized that modifiable factors could be identified, unique to the young high-risk population, that could potentially be addressed to help improve tamoxifen initiation. Methods: From 2005 to 2012, we identified 162 premenopausal, < 45, high-risk women (BRCA mutation, lobular carcinoma in situ, atypical ductal hyperplasia, atypical lobular hyperplasia, flat epithelial atypia, strong family history) who had not undergone surgical prophylaxis with bilateral mastectomy or oophorectomy. Women younger than 35 (n = 81), for whom tamoxifen was not indicated, were excluded. For the study population of 81 patients, factors associated with tamoxifen use were examined. Results: Mean age of the study population was 41 and the majority of patients were diagnosed with ADH (27, 33%). Half the study population was nulliparous (43, 53%). Tamoxifen use was discussed with 56 (69%) patients, and initiated in 10 (12%). For those patients offered tamoxifen, the primary reasons for lack of initiation were fertility concerns, concerns about side effects, and perceived minimal treatment benefit; 39% of these patients opted for radiographic screening alone. The average age of the women who initiated tamoxifen was 42, and the majority had an ADH diagnosis and a family history of breast cancer. Conclusion: This study highlights the lack of tamoxifen initiation in a young high-risk patient population. Improving physician-patient communication regarding the beneficial impact of tamoxifen chemoprevention and options for

implementation of fertility preservation may help to improve tamoxifen initiation. Just as young breast cancer patients are treated with a multidisciplinary approach, young women at high-risk for breast cancer should be counseled with a focus on cancer prevention and survivorship concerns.

PT7

Significant Discordance of Lymphovascular Invasion Between Breast Cancer Core Biopsies and Surgical Specimens Limits Its Role as a Preoperative Prediction Tool C.K. Harris,* R. Scott, C. Mylander, M. Rosman, S. Robbins, L. Tafra, R.S. Jackson. *Breast Surgery, Anne Arundel Medical Center, Annapolis, MD.*

Introduction Many breast cancer nomograms have been developed from resected tumor pathology, but are intended to be used preoperatively based on core biopsy results. One such example is the Memorial Sloan Kettering Cancer Center (MSKCC) nomogram, which uses lymphovascular invasion (LVI) as one criteria to predict the likelihood of sentinel lymph node metastasis. In this study we examined whether LVI on resected tumor pathology is accurately identified on core biopsy. Methods We reviewed cases of invasive breast cancer from 2/04/2011 - 9/30/2014, excluding those with neoadjuvant therapy, recurrent cancer, histology other than ductal/lobular/mixed, or stage IV disease. LVI was categorized as absent, present, or suspicious, as indicated in the pathology report, and compared on core biopsy vs. resected tumor. Final LVI was considered positive if core biopsy and/or resected tumor showed present LVI, or if resected tumor was suspicious for LVI. Results We analyzed 614 cases for LVI discordance. Of 147 cases with final LVI positive by the above criteria, 76 (51.7%) were negative for LVI on core biopsy (Table 1). By pathology report, of cases with present LVI on core biopsy, 33.3% were negative for LVI on resected tumor. Of cases suspicious for LVI on core biopsy, LVI status on resected tumor was negative in 44.6%. Conclusion Our study demonstrates that preoperative core biopsy misses the majority of cases of LVI, which were considered positive on final surgical pathology. This would substantially influence MSKCC nomogram estimates, since presence of LVI increases the probability of having sentinel node metastasis by approximately 25%. Postoperative data (e.g. pathology from resection) is often used to develop nomograms for preoperative use, on the assumption that the core biopsy information will correlate with the resected tumor. This study shows that LVI on core biopsy does not correlate well with resected tumor pathology, demonstrating a limitation to the practice of using postoperative data to develop nomograms for preoperative use, as well as predicting breast cancer prognosis from LVI absence on core biopsy.

Table 1: Lymphovascular invasion on core biopsy vs. resected tumor (row percentages in parentheses)

		Resected tumor		
		Negative for LVI (n=477)	Suspicious for LVI (n=10)	Positive for LVI (n=127)
Core biopsy	Negative LVI (n=510)	434 (85%)	6 (1%)	70 (14%)
	Suspicious for LVI (n=74)	33 (45%)	3 (4%)	38 (51%)
	Positive for LVI (n=30)	10 (33%)	1 (3%)	19 (63%)

PT8

Risk of Early-Onset Breast Cancer and Neurofibromatosis Type 1: Are Early Breast Cancer Screening Guidelines Needed in This High-risk Population? A Quantitative Systematic Review and Meta-analysis of Cohort Studies L. Suarez-Kelly,* L. Yu, D. Kline, W.E. Carson III. *The Ohio State University, Columbus, OH.*

Introduction: Neurofibromatosis type 1 (NF1) is a cancer predisposing syndrome. Studies have suggested that women < 50 years of age with NF1 have an increased breast cancer (BC) incidence and BC associated mortality. However, this has not been widely recognized secondary to the small study populations. Methods: A systematic literature review was conducted through database searches for BC and NF1: 3,455 articles identified, 165 reviewed, 64 used for descriptive analysis, and 4 utilized for meta-analysis. Fisher's exact tests, Kaplan-Meier curves, and random-effects models were used for analysis. Results: Two hundred and eighty-five cases of NF1 and female BC were identified. Descriptive analysis demonstrated a mean age of 49.3 years; 53% were < 50, 28% were 35-44, and 15% were < 35. Distribution of patients based on their age at the time of diagnosis revealed a peak age of diagnosis between the ages of 34 to 44 years. Women < 50 presented with more advanced disease vs. those ≥ 50 (56% vs. 22% Stage III-IV, p = 0.005). Median survival for the entire cohort was 5 years compared to the reported median BC survival of over 20 years in the general population using the SEER data base. However, median survival was 5.58 years if < 50 and over 15 years if ≥ 50. Mean age at BC death was 45.7 years; 64% of deceased patients were < 50, 38% were 35-44, and 10% were < 35. Meta-analysis of a total of 4,187 female patients with NF1 revealed a BC standardized incidence ratio (SIR) of 3.07 (95%CI 2.16-4.38) for women with NF1 vs. the general population. However, women < 50 years of age demonstrated a higher SIR of 5.08 (95%CI 3.77-6.81) compared to 1.92 (95%CI 1.40-2.63) if ≥ 50 years of age. Conclusions: This systematic literature review and meta-analysis suggests that women with NF1 < 50 years of age have a fivefold increased risk of BC, present with more advanced disease, and may have an increased BC related mortality. Early breast cancer screening guidelines should to be implemented for this high-risk patient population.

PT9

Sentinel Lymph Node Biopsy in Elderly Women with Hormone Receptor Positive Breast Cancer: Do Results Influence Treatment? R.E. Morgan,* A.M. Naik, R.F. Pommier, J.T. Vetto, S.J. Pommier, M. Heath, K. Massimino. *Oregon Health & Science University, Portland, OR.*

Introduction: As part of the Choosing Wisely® initiative, the Society of Surgical Oncology recently recommended to not routinely offer sentinel lymph node biopsy (SLNB) in clinically node negative women ≥ 70 years of age with hormone receptor positive breast cancer. Reports examining the impact of SLNB on treatment decisions in elderly patients are limited. Methods: Records of women ≥ 70 years of age who underwent breast operation at our institution between January 2011 and August 2016 were reviewed. Women with pT1-pT3, clinically node negative, hormone receptor positive tumors were included. Demographic and treatment data, outcomes, complications of SLNB and impact of SLNB on treatment decisions were recorded. Results: Ninety-five women met inclusion criteria. Mean age was 76 years. Seventy-five women (79%) underwent lumpectomy. SLNB was performed in 87 patients (92%). Thirteen of 87 patients (15%) had a positive SLNB and 5 underwent completion axillary lymph node dissection; 9 had no further axillary treatment, 4 of whom underwent breast conservation therapy. Sixty-eight women (72%) received endocrine therapy. Twenty-seven women (28%), all of whom had SLNB, had Oncotype DX® scores. Adjuvant cytotoxic chemotherapy was recommended to 3/13 (23%) women with positive SLNB. For 2 of these 3 women, a high Oncotype DX® score was cited as the reason. Six women received cytotoxic chemotherapy after negative SLNB, with tumor characteristics, Oncotype DX® score and HER2 status cited as the reason. On multivariate analysis, HER2 status and high Oncotype DX® score were significantly associated with recommendation for cytotoxic chemotherapy ($p<0.001$) while positive SLNB and tumor size were not. Ten women had axillary complications (11%). At a mean follow up of 30 months there were no breast cancer specific deaths, no axillary recurrences and two patients were alive with disease. Conclusion: Sentinel lymph node biopsy has little influence on the decision to recommend cytotoxic chemotherapy in this study population. Furthermore, this dataset reminds that SLNB is not without morbidity.

PT10

MarginProbe Assessment of Lumpectomy Margins and Rates of Surgical Re-excision in a Rural Community Teaching Hospital M. Kryskow,* R. Knowles, M. DiSiena. *Surgery, Berkshire Medical Center, Pittsfield, MA.*

BACKGROUND: Breast-conserving surgery (BCS) for early stage breast cancer is standard of care with 75% of women electing lumpectomy with sentinel node biopsy. Obtaining negative margins improves breast relapse-free survival. The extent of disease is not obvious and the microscopic margin is difficult to assess intraoperatively. Studies indicate 20% of patients need re-excision of positive margins in patients undergoing BCS. Recent technology called the MarginProbe (MP, Dune Medical Devices) may provide the surgeon with intraoperative evaluation of margins using radiofrequency spectroscopy. The device measures local electrical properties in breast tissue and calculates a positive/negative margin with a documented sensitivity 70–100% and specificity 70–87%. Our study aimed to measure the sensitivity and specificity of the MP and ascertain whether one surgeon's re-excision rate (RER) changed secondary to intraoperative MP assessment of margins. METHODS:

A retrospective review of RER in a single surgeon case series of 173 patients undergoing partial mastectomy for early stage breast cancer from 07/01/2011-01/01/2014 was compared to the same surgeon's RER of 46 patients during the trial of the MP from 4/28/2015 to 4/26/2016. During the MP trial, specimens were probed on 6 margins (medial, lateral, superior, inferior, anterior and posterior) for residual disease. Subsequent shave excisions were taken based on MP directed positive margins. RESULTS: 173 patients undergoing BCS during the pre MP trial era had a RER of 10/173, 6%. During the MP trial 46 patients underwent BCS with intraoperative MP assessment of 266 margins. RER during this time period was 4 of the 46 (8%). There were 7 False-negative, 73 false-positive, 10 True-positive and 174 true-negative margins. CONCLUSIONS: Our assessment of MP sensitivity and specificity was 59% and 70% respectively compared to previously reported sensitivities of 70–100% and specificities 70–87%. During the MP trial our RER increased from 6% to 8%. We conclude that the MP does not decrease rates of reoperation and as such does not seem cost effective/justified for use in rural community teaching hospitals.

PT11

Treatment Strategies in Octogenarians with Early-Stage High-risk Breast Cancer A. Mamtani,* J.J. Gonzalez, D. Neo, R.S. Friedman, A. Recht, M.R. Hacker, R. Sharma. *General Surgery, Beth Israel Deaconess Medical Center, Boston, MA.*

Background: Octogenarians with early-stage breast cancers often have low-risk tumor biology. However, optimal treatment strategies and outcomes for octogenarians with high-risk biology remain unclear. Methods: We reviewed medical records of all women aged 80-89 years with biopsy-proven Stage I or II invasive breast cancers referred for surgical evaluation from 01/2001 to 12/2010. "High-risk" disease was defined as HER2-positive (HER2+), triple-negative (TN) receptor phenotype, or histologic grade 3. Results: Table 1 summarizes clinicopathologic features and locoregional treatment of the 178 patients who met the inclusion criteria. Forty (22%) had high-risk disease features: 12 had grade 1–2 cancers (10 HER2+, 2 TN); 28 had grade 3 cancers (7 HER2+, 6 TN, 15 ER+/HER2–). Compared to those with low-risk biology, high-risk patients had larger tumors, and more often had ductal histology and lymphovascular invasion. High-risk women were more likely to have a mastectomy (18% vs. 5%, p=0.02) and more frequently had radiotherapy (RT) (55% vs. 36%, p=0.03) and chemotherapy (10% vs. 0%, p=0.002). Receipt of endocrine therapy was similar among ER+ patients in both groups (70% vs. 62%, p=0.42). Among high-risk patients who had RT, 23% had comprehensive nodal irradiation in addition to breast or chest wall irradiation. Of the 22 (55%) high-risk patients who had systemic therapy, 3 (8%) had chemotherapy alone, 18 (45%) had endocrine therapy alone, and 1 (3%) received both. All patients given chemotherapy were HER2+ and treated after 2007 with trastuzumab-based regimens, without any reported early or late complications. At median follow-up of 67 months (range, 5–108 months) 10% of high-risk women had a recurrence: 3 were distant only, and 1 was simultaneous locoregional (chest wall) and distant in a patient treated with mastectomy without RT. Three of 4 recurrences occurred within 2 years of diagnosis. Conclusion: Tailored locoregional and systemic therapy resulted in a low failure rate in these octogenarians with high-risk cancers with low morbidity. In the absence of significant comorbidities, the use of modern adjuvant therapies should be considered in elderly women with high-risk cancers.

Table 1: Clinicopathologic characteristics and locoregional treatment

Characteristic	High Risk N = 40	Low Risk N = 138	P
Age at diagnosis, years	83 (80 – 86)	83 (81 – 85)	0.88
Pathologic tumor size, mm	19 (13.5 – 26)	13 (8 – 22)	0.002
ECOG status < 2	23 (58%)	84 (61%)	0.7
Ductal histology	37 (93%)	106 (77%)	0.32
Histologic grade: *			
1	0 (0%)	61 (45%)	<0.0001
2	12 (30%)	73 (54%)	
3	28 (70%)	0 (0%)	
Lymphovascular invasion **	12 (30%)	12 (9%)	0.0007
Local Treatment:			
None	0 (0%)	3 (2%)	<0.0001
Lumpectomy Alone	13 (33%)	80 (58%)	
Lumpectomy + RT	20 (50%)	48 (35%)	
Mastectomy Alone	5 (13%)	5 (4%)	
Mastectomy + RT	2 (5%)	2 (1%)	
Axillary Treatment:			
None	17 (43%)	53 (38%)	0.36
SLNB (± RT)	10 (25%)	39 (28%)	
ALND (± RT)	10 (25%)	23 (17%)	
Nodal RT, No Surgery	3 (8%)	23 (17%)	

Data presented as median (interquartile range) and n (%)
* Grade unknown for n = 4 cases in the Low Risk group
** Lymphovascular invasion unknown for n = 3 cases in the Low Risk group
ECOG: Eastern Cooperative Oncology Group; RT: Radiotherapy; SLNB: Sentinel lymph node biopsy; ALND: axillary lymph node dissection

PT12

Immediate Breast Reconstruction for Inflammatory Breast Cancer in the United States: When Survival Matters S. Patel,[1] M. Ng,[1]* S. Nardello,[2] K. Ruth,[3] R.J. Bleicher.[2] *1. Division of Plastic Surgery, Fox Chase Cancer Center, Philadelphia, PA; 2. Department of Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 3. Department of Biostatistics, Fox Chase Cancer Center, Philadelphia, PA.*

Background Inflammatory breast cancer (IBC) is an aggressive breast disease with a poor prognosis. Traditionally, reconstruction is not offered due to concerns about delay of multimodality treatments, margin positivity, recurrence, and poor long-term survival. There is a paucity of literature, however, evaluating whether immediate breast reconstruction (IR) is associated with greater mortality in patients with IBC. Methods A population-based study was conducted via the SEER-Medicare linked database. Female patients were reviewed who had mastectomy and reconstruction claims for non-metastatic IBC diagnosed in 1991 through 2009. Competing risk and Cox regression were used to assess whether IR was associated with higher breast cancer-specific mortality (BCSM) or overall mortality (OM). Results Of the 552,936 patients (1991-2009), 1,574 (median age 74 years) were diagnosed with IBC and had a mastectomy. Forty-seven patients (3%) underwent IR. Younger age (p=0.012), a lower Charlson comorbidity score (p=0.014) and a greater median income (p=0.029) were predictors of IR use. IR patients had lower OM risk compared to patients not having IR (hazard ratio [HR] 0.61; CI 0.42-0.91; p=0.014), but this difference was no longer significant after adjusting for age, co-morbidities and other covariates. Tumor grade, receptor and lymph node status were independent predictors of adjusted-OM and BCSM. There was no difference by IR status in BCSM or covariate-adjusted BCSM (sHR 1.02; CI 0.7-1.51; p=0.90 and sHR 1.16; CI 0.75-1.80; p=0.51, respectively). Cumulative incidence of all-cause mortality was lower among IR patients (p=0.013), and IR did not influence the cumulative incidence of BCSM (p=0.91) (Figure 1). Conclusion Immediate breast reconstruction was not associated with increased overall and BCSM mortality. Although further study of IR in the IBC setting may be of value, these data suggest that IBC should not be considered an absolute contraindication to immediate breast reconstruction.

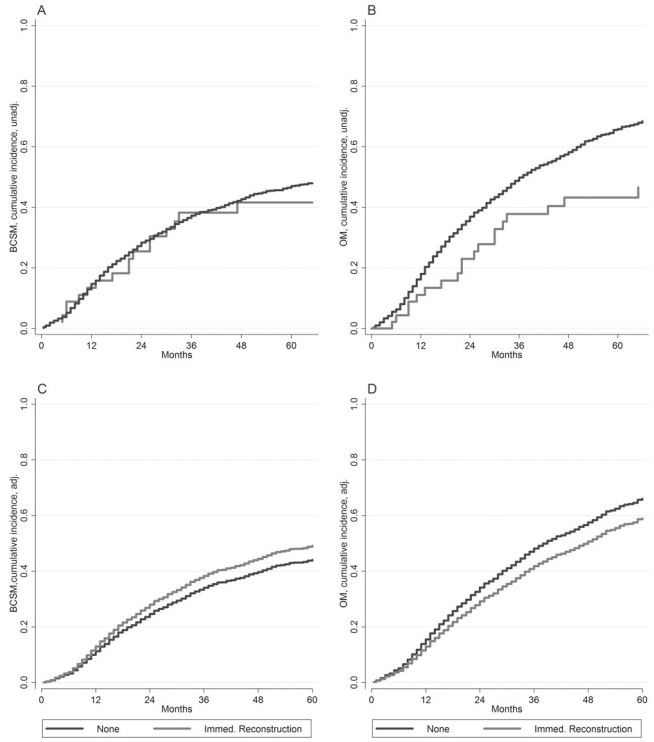


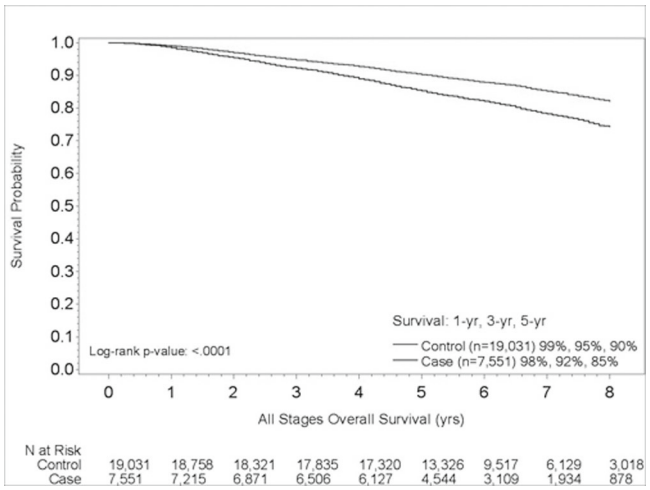
Figure 1. Breast cancer-specific and overall mortality for Surveillance, Epidemiology, and End Results (SEER)-Medicare inflammatory breast cancer patients and immediate breast reconstruction status.

A, Unadjusted cumulative incidence of breast cancer-specific mortality was no different between reconstruction groups (Gray's test, p=0.91). B, Unadjusted cumulative incidence of overall mortality was lower in the immediate reconstruction group (Log rank test, p=0.013). C and D, Adjusted cumulative incidence of breast cancer-specific mortality and overall mortality were not influenced by immediate reconstruction (sHR 1.16; CI 0.75-1.8; adjusted p=0.51 and adjusted HR 0.83; CI 0.56-1.23; adjusted p=0.34, respectively).

PT13

Insurance Status Predicts Survival in Women with Breast Cancer: Results of Breast and Cervical Cancer Prevention and Treatment Program in California Z. Bostanci,* R. Nelson, V. Jones, J.E. Mortimer, A.C. Polverini, L. Taylor, C. Vito, J.H. Yim, L. Kruper. *Breast Surgery, City of Hope, Duarte, CA.*

Introduction: In 2000, Congress passed the Breast and Cervical Cancer Prevention and Treatment Act, mandating states to provide insurance coverage for uninsured women diagnosed with breast or cervical cancer. The purpose of our study is to determine whether a survival difference exists between breast cancer patients with pre-existing insurance versus insurance provided under the Breast and Cervical Treatment Program (BCCTP). Methods: Women with Stage I-III breast cancer covered under California's BCCTP (2005-2009) were identified from the CA Dept of Health Care Services (N = 7551) and matched with California Cancer Registry (CCR) controls (N=19031) on age, race/ethnicity and stage. Univariate and multivariate Cox proportional hazard models were used to assess factors related to overall survival. Results: Although cases were matched, differences between the 2 cohorts existed: BCCTP patients were more likely to be Hispanic (47% vs 37%, p<0.001); in the lowest socio-economic status (SES) quintile (24% vs 9%, p<0.001), and less likely to be married (46% vs 68%, p<0.001). Variables associated with improved survival were higher SES (HR 0.73; 95%CI, 0.64-0.82 highest quintile compared to the lowest), Hispanic (HR 0.88; 95% CI, 0.81-0.95) and Asian (HR 0.77; 95%CI, 0.7-0.85) race/ethnicity, hormone therapy (HR 0.91; 95%CI 0.84-0.99), and chemotherapy (HR 0.82; 95%CI 0.75-0.89). Variables associated with decreased survival were ER negative status (HR 1.23; 95% CI, 1.11-1.36), increasing stage (HR 4.71; 95% CI, 4.23-5.25 Stage III), increasing age (HR 1.21; 95%CI 1.11-1.32 age 60-69; HR2.25; 95%CI 1.9-2.67 age >70), African-American race (HR 1.31; 95% CI, 1.18-1.46) and BCCTP status (HR 1.34; 95%CI 1.25-1.43). Conclusion: BCCTP provides essential coverage to uninsured women with breast cancer. Although the aim of the BCCTP is to provide timely and comprehensive care to women with breast cancer, disparities in outcomes in this group exist. Survival differences among BCCTP patients are most likely multifactorial, related to lower SES and potential barriers to care.



BCCTP Patients Have Decreased Overall Survival

PT14

Surgical Management of Flat Epithelial Atypia Diagnosed on Core Needle Biopsy S.M. Wong,* A. Misariu, M. Ma, A. Omeroglu, S. Meterissian. *Surgery, McGill University Health Centre, Montreal, QC, Canada.*

Background: Flat epithelial atypia (FEA) is an atypical breast lesion of uncertain clinical significance that is increasingly diagnosed on core needle biopsies for mammographic abnormalities. The purpose of this study was to evaluate the presence of malignancy in excised FEA specimens. Methods: Using a prospectively maintained institutional database, we reviewed all cases with a diagnosis of FEA made on core needle biopsy between 2008 and 2016. Differences in clinical characteristics and rates of malignancy on excision between patients with FEA with associated atypical hyperplasia and pure FEA were compared. Results: We identified 126 patients with FEA diagnosed on core needle biopsy specimens. The median age of the cohort was 52 years (range, 38-78), with 109 (89.3%) patients presenting with microcalcifications on screening mammography. On biopsy, 82 (65.1%) patients were diagnosed with FEA with atypical hyperplasia, and 44 (34.9%) patients with pure FEA. Excision was performed in 100 patients, with 6 cases demonstrating ductal carcinoma in situ (DCIS), 3 cases demonstrating invasive ductal carcinoma (IDC), and 2 cases demonstrating invasive lobular carcinoma (ILC), yielding an overall upgrade rate to in-situ or invasive malignancy of 11.0%. The incidence of malignancy on excisional pathology did not differ significantly between the pure FEA (9.1%) and FEA with atypical hyperplasia groups (11.9%; p =0.67). Of those who opted for mammographic surveillance (n=22), no cancers were diagnosed at a median follow up of 3.2 years. Conclusion: FEA diagnosed on core needle biopsy was associated with malignancy on final pathology in 11.0% of cases. The incidence of in situ or invasive malignancy was not statistically different between pure FEA and FEA with atypical hyperplasia groups, suggesting that surgical excision may be warranted in all cases of biopsy-proven FEA until further studies are available to better predict factors associated with malignancy.

PT15

To Excise or Not to Excise: Can Methylated Markers Predict Upgrade of Benign Breast Papillomas? M. Rizzo,[1]* M. Fackler,[2] W. Teo,[2] S. Cho,[2] L. Cope,[2] E. Gabrielson,[2] M. Mosunjac,[1] D. Sgroi,[3] M. Sullivan,[4] E. Alonsozana,[5] S. Jeter,[2] A. Gerbasio,[5] D. Euhus,[2] S. Gabram,[1] N. Friedman,[5] S. Khan,[4] S. Sukumar.[2] *1. Department of Surgery, Division of Surgical Oncology, Emory University, Atlanta, GA; 2. Johns Hopkins, Baltimore, MD; 3. Dana Farber Cancer Institute, Boston, MA; 4. Lynn Sage Cancer Center, Northwestern University, Chicago, IL; 5. Mercy Medical Center, Baltimore, MD.*

Introduction: The clinical management of breast papillomas remains controversial. Although benign on core biopsy, nearly 25% upgraded to ADH or DCIS on surgical excision. Methylated genes showed potential to distinguish benign and malignant lesions in women with spontaneous nipple discharge. The objective of this study was to validate a methylated gene marker panel for detecting occult DCIS or invasive cancer in pathologically benign breast papillomas on core biopsy. Methods: Coded slides of breast core biopsy and subsequent surgical excision were collected in four major academic centers and analyzed independently by four pathologists. Two to four formalin fixed paraffin embedded sections of cases defined as papillomas on core that upgraded to DCIS and controls were analyzed. T-tests and receiver operator characteristic (ROC) analysis were performed to characterize the predictive power of the candidate markers. Results: 51 papillomas that were upgraded to DCIS on the surgical excision within 6 months from the core, and 118 controls were analyzed by quantitative, multiplexed methylation specific PCR (QM-MSP) on 12 genes frequently methylated in breast cancer. DNA methylation levels for all 12 genes were higher in core biopsy of cases that were upgraded to DCIS compared to controls of benign papilloma with no upgrade. RASSF1A achieved statistical significance (t-stat=2.61, p =0.012). A score of average DNA methylation for the 12 genes was significantly associated with upgrade to DCIS (t-stat=2.83, p =0.006). A total of six-gene RASSF1A, TWIST1, HIN1, CCND1, APC, RARB achieved statistically significant association as well. The 3-gene signature (RASSF1A, HIN1, and TWIST1) provided the best discrimination, with an area under the ROC curve of 0.62. Conclusions: Although DCIS was associated with increased DNA methylation levels compared to benign disease, these markers were not sufficiently informative to allow reliable discrimination of benign breast papilloma from those that were upgraded to DCIS. Therefore, at this time, surgical excision for all benign breast papilloma to identify possible ADH or DCIS is recommended.

PT16

Pre-treatment Neutrophil/Lymphocyte Ratio Predicts 5-Year Survival in Stage 1-3 Triple Negative Breast Cancer Patients B. Azab,* D. Yakoub, H. Stuart, A. Cioci, E. Avisar, F. Moffat, A.S. Livingstone, N. Merchant, D. Franceschi. *University of Miami, Miami, FL.*

Background: We have previously shown that pretreatment neutrophil lymphocyte ratio (NLR) is an independent predictor of survival among breast cancer patients. Recent studies have reported similar results in triple negative breast cancer (TNBC) patients. Axillary lymph node status also remains a valuable prognostic factor for breast cancer patients. The aim of this study was to determine the predictive value of NLR based on nodal status (pN) and chemotherapy status of women with TNBC. Methods: 125 TNBC patients who had breast surgery and blood counts obtained prior to surgery or neoadjuvant therapy were included. The 5-year overall and disease-free survival status (OS and DFS) were obtained. The previously reported NLR value of 2 was used to divide patients into high and low NLR groups. Results: Median follow-up time was 52 months (range 24 to 110 months). The 5 yr OS: low NLR - 84% vs high NLR – 67%, HR 2.8, CI 1.3-5.9, p<0.001; 5yr DFS: low NLR- 73% vs high NLR – 54, HR 2.3, CI 1.2-4.2, p<0.001). Cox regression multivariate analysis adjusting for age, T and N stages, radiotherapy and chemotherapy status, revealed that high NLR was an independent predictor for both 5-year OS (HR 5.5, CI 2.2-13.7, p<0.0001) and 5-year DFS (HR 5.2, CI 2.3-11.6, p<0.0001). Categorization of TNBC patients by NLR and pN status resulted in 4 groups of patients with distinctly different Kaplan-Meier survival curves (log rank p<0.0001, Figure 1A). Patients with high NLR receiving chemotherapy (neoadjuvant and/or adjuvant) showed statistically improved OS (p<0.0001) and DFS (p<0.001) compared to high NLR women not receiving chemotherapy. No statistical difference in OS (p=0.65) or DFS (p=0.07) survival was noted with or without chemotherapy in those with low NLR (Figure 1B). Conclusion: High pretreatment NLR is an independent predictor of poor OS and DFS amongst TNBC patients. Among TNBC patients, combining NLR and pN provides improved prognostic discrimination than either factor alone. Chemotherapy results in improved OS and DFS only in patients with high NLR but not in patients with low NLR. Larger prospective studies are needed to validate these findings.

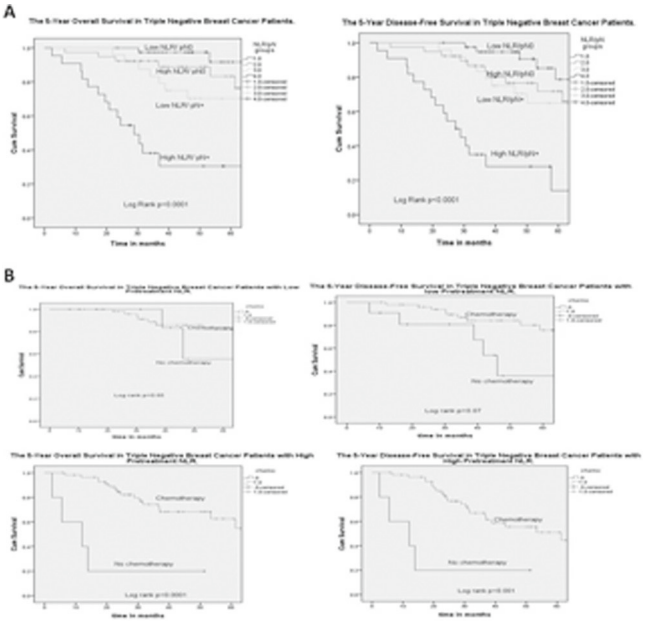


Figure 1A: The 5-year overall and disease-free survival statuses according to the pretreatment Neutrophil Lymphocyte Ratio (NLR) among pathological nodal negative (pN0) triple negative breast cancer patients.
Figure 1B: It illustrates the 5-year overall and disease-free survival statuses among the triple negative breast cancer patients according to their chemotherapy statuses in low and high Neutrophil Lymphocyte Ratio (NLR) subgroups.

PT17

Clinicopathologic Features and Models Predicting for High-risk 21-Gene Recurrence Score (RS) are Unreliable in Predicting Primary Tumor Downstaging with Neoadjuvant Chemotherapy (NACT) K. Park,* S. Choi, H. Ali, G. Divine, J. Bensenhaver, D. Nathanson, E. Proctor, L. Petersen, L. Newman. *General Surgery, Henry Ford Health System, Detroit, MI.*

10-25% of hormone receptor-positive (pos), HER2/neu-negative (neg), node-neg breast cancer patients (pts) will have a high-risk RS, indicating survival advantage associated with adjuvant chemotherapy. Samples for RS testing are typically selected from primary surgery specimens. Extent to which elevated RS or models predicting for an elevated score might identify pts that would benefit from NACT to downstage the primary tumor/improve lumpectomy eligibility is uncertain. Neoadjuvant endocrine therapy is limited in improving lumpectomy eligibility. Our goal was to determine whether clinicopathologic features and models predicting for high-risk RS could accurately identify pts that respond to NACT. We queried an IRB-approved, prospectively-maintained database to evaluate pts with hormone receptor-pos, HER2-neg breast cancer 2009-2016 that had primary surgery with RS testing or that received NACT without RS. Clinicopathologic features, including MIB1/Ki67 proliferative index and the web-based Magee scores were evaluated for accuracy in identifying (i) cases with high-risk RS (≥31) and (ii) cases with significant tumor downstaging from NACT likely to improve lumpectomy eligibility (defined as complete pathologic response or ≥1 centimeter decrease in primary tumor size). 302 primary surgery pts had RS; 21 (7%) had high-risk score. Univariate features associated with high-risk score were: high Ki67 and grade (p<0.001); lower ER/PR expression (p<0.001) and high Magee score (p<0.001). Among 38 NACT pts, 6 (15.8%) had complete pathologic response; 29 (76.3%) had significant tumor downstaging. None of the clinicopathologic

features associated with elevated RS were significantly associated with tumor downstaging (p-values 0.112 to 1.0) but younger pts were more likely to be downstaged (median age 49.1 vs. 58.6; p=0.03). Standard clinicopathology and existing models that predict for high-risk RS do not reliably predict for response to NACT and improved lumpectomy eligibility. Hormone receptor-pos, HER2-neg breast cancer pts should undergo primary surgery.

PT18

Patterns of Loco-Regional Relapse in Curatively Treated Locally Advanced Breast Cancer (LABC) Patients: A Single Centre Retrospective Study A. Jakhetiya,* S.S. Deo, N.k. Shukla, A. Gogia, D. sharma, D. Muduly, S. Mathur, V. Sreenivas. *Surgical oncology, All India Institute of Medical Sciences, Delhi, India.*

Introduction Locally advanced breast cancer (LABC) constitutes 40 to 60% of the breast cancer burden in low and middle income countries (LMIC) with gross disparity in results and poor survival outcomes. We undertook this study to identify clinical spectrum, treatment details and loco-regional relapse patterns in LABC patients treated with curative intent. Methods A retrospective analysis of prospectively maintained computerized breast cancer database at Dr BRA-IRCH, AIIMS, Delhi was performed. All consecutive LABC patients who underwent surgery from January 1995 to December 2012 were included for present analysis. The Combination of AJCC (2010) staging and clinicopathologic features were used for staging. All patients underwent standard protocol based trimodality (surgery, chemotherapy, radiotherapy) treatment including quality controlled surgery. Results A total of 2336 breast cancer patients underwent surgery. Out of these 1293 (55%) were LABC. Final stage distribution of IIIA, IIIB and IIIC were 20%, 52%, and 28% respectively. Luminal variants constituted 53%, HER2 positive 22% and TNBC 25%. Majority underwent mastectomy (94%) and a selective subset (6%) underwent breast conservation. Total of 90% received chemotherapy, 80% received adjuvant radiotherapy and 61.25% received adjuvant hormonal therapy. After a median follow-up of 28.63 months, a total of 456 (35.27%) patients had documented recurrence. Almost 80% of the recurrences occurred before 2.5 years of follow-up. The most common site of recurrence was systemic (75.66%), followed by regional (3.63%) patients and local (6.41%). Isolated local recurrence and regional recurrences were 2.08% and 0.54% respectively. The 5 year disease free and overall survival for the whole cohort of LABC was 54 % and 74.7% respectively. Conclusion LABC is heterogeneous disease spectrum with wide variation in clinical profile. Results of the present study show that LABC constitutes more than 50% of Indian breast cancer burden. Excellent loco-regional control can be achieved with good quality control surgery and protocol based multimodality treatment.

PT20

Barriers, Beliefs and Practice Patterns for Breast Reconstruction: A Provincial Survey C.J. Coroneos,[1] K.V. Roth-Albin,[2] A.S. Rai,[3] A.S. Rai,[4] S.H. Voineskos,[1] R. Avram,[1] M.C. Brouwers,[1] B. Heller.[1]* *1. Surgical Oncology, McMaster University, Hamilton, ON, Canada; 2. Cambridge Memorial Hospital, Cambridge, ON, Canada; 3. Wayne State University, Detroit, MI; 4. University of Toronto, Toronto, ON, Canada.*

Background: The purpose of this study was to characterize beliefs and practice patterns for breast cancer reconstruction among physicians who treat patients with breast cancer, in order to delineate current clinical practice. This survey was administered prior to Cancer Care Ontario (CCO) guideline publication. Method: Survey questions addressed four domains: survival, delayed or obscured recurrence detection, delayed adjuvant therapy, and aesthetics. The survey was administered to 1160 Ontario plastic and general surgeons and radiation and medical oncologists. Data were compared to published guidelines. Results: The overall response rate was 48%, with 57% of respondents treating breast cancer. Of those treating breast cancer, 75% are affiliated with an academic center. Immediate breast reconstruction (IBR) is not available to 28%. Autologous reconstruction is thought to interfere with recurrence detection by 23% (oncologists 30%, surgeons 19%, p=0.04). For patients not expected to require radiation therapy, IBR is not supported by 30%. Autologous IBR is believed to delay delivery of adjuvant chemotherapy by 45% (oncologists 55%, surgeons 41%, p=0.02). Up to 42% of respondents believe delays in adjuvant therapy delivery following IBR are due to insufficient health care resources (ie. coordinating an oncologic and reconstructive surgeon). Radiation therapy following reconstruction is believed to have negative aesthetic outcomes, and increase the need for revision surgery. Conclusions: This study is the first to analyze beliefs and practice patterns for breast reconstruction in Ontario. Findings are most noteworthy for speciality variation in IBR support, interference with recurrence detection, and adjuvant chemotherapy delay. These beliefs do not reflect CCO recommendations. Insufficient resource, specifically operative resource to coordinate oncologic and reconstructive surgeons, was identified by all groups surveyed as a barrier to IBR and timely adjuvant therapy.

PT21

Cancer Upgrade Rate Upon Excision of Isolated Flat Epithelial Atypia Found on Core Biopsy of Pure Microcalcifications A. Sevrukov,[1] T. Kaufman,[2] S. DeWyngaert,[1] T.B. Eisenberg,[1] E. Hsu,[1] N. Wasti,[1] A. Wilkes,[1] L. Zorn,[1] A. Berger,[1] M. Lazar,[1]* T. Tsangaris.[1] *1. Thomas Jefferson University, Philadelphia, PA; 2. Abington Jefferson Health, Philadelphia, PA.*

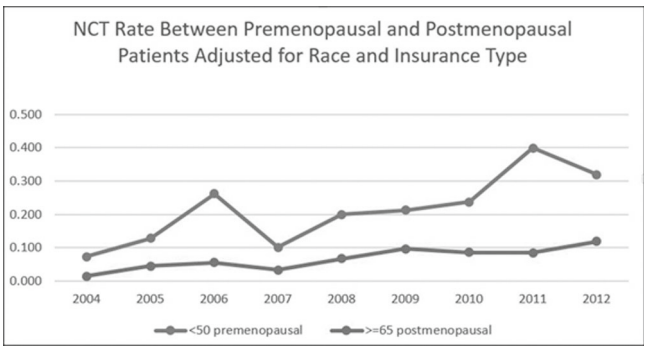
Flat epithelial atypia (FEA) is a relatively uncommon atypical lesion found on core biopsy of breast calcifications. Recent literature on surgical excision of isolated FEA found on large core biopsy of calcified and non calcified lesions reported upgrade rates to ductal carcinoma in situ (DCIS) or invasive cancer between 4 and 18%. However, reports on upgrade rates upon excision of isolated FEA associated with pure microcalcifications are few. We examined these rates in a cohort of women recalled from screening. 67 cases of isolated FEA were diagnosed between 2008 and 2015 on 8-10 gauge vacuum assisted stereotactic core biopsy performed for suspicious microcalcifications in asymptomatic women with no personal history of cancer or atypia. 49 women went on to have a wire-localization surgical excision of the biopsy site. 13 women elected mammographic surveillance with no evidence of cancer at follow up, range 1-6 years. 5 women were lost to follow up. Results 26/49 (53%) excisions showed no residual atypia or cancer. 20/49 (41%) showed some atypia and no cancer. Of these 20 cases, residual atypia was qualified as isolated FEA in 6 cases, ADH in 2 cases, and a mixture of FEA, ADH, lobular neoplasia, radial scar and papilloma in the remaining 12 cases. 3/49 (6%) cases were upgraded to cancer. In two of these cases, a focus of low-to-intermediate grade DCIS arose in a background of extensive multifocal atypia. One case showed intermediate-grade multifocal DCIS with a single focus of low grade invasive ductal carcinoma. Conclusion Isolated FEA on core biopsy of pure microcalcifications in our cohort carried a 6% risk of upgrade to cancer and a 41% risk of finding more and potentially higher-risk atypia on surgical excision. The 6% risk of upgrade to cancer is at the lower end of the published spectrum. However, it exceeds the accepted threshold of 2% for the probably benign category and makes imaging surveillance inappropriate for the management of FEA. Our data support surgical excision as appropriate management for isolated FEA on vacuum-assisted large core biopsy of microcalcifications.

PT22

Age Disparity Exists in the Use of Neoadjuvant Chemotherapy for Breast Cancer J. Carr,* C. Baggett, K.P. McGuire. *Surgery, UNC Hospitals, Chapel Hill, NC.*

Introduction: Neoadjuvant chemotherapy (NCT) is increasingly used for locally advanced and early stage breast cancer; often with younger patients experiencing greater response than older patients. However, most studies of NCT use populations that underrepresent younger patients. The aim of this study was to evaluate clinicopathologic differences in younger vs. older women receiving NCT and to determine the rate of NCT use in both cohorts. We hypothesized that younger women receive NCT more often and for lower stage tumors than older women. Methods: Using ICISS (Integrated Cancer Information and Surveillance System), we identified women undergoing NCT in North Carolina between 2004 and 2012, and compared yearly rates of NCT in the premenopausal ("PRE", <50) and postmenopausal ("POST", ≥65) populations. Using Poisson regression, adjusted annual rates of NCT use were calculated for PRE and POST groups. Comparisons between groups were made using chi-square. P-values of 0.05 or less were considered significant. Results: A total of 516 women, 284 PRE and 262 POST, were identified. The distribution of women diagnosed each year was equal. T stage at presentation was lower in PRE vs. POST (p = 0.002). Mastectomy after NCT was more common in PRE vs. POST women (70% vs. 61%, p = 0.022). Black race was more common in PRE vs. POST (29 vs. 21%, p = 0.030). N stage, tumor grade and hormone receptor status did not differ. While the rate of NCT receipt remains stable in the POST population, it has risen in the PRE group over the study period (Figure). Conclusion: NCT is more common among PRE women with early

stage tumors. Furthermore, the rate of use of NCT is increasing among PRE women but not among POST women. Despite this trend, mastectomy remains more common in the PRE population after NCT. These findings suggest that young women are receiving more aggressive treatment of their breast cancers than they previously received, and as compared to their older counterparts. Further study into this trend, as well as socioeconomic differences between the groups, is ongoing.



PT23

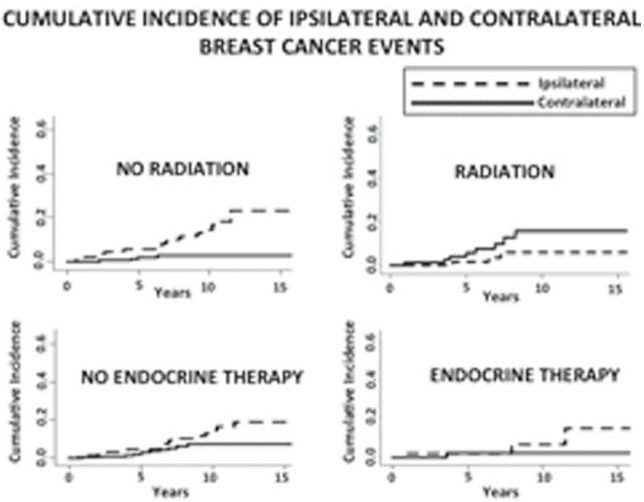
Predictors for Omission of Postmastectomy Radiotherapy After Neoadjuvant Chemotherapy in the United States J.L. Crawford,[1]* E.A. Handorf,[2] E.R. Sigurdson,[1] C.T. Murphy,[4] A. Aggon,[1] S.E. Weiss,[3] S.B. Hayes,[3] P.R. Anderson,[3] R.J. Bleicher.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Biostatistics, Fox Chase Cancer Center, Philadelphia, PA; 3. Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA; 4. Radiation Oncology, McGlinn Cancer Institute at Reading Hospital and Medical Center, West Reading, PA.*

Introduction: Studies demonstrate an overall survival (OS) benefit to post-mastectomy radiotherapy (PMRT) in the adjuvant chemotherapy setting but there is little data regarding PMRT in the neoadjuvant chemotherapy (NAC) setting. In this analysis of data from the National Cancer Database (NCDB), we evaluate predictors for omission of PMRT in women who received NAC and factors affecting OS. Methods: All women were diagnosed between 2003-2012 with clinical stage 2-3 unilateral invasive breast cancer, treated with NAC and mastectomy. Relationships between patient, facility, and tumor characteristics were compared using univariate chi-squared, tests for trend, and t-tests, and multivariate logistic regression. Multivariate proportional hazards regression determined the relationship between PMRT and OS. Results: Among 19,763 women reviewed, PMRT was omitted in 30.8%, with 30.8% of black and 30.8% of white patients not receiving it. Median age and tumor size in those receiving and not receiving PMRT was 51.0 and 51.4 years ($p<0.0001$), and 4.3 and 5.1 cm ($p<0.0001$), respectively. On multivariable analysis, significant factors associated with PMRT omission after NAC were older age, increasing Charlson-Deyo score, Medicare or Medicaid insurance, living farther from the treating facility, US region, diagnosis and treatment at the same facility, diagnosis year, ductal histology, ER/PR+ status, HER2/neu+ status, smaller clinical tumor size and nodal status, no change in tumor size and nodal status, and no receipt of endocrine therapy. US region had the widest odds ratio range (0.83-1.79). When accounting for all other factors to remove confounders, PMRT was associated with improved survival (HR=0.79, $P<0.001$). Conclusions: Approximately 1/3 of patients do not receive PMRT after NAC, although PMRT improves OS when accounting for other factors. No racial disparities were evident. With US region predicting PMRT omission so variably, there seems to be little consensus about its indications after NAC. The recent SSO/ASCO/ASTRO consensus guidelines serve as a starting point for needed refinement of its indications, along with upcoming results from clinical trials.

PT24

Outcomes of Women with Minimal Volume Ductal Carcinoma In Situ Completely Excised on Core Biopsy S. Muhsen,* A.V. Barrio, C. Olcese, S. Patil, M. Morrow, K.J. Van Zee. *Breast Surgical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Overdiagnosis of DCIS is a concern, especially in women with low volume screen-detected DCIS. We sought to evaluate outcomes in such patients. Methods: Using a prospectively maintained database of DCIS patients undergoing BCS from 1990–2011, women with minimal volume DCIS (mDCIS, defined as diagnosed by core biopsy and no residual DCIS on surgical excision) were identified. Local recurrence (LR) and contralateral breast cancer (CBC) risk were compared by competing-risk (CR) analysis. Kaplan–Meier (KM) estimates and log-rank tests were used to evaluate covariates. Results: 290 cases of mDCIS were identified; median age was 53yrs (range, 26-86). 80(28%) received radiation (RT) and 47(16%) received endocrine therapy (ET). Median follow-up was 6.8yrs. 25 had LR; 18(72%) were DCIS, 6(24%) invasive and 1(4%) unknown. Overall, 5- and 10-yr KM LR rates were 4.3% and 12%. 5- and 10-yr LR rates for those receiving neither adjuvant RT nor ET (n=178) were 5.7% and 15%, while 0 of 19 women that received both RT and ET had LR. Women receiving no RT trended towards higher LR, with 5- and 10-yr KM LR rates of 5.4% and 15%, compared to 1.6% and 6.5%, respectively, for those receiving RT ($p=.067$). Age, grade and ET were not significantly associated with LR ($p>0.3$). CBC occurred in 13 patients. Overall, 5- and 10-yr KM CBC rates were 2.5% and 6.4%. Among those not receiving RT, 5- and 10-yr CR LR rates (5.4% and 14%) were higher than CBC rates (1.8% and 2.7%). However, in patients receiving RT the 5- and 10-yr CR LR rates (1.5% and 6.0%) were lower than CBC rates (4.1% and 16%). Conclusions: Among patients with mDCIS, LR risk without RT was substantially higher than CBC risk, demonstrating that even DCIS of very low volume is associated with clinically relevant disease. Women with mDCIS receiving RT experienced lower risk of LR than CBC suggesting that RT effectively treated the excess ipsilateral risk associated with mDCIS. The finding that LR risk is greater than CBC risk supports current strategies treating DCIS as a precursor rather than a risk marker. Further work is necessary to identify mDCIS that is at negligible risk of LR in the absence of adjuvant therapy.



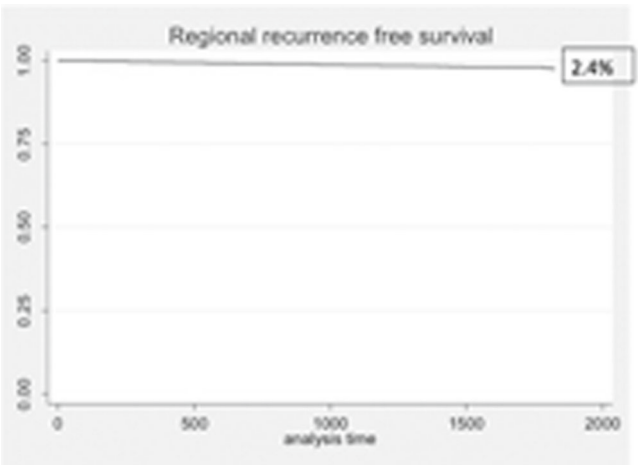
Cumulative Incidence of Ipsilateral and Contralateral Breast Cancer Events

PT25

Regional Recurrence in Breast Cancer Patients with a Negative Sentinel Node Procedure; The True False Negative Rate? M. Roos,[1]* K. Aalders,[1] I. Burgmans,[1] S. Siesling,[2] S. Elias,[3] T. van Dalen.[1] *1. Surgery, Diakonessenhuis Utrecht, Utrecht, Netherlands; 2. IKNL, Utrecht, Netherlands; 3. Julius Centrum UMC Utrecht, Utrecht, Netherlands.*

Introduction Although the false negative rate (FNR) of the sentinel lymph node biopsy (SLNB) is approximately 7%, reported regional recurrence rates after a negative SLNB are much lower. Additional adjuvant treatment modalities likely contribute to the discrepancy between the FNR of the SLNB and

the reported regional recurrence rates in breast cancer patients. We evaluate the 5-year risk of developing a regional recurrence after a negative SLNB in breast cancer patients who do not undergo radiotherapy and who are not treated with adjuvant systemic therapy. Methods All patients operated for primary unilateral invasive breast cancer from 2005-2008 were identified in the Netherlands Cancer Registry. We selected patients who underwent amputation of the breast and who had a tumour negative SLNB, who did not undergo axillary lymph node dissection, were not treated with radiotherapy and did not receive (neo-)adjuvant systemic therapy. The 5-year regional recurrence rate was estimated by Kaplan-Meier analysis. Possible influence of prognostic factors on the risk of development of a regional recurrence was analyzed univariately. Results 34.734 patients were surgically treated for primary breast cancer, of which 13.452 patients had a negative SLNB. We identified 2.012 sentinel node negative patients who underwent breast amputation without axillary lymph node dissection, and who did not receive radio- or adjuvant systemic therapy. The cumulative 5-year regional recurrence rate of this group was 2.4%, compared to a cumulative 5-year regional recurrence rate of the total group of 13.452 sentinel node negative patients of 1.3%. Univariate analysis showed no significant influence of patient- and tumor characteristics on development of a regional recurrence. Conclusion Elimination of the effect of radiotherapy and adjuvant systemic therapy in breast cancer patients with a negative SLNB treated with mastectomy resulted in a cumulative 5-year regional recurrence rate of 2.4%. This risk is 2 to 3 times lower than the risk that might be expected based on the percentage of false-negative lymph node procedures. More regional recurrences may develop over a longer period of time.



Five-year regional recurrence-free survival in 2012 sentinel-node negative patients treated without adjuvant radio- or systemic therapy

PT26

Concordance of Local Immunohistochemistry with TargetPrint Microarray Based Assessment of ER, PR and HER2 and BluePrint Molecular Subtyping in the Triple A Study A. Kuijer,[1] J. van Steenhoven,[1]* M. Straver,[1] S. Elias,[2] C. Smorenburg,[3] J. Wesseling,[3] S. Linn,[3] E. Rutgers,[3] S. Siesling,[4] T. van Dalen.[1]
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PURPOSE: A decade ago intrinsic biological breast cancer subtypes were identified which have proven to be of clinical importance. The aim of the current study is to assess concordance between subtypes determined by local immunohistochemistry (IHC) assessment of estrogen receptor (ER), progesterone receptor (PR) and Her2-receptor status and microarray based molecular subtyping in a subset of ER+ early stage breast cancer patients. METHODS: In this prospective observational study information on local pathology assessment and BluePrint/TargetPrint (BP/TP) results were obtained in ER+ early stage breast cancer patients in whom a 70-gene profile was used as there was controversy regarding the additional value of CT. Local assessment of ER, PR and Her2-status were compared with microarray based assessment (TP/BP) of these characteristics. Concordance was assessed by Kappa statistic. Furthermore, concordance between the clinical subtypes based on local pathology (Luminal-type: ER+/PR+ & Her2-; Her2-type: Her2+ disease) and molecular subtyping was assessed. RESULTS: Between October 1 2013 - December 31 2015 660 patients, treated in 31 hospitals, were enrolled and in 564 (85%) BP andTP was performed. The majority of patients had ER+/Her2- disease and TP reclassified 1% (n = 7) of patients as ER-negative. TP reclassified 7% (n = 40) and 2% (n = 11) of patients for PR and Her2 status respectively (table 1, kappa = 0.67 and 0.34, indicating substantial and fair agreement, respectively). Based on IHC 545 (98%) patients were regarded as luminal-type and the remaining 2% as Her2-type. BP reclassified 2% of the clinical luminal-type patients: 4 (1%) patients were reclassified as basal-type and 3 (0%) patients as Her2-type. Of the clinical Her2-type patients 80% (n=8) was reclassified by BP as molecular luminal-type. CONCLUSION: We observe high concordance between microarray-based assessment of ER, PR and Her2 and local pathology in Dutch ER+ early stage breast cancer patients. In the small subset of ER+ patients with HER2+ tumors by IHC molecular typing of HER2 status is of additional value.

Table 1. Concordance between ER, PR and Her2 assessment by immunohistochemistry and TargetPrint.

	TargetPrint Result (ER, PR and Her2, respectively)				
Immunohistochemistry	Positive	Negative	Overall discordance	Kappa (95% CI)	p-value
Estrogen Receptor Status					
Positive	557 (97%)	6 (1%)			
Negative	n.a.	n.a.	1%	n.a.	n.a.
Progesterone Receptor Status					
Positive	474 (96%)	18 (4%)			
Negative	22 (31%)	48 (69%)	7%	0.67 (0.57 - 0.73)	<0.001
Her2-Neu Status					
Positive	3 (30%)	7 (70%)			
Negative	4 (3%)	546 (97%)	2%	0.34 (-0.04 - 0.73)	<0.001
Equivocal	0 (0%)	3 (1%)			

PT27

A Comparison of SAVI SCOUT Radar to the Radioactive I125 Seed in the Localization of Non-palpable Breast Cancer L.M. Rico,* K.M. Raque, E. Yu, M. Truax, B. Carter, T. Frazier. *Surgery, Bryn Mawr Hospital, Philadelphia, PA.*

Background Radioactive seed localization (RSL) is an effective method for localizing non palpable breast lesions in breast conserving therapy (BCT). The logistical coordination required to implement the use of RSL in the hospital setting is difficult. The SAVI SCOUT radar technology removes the cumbersome logistics and allows for convenient localization of the tumor. This IRB approved study evaluates radar to determine its equivalence to RSL. Methods 119 patients with early stage breast cancer treated with BCT were retrospectively reviewed after having either RSL or radar localization. 2 surgeons participated in this study. All patients requiring localization were enrolled and had BCT. 59 agreed to radar and 60 patients had RSL. The tissue was oriented and assessed clinically and radiographically (Kubtec's XPERT 40) in the operating room. All specimens were evaluated to assure that the localization device was removed. RSL and radar were assessed with total volume resected (VR), margins, and return to the OR (RTO). Surgeon A who had more experience with RSL was also compared to surgeon B who was less familiar. Results 119 patients had successful removal of the marker. Average VR for RSL was 94.7cm3 vs 77.7cm3 with radar. p=0.141. P=86%. Within the RSL group 7 of 60 (12%) patients had RTO for re-excision secondary to 8 positive margins while in the radar group 8 of 59 (13.5%) patients had RTO due to 12 positive margins. Surgeon A had a 5.5% re-excision rate for both RSL and radar. Average VR for Surgeon A was 121cm3 with RSL and 97.2cm3 with radar. Surgeon B had a 20.8% re-excision rate with the RSL vs 26% with the radar. Average VR for Surgeon B was 55.2 cm3 with RSL and 47.3cm3 with radar. Conclusion The use of radar tumor localization was equivalent to RSL when comparing volume of resection and return to OR. Surgeon A and Surgeon B had similar VR and RTO regardless as to whether their patients had RSL or SSR. We conclude that SAVI SCOUT localization is an excellent alternative in breast cancer localization and can be safely implemented in most hospitals for BCT.

PT28

Risk for Second Primary Malignancies Among Breast Cancer Patients M. Yi,[1]* B. Smith,[2] E.A. Mittendorf,[1] D.M. Black,[1] L.H. McNeill,[3] T.B. Bevers,[4] K.K. Hunt.[1] *1. Department of Breast Surgical Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX; 2. Department of Radiation Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX; 3. Department of Health Disparities Research, University of Texas M.D. Anderson Cancer Center, Houston, TX; 4. Department of Clinical Cancer Prevention, University of Texas M.D. Anderson Cancer Center, Houston, TX.*

Background: Breast cancer survivors are at risk for developing a second primary breast cancer and other primary malignancies. Our purpose was to examine the incidence of second primary malignancies (SPM) in breast cancer patients in order to inform screening practices. Methods: A population-based cohort of female patients diagnosed with breast cancer as the first primary cancer between 1992 and 2013 was identified from Surveillance, Epidemiology, and End Results Program data (SEER 13 registries only). SEER*Stat MP-SIR session was used to calculate standardized incidence ratio (SIR) which was calculated on the basis of incidence in the general population. Results: Compared to the general population, breast cancer patients had a higher overall risk for SPM (SIR: 1.23). The risk increased significantly for cancers of the breast, uterus, ovary, thyroid, stomach, small intestine, lung and bronchus, and kidney and leukemia, while the risk was decreased for cancers of liver, cervix, brain and lymphoma. Patients with estrogen receptor (ER) positive or negative tumors had similar risks for most cancer sites except ER negative patients had a higher risk of ovary (SIR: 1.84) and lung and bronchus cancers (SIR: 1.18). Younger patients (<40 years old) had the highest overall risk for SPM (SIR: 6.10) while other age groups had lower SIRs (range from 1.11 to 2.43). Younger patients also had the highest risk of developing cancers of lung and bronchus (SIR: 5.15), ovary (SIR: 5.28), kidney (SIR: 4.71) and leukemia (SIR: 11.34). We found a similar age trend when we combined ER status and different age groups except younger patients with ER positive tumors had a higher risk of thyroid cancer (SIR: 2.78) while younger patients with ER negative tumors did not. Excess risks of SPM were low (< 6 per 10,000) for most cancer sites except breast cancer (highest 75.5 per 10,000 for younger patients with ER negative tumor). Conclusion: Our study shows that breast cancer patients have an increased risk of developing some SPMs over the general population. Given the overall low excess risks, screening practices for SPM should be based on routine cancer screening guidelines, family history and genetic information.

PT29

Surgical Management of Lobular Carcinoma In Situ: Analysis of the National Cancer Data Base L. Taylor,* J. Steiman, J.R. Schumacher, L. Wilke, C. Greenberg, H. Neuman. *Surgery, University of Wisconsin, Madison, WI.*

Background: Current guidelines for management of lobular carcinoma in situ (LCIS) recommend excisional biopsy for definitive diagnosis and counseling regarding risk-reduction strategies. Bilateral mastectomy can be used for risk reduction in certain circumstances, but there is no indication for unilateral mastectomy in the diagnosis or management of LCIS. However, prior studies suggest growing use of mastectomy. We sought to investigate national practice patterns and factors associated with surgical treatment of LCIS. Methods: We used the National Cancer Data Base to identify women diagnosed with LCIS from 2004 to 2013, excluding those with concurrent invasive cancer or ductal carcinoma in situ. We used descriptive statistics to describe the first course of surgical treatment and multivariable logistic regression to identify temporal, patient and facility-level factors associated with receipt of mastectomy. Results: We identified 30,979 women with LCIS; median age at diagnosis was 52 years (range 21-90). 5.4% received no surgery, 82.9% underwent excision alone, 1.5% received excision and radiation, and 9.1% underwent mastectomy. On adjusted analysis, young age ($p<0.001$), white race ($p<0.001$), having insurance ($p<0.001$), geographic region ($p<0.001$) and more recent year of diagnosis ($p=0.03$) were associated with receipt of mastectomy. Mastectomy rates within geographic regions ranged from a low of 5.4% in New England to 21.5% in the South. Of the 2,808 women treated with mastectomy, 44.3% received a unilateral as opposed to bilateral procedure. Conclusions: This population-based analysis demonstrates concerning overuse of mastectomy for initial management of LCIS with significant geographic variability. Family history of breast malignancy is not available in the database and therefore could not be accounted for in this analysis. However, the relatively high rate of unilateral mastectomy suggests that many of these procedures are not being performed for risk reduction. Our findings identify an opportunity to reduce unnecessary care through improved provider and patient education regarding optimal management of LCIS and clinical scenarios that warrant risk-reducing surgery.

PT30

Disparities in Compliance with the 21-Gene Reverse Transcription Polymerase Chain Reaction Assay for Breast Cancer in the United States: A National Cancer Data Base Assessment Z. Kozick,* A. Hashmi, J. Dove, M. Hunsinger, T. Arora, J. Wild, M. Shabahang, J. Blansfield. *Surgical Oncology, Geisinger Medical Center, Danville, PA.*

Background Oncotype DX (ODX) is a commercial multi-gene tumor assay for early-stage invasive breast cancer patients. To guide adjuvant treatment, ODX classifies patients as low, intermediate, or high recurrence risk. Our objective is to assess eligible ODX patients' compliance to (1) be tested and (2) follow recommendations for their respective risk. Methods We retrospectively analyzed compliance in patients eligible for ODX using the National Cancer Data Base from 2010-2012. Inclusion criteria was consistent with national guidelines to receive the test. Results A total of 158,235 patients met ODX eligibility criteria. Sixty-four percent of patients did not receive the test. Testing non-compliance rose with age (OR: 0.645 95% CI: 0.638-0.653). White patients were more likely to be tested (56%) versus black patients (46%, $p<0.0001$). Testing compliance was highest at academic facilities (40%) and lowest in community cancer programs (31%, $p<0.001$). Privately insured patients were more likely to get tested compared to uninsured (45 versus 34%, $p<0.0001$). The highest income quartile was also more likely to be tested ($p<0.001$). For low-risk patients, 5% did not comply with guidelines to omit chemotherapy. Median age was higher in the compliant group (59 versus 50 years old, $p<0.001$). Facility type again predicted compliance. Year of diagnosis, tumor grade and size were all predictors of compliance. Ten percent of high-risk patients were not compliant to receive chemotherapy. These patients showed worse compliance if they were older, had smaller tumors, and well-differentiated tumor grades. Forty-four percent of patients in the intermediate-risk group underwent chemotherapy. Younger age, poorly-differentiated tumor grade and larger size demonstrated higher odds of chemotherapy. In addition, as ODX score increased in this category there was a higher likelihood of undergoing chemotherapy. CONCLUSION ODX is under-utilized, with racial and socio-economic factors influencing testing compliance. Further studies are necessary to identify ways to remove these disparities and increase testing compliance.

PT31

Axillary Lymph Node Dissection After Sentinel Node Biopsy in Patients with Mastectomy and Pathological N1 Breast Cancer Y.B. Olimpiadi,[1]* D. Chung,[2] J. Gornbein,[2] H. Chang.[2] *1. Surgery, University of Southern California, Los Angeles, CA; 2. University of California Los Angeles, Los Angeles, CA.*

ABSTRACT Background. Until 2009, positive sentinel lymph node biopsy (SLNB) was followed by axillary lymph node dissection (ALND) for nodal staging in patients with breast cancer. In 2010, the American College of Surgeons Oncology Group Z0011 trial (ACOSOG) demonstrated that ALND did not affect recurrence and overall survival rates in the patients with T1 or T2 disease with up to two positive sentinel lymph nodes who underwent lumpectomy. Since then, the surgical practice has changed in patients with lumpectomy and N1 breast cancer found by SLNB. However, the effectiveness of post-mastectomy radiation in patients with SLNB detected N1 disease has not been clearly addressed. This study aimed to examine the role of post-mastectomy radiation in patients with SLNB-detected N1 metastasis in the California Cancer Registry. Materials and Methods. The study retrospectively analyzed 25,343 patients identified from the California Cancer Registry who had invasive non-metastatic breast cancer with N1 disease treated between 2002 and 2014. The patients were divided into four subgroups, based on the types of nodal surgery and the presence or absence of post-mastectomy radiation. Relapse-free survival (RFS) and overall survival (OS) were compared among the groups. Results. Our study demonstrated that the OS and RFS were significantly better in those who received radiation than those who did not in

both ALND (HR=0.68, p < 0.001) and SLNB (HR=0.67, p < 0.001) groups. There was no significant difference between SLNB and ALND without radiation (HR=1.08, p=0.1901) and in the two groups with radiation (HR=1.07, p=0.3241) after a median follow-up of 45 weeks (4 to 107 weeks). Conclusions. Post-mastectomy radiation without ALND appears to be effective in treating breast cancer patients who have N1 disease detected by SLNB. Considering that SLNB is less morbid, ALND may be spared in patients with mastectomy and limited nodal metastasis as long as they receive post-mastectomy radiation.

PT32

In Breast Tumor Recurrence (IBTR) After Intraoperative Radiation Therapy (IORT) D.K. DePeralta,* K. Reno, W. Sun, J. Zhou, R. Diaz, M. Lee. *Surgical Oncology, Moffitt Cancer Center, Boston, MA.*

Introduction: Adjuvant external beam radiotherapy (EBRT) following lumpectomy is a standard treatment for breast cancer but can be a hardship. IORT alone is an appealing alternative, eliminating many EBRT-associated barriers. In the TARGIT-A trial, 5-year IBTR was 3.3% compared with 1.3% for EBRT. We examined our IORT population with focus on IBTR and associated factors. Methods: An IRB-approved, single-institution retrospective chart review of patients receiving lumpectomy + IORT from 1/2011-2/2014 was conducted. IORT eligibility: age>60yrs, index invasive ductal cancer<3.1cm, ER+, clinically N_0. Demographics, clinical-pathological factors, operative data, adjuvant treatment, and follow-up data were collected to compare pts with IBTR vs. no IBTR. Statistical analysis was performed using Wilcoxon rank-sum and Fisher exact test. Results: During the study period, 114 post-menopausal women with breast cancer underwent lumpectomy with IORT; median age was 71yrs (range 51-88) with median tumor size 1.0cm (range 0.2-3.5). After median 40 months follow-up [range 2-66mos], 7/114 (6.3%) developed an IBTR with no distant recurrences. No difference was noted in clinical pathologic features, except that histologic grade of the biopsy favored low-intermediate grade in pts without IBTR (p=0.031) There was no difference on surgical specimen. Of 7pts with IBTR, 5 developed tumors in the index quadrant and 2 lesions were outside of the radiation field. While 95% of pts were candidates for hormonal therapy (Aromatase Inhibitor, AI), 5/7 (71.4%) endocrine eligible pts that developed IBTR declined AI versus 23/104 (22.1%) endocrine eligible pts without IBTR. Conclusion: IBTR occurred in 6.3% of pts treated with single-dose targeted IORT to the lumpectomy cavity after 3.5 years median follow-up. Pts that developed IBTR were less compliant with adjuvant aromatase inhibitor therapy. In women where adjuvant EBRT may not be desired or feasible, compliance with endocrine therapy is paramount.

	No IBTR (n=104)	IBTR (n-7)	P-value
Mean Age at Diagnosis (yrs)	70	72	0.1528
Median Tumor Size (cm)	1.0	0.7	0.3985
Final Margin Status Negative	92.5%	85.7%	0.4468
Median Oncotype RS	19	15.5	0.4335
Compliance with Aromatase Inhibitor	77.6%	28.6%	0.0113
Follow-Up Time (mos)	40	43	0.9313

PT33

Neoadjuvant Chemotherapy Increases Breast Conservation Rates and Decreases Extent of Axillary Surgery in Patients with Estrogen Receptor Positive Breast Cancer J. Lee,[1]* E.J. Diego,[1] A. Soran,[1] D. Farrugia,[2] A. Landmann,[3] M. Bonaventura,[1] R.R. Johnson,[1] P.F. McAuliffe,[1] G.M. Ahrendt.[1] *1. Surgical Oncology, Magee-Women's hospital of UPMC, Pittsburgh, PA; 2. Centegra Gavers Breast Center, Crystal Lake, IL; 3. Oklahoma University Health Sciences Center, Oklahoma City, OK.*

Introduction Response to neoadjuvant chemotherapy (NAC) differs based on breast cancer (BC) phenotype, with a low pathologic complete response (pCR) rate in patients (pts) with estrogen receptor positive, HER2-neu negative (ER+/HER2-) BC. However, a partial response can be seen in most ER+/HER2- BC after NAC. We hypothesize that in ER+/HER2- BC, NAC can decrease the extent of breast and axillary surgery required. Methods A retrospective review was performed on a prospectively maintained NAC database at a single institution from 2010-2015. Pts with ER+/HER2- BC were identified. Pt demographics, clinicopathologic information, surgical plans and outcomes pre- and post-NAC were collected. Results Of 651 pts treated with NAC, 153 had ER+/HER2- BC. Mean age was 51. 84 (55%) were pre-menopausal. 133 (87%) had invasive ductal carcinoma. At diagnosis, 144 (94%) had clinical stage II or III BC and 97 (63%) had a positive lymph node biopsy (LN+). 136 (89%) completed NAC, and most received doxorubicin, cyclophosphamide, and paclitaxel. 21 (14%) achieved pCR both in breast and axilla: 10 had ER H-score <100 and 15 had Ki-67 >50%. 78 (51%) achieved >50% tumor volume reduction (TVR). Only 15 (10%) pts were candidates for breast conservation therapy (BCT) pre-NAC based on tumor-to-breast ratio and/or due to multicentricity. 58 (38%) were BCT candidates post-NAC. Of these 58 pts, 52 had an attempt at BCT and 45 were successful, increasing the BCT rate from 10 to 29%. Of these 45 pts with successful BCT, 30 had >50% TVR with NAC. 34 of the 97 LN+ pts (35%) became clinically and radiographically node negative post-NAC, allowing for a sentinel lymph node biopsy (SLNB). Of these 34 pts, 13 had no residual axillary disease based on post-NAC SLNB and did not undergo axillary lymph node dissection, resulting in axillary downstaging of 13%. Conclusion In pts with ER+/HER2- BC, NAC reduces the extent of both breast and axillary surgery, even without pCR. These findings confirm that NAC should be considered in this group of pts, despite the low likelihood of pCR.

Table 1. Patient Demographics and Clinicopathologic Outcomes, N=153

Age, in Years	Mean (range)	51 (24-78)	
Menopausal Status	Post-menopausal	69	45%
	Pre-menopausal	84	55%
Histology	Invasive ductal carcinoma	133	87%
	Invasive lobular carcinoma	20	13%
Estrogen Receptor H Score	1-100	29	19%
	101-200	30	20%
	201-300	94	61%
Ki-67	1-50%	93	61%
	51-100%	53	35%
Pre-NAC Clinical AJCC Stage	I	9	6%
	II	84	55%
	III	60	39%
Pathologic Response (TVR%)	100%	21	14%
	51-99%	78	51%
	0-50%	45	29%
Breast Surgery			
	BCT candidate pre-NAC	15	10%
	BCT candidate post-NAC	58	38%
	BCT	45	29%
	TM	108	71%
Axillary Surgery		N=97	
	LN+ pre-NAC	97	100%
	LN+ downstage to LN- post-NAC	34	35%
pCR by Subgroup		N=21	
Estrogen Receptor H Score	1-100	10	48%
	101-200	3	14%
	201-300	8	38%
Ki-67	1-50%	6	29%
	51-100%	15	71%

NAC neoadjuvant chemotherapy, AJCC American Joint Committee on Cancer, TVR tumor volume reduction, pCR pathologic complete response, BCT breast conservation therapy, TM total mastectomy, LN+ positive lymph node biopsy, LN- negative lymph node biopsy

PT35

Mammographic Screening for Identification of Breast Cancer in Women Under 50: Low-risk is Not Protective T. Sutton,[2]* N. Johnson,[1] J.R. Garreau.[1] *1. Surgical Oncology, Legacy Good Samaritan Hospital, Portland, OR; 2. Oregon Health & Science University, Portland, OR.*

Introduction: In 2009, the US Preventive Services Task Force (USPSTF) changed the previously recommended age to begin routine annual screening mammography from 40 to 50 years of age for women who did not fall into a "high risk" category. Subsequently, the American Cancer Society (ACS) reviewed data and in 2015 issued guidelines suggesting that women should start screening mammograms at age 45 unless they were high risk. High risk patients were recommended to be screened annually beginning at age 40. The underlying assumption of these recommendations is that women who develop breast cancer under the age of 50 have identifiable risk factors. Our hypothesis is that most of these women don't actually have any risk factors and that current screening recommendations are flawed. Methods: We retrospectively reviewed data between January 2013-December 2015 for women <51 years diagnosed with breast cancer. Validated risk assessment models were used to define risk. If no score was assigned, then we entered patient data into the modified Gail

model to assign a risk score. Low risk was considered a lifetime risk <15% and high risk >20%. Results: 249 women were identified. Of these, 170 (68%) were classified as low risk. 79 (32%) women were classified as high risk. 66% of women classified as low risk had Stage I/II breast cancer compared to 73% in the high risk group. Refer to Table I for details. Conclusions: Current ACS screening recommendations state that women should not start screening mammograms until the age of 45 (50 for USPSTF) unless they are at high risk. In our population, only 32% of women diagnosed with breast cancer in this age group met high-risk criteria by validated risk assessment models. This suggests that using current recommendations, over 70% of women who will develop breast cancer in this age range would not be instructed to start screening. Counseling patients in this age range against screening with standard risk models leaves much to chance. Based on this review, we argue that women should be counseled to get annual screening mammograms starting at age 40 because being low risk by current measures is not protective.

Classification of patients based on risk, stage and prognostics

	Stage O	Stage I	Stage II	Stage III	Stage IV	ER+	Her-2/neu+	Total
Low risk	23% (39)	35% (60)	31% (53)	9% (15)	2% (4)	82% (139)	12% (20)	170
High risk	15% (12)	44% (35)	29% (23)	6% (5)	5% (4)	84% (66)	9% (7)	79
Total								249

Differences between the groups were not statistically significant, p>0.05

PT36

Model to Predict Node Negative Disease After Neoadjuvant Chemotherapy Using Data from the National Cancer Data Base

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Introduction Axillary staging after neoadjuvant chemotherapy (NAC) involves axillary dissection (ALND) or sentinel lymph node (SLN) surgery. We created a clinical prediction model using data from the National Cancer Database (NCDB) to identify patients (pts) likely to have ypN0 status, who would be good candidates for SLN surgery and may avoid ALND. Methods We identified pts in the NCDB from 1/2010-12/2012 with cT1-T4c breast cancer who received NAC. The effects of patient and tumor factors on pathologic node status was assessed by multivariable logistic regression. The model was developed using NCDB data and its performance evaluated in a cohort of NAC pts treated at our institution (1/2013-7/2016). Model discrimination was assessed by estimating the area under the curve (AUC). Results We identified 16,153 pts from the NCDB; 6659 (41%) cN0 and 9494 (59%) cN+. Biologic subtype was ER+/Her2- 42%, ER-/Her2- 32%, ER+/Her2+ 16%, and ER-/Her2+ 11%. At surgery 8508 (53%) pts were ypN0 (35% of cN+ pts and 78% of cN0 pts). The external validation sample included 374 pts, 194 (52%) cN0 and 180 (48%) cN+. Multivariable analysis [Table] showed biologic subtype as the strongest independent predictor of ypN0 status, with odds of 5.2 (cN0) and 5.3 (cN+) for ER-/Her2+ vs ER+/Her2- disease (p<0.001). Higher grade and IDC (vs ILC) were associated with higher likelihood of ypN0 status in both subgroups. Lower cT stage (cT1/T2 vs cT3/T4) was associated with increased odds of ypN0 in cN0 pts but not in cN+ pts. In cN+ pts, cN1 vs cN2/cN3 disease were more likely to be ypN0 (OR 1.5, p<0.001). Among cN0 pts, the multivariable model demonstrated good discrimination with AUC 0.73 (95% CI: 0.72-0.74) in NCDB and AUC 0.77 (95% CI: 0.68-0.85) in external validation. Similarly, the model for cN+ pts showed AUC 0.71 (95% CI: 0.70-0.72) in NCDB and AUC 0.74 (95% CI: 0.67-0.82) in external validation. Conclusion Our model using patient age, cT stage, cN stage, grade, biologic subtype, and histology showed good discrimination for predicting ypN0 status following NAC in cN0 and cN+ pts.

Multivariable models predicting ypN0 status following NAC in cN0 and cN+ pts

cN0			cN+		
Variable	Odds Ratio (95% Confidence Interval)	p-value	Variable	Odds Ratio (95% Confidence Interval)	p-value
Age			Age		
<40	1.0 (Reference)		<40	1.0 (Reference)	
40-49	0.79 (0.65-0.98)	0.03	40-49	0.94 (0.82-1.08)	0.38
50-59	0.82 (0.67-1.01)	0.06	50-59	0.79 (0.69-0.91)	<0.001
60-69	0.85 (0.68-1.06)	0.15	60-69	0.67 (0.57-0.78)	<0.001
≥70	0.82 (0.60-1.11)	0.20	≥70	0.54 (0.43-0.67)	<0.001
Clinical T stage			Clinical T stage		
cT1/cT2	1.72 (1.50-1.96)	<0.001	cT1/cT2	1.09 (1.0-1.20)	0.06
cT3/cT4	1.0 (Reference)		cT3/cT4	1.0 (Reference)	
Grade			Grade		
Well differentiated	1.0 (Reference)		Well differentiated	1.0 (Reference)	
Moderately differentiated	0.99 (0.80-1.24)	0.95	Moderately differentiated	1.50 (1.13-1.99)	0.005
Poorly differentiated	1.57 (1.25-1.98)	<0.001	Poorly differentiated	1.97 (1.48-2.61)	<0.001
Biologic subtype			Biologic subtype		
ER+/Her2-	1.0 (Reference)		ER+/Her2-	1.0 (Reference)	
ER+/Her2+	2.42 (2.02-2.91)	<0.001	ER+/Her2+	3.12 (2.74-3.56)	<0.001
ER-/Her2+	5.18 (3.88-6.93)	<0.001	ER-/Her2+	5.31 (4.58-6.14)	<0.001
ER-/Her2-	3.85 (3.25-4.56)	<0.001	ER-/Her2-	3.01 (2.67-3.39)	<0.001
Histology			Histology		
IDC	1.0 (Reference)		IDC	1.0 (Reference)	
ILC	0.77 (0.61-0.96)	0.02	ILC	0.51 (0.38-0.68)	<0.001
IMC	0.78 (0.58-1.05)	0.10	IMC	0.71 (0.54-0.94)	0.02
Other	1.68 (0.93-3.05)	0.09	Other	0.81 (0.59-1.11)	0.20
			Clinical N stage		
			cN1	1.51 (1.35-1.68)	<0.001
			cN2/cN3	1.0 (Reference)	

PT37

Cosmetic Outcome Determines Quality of Life After Breast Conserving Therapy

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Introduction Secondary outcomes, including cosmetic outcome and quality of life (QoL) are becoming increasingly important in the treatment of breast cancer. Most studies analyzing the effects of cosmetic outcome on QoL are retrospective without baseline measurements and are not taking into account important factors other than cosmetic outcome influencing QoL. We aim to report the longitudinal analysis of QoL and cosmetic outcome after breast conserving therapy (BCT) and to describe the relationship between QoL and cosmetic outcome, measured both subjectively and objectively. Methods 128 patients with early stage invasive breast cancer who underwent BCT were included as part of a prospective randomized controlled trial. Qol was measured using the EORTC QLQ-C30 and QLQ-BR23 at baseline, 3, 6, 12 and 36 months postoperatively and digital photographs of the breasts were taken. Cosmetic outcome was determined by patient self-evaluation, panel-evaluation and BCCT.core software. Results After 6 months all QoL subscales decreased compared to baseline except for emotional functioning and sexual enjoyment. All returned back to baseline or improved after 36 months except for physical functioning and arm symptoms. Cosmetic outcome was significantly worse after 36 months compared to 3 and 6 months for panel and BCCT. core evaluation. No difference in cosmetic outcome after 12 and 36 months were seen for all three evaluation methods. After adjustment for patient and tumour-characteristics, a significant worse Qol for fair/poor cosmetic outcome compared to good/excellent outcome after patient self-evaluation was seen in the subscales pain, arm symptoms, breast symptoms, body image and sexual enjoyment. This negative correlation was also seen for panel-evaluation in the subscales pain, arm symptoms, breast symptoms and body image. Objectively measured cosmetic outcome showed no correlation with QoL. Conclusion. During pre- and postoperative counseling physicians must be aware of the decreasing cosmetic outcome and QoL during the first year and the recovery of most QoL factors after 3 years. Subjectively measured poor cosmetic outcome after BCT is a time-independent factor which negatively influences QoL.

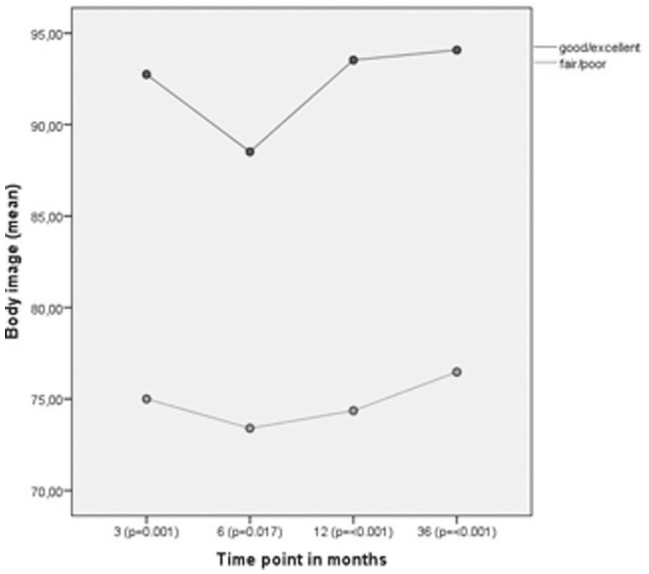


Figure 1 shows the mean outcome of QoL subscale Body-image in time for good/excellent and fair/poor cosmetic outcome. P-values represent the difference QoL between good/excellent versus fair/poor cosmetic outcome at the given time point.

PT38

Extracapsular Extension of Sentinel Lymph Node: A Marker of Poor Prognosis in cT1-2N0 Breast Cancer Patients? M. Vane,[1]* M. Willemsen,[1] L. van Roozendaal,[2] S. van Kuijk,[1] L. Kooreman,[1] S. Siesling,[3] S. Engelen,[1] H. de Wilt,[4] M. Smidt.[1] *1. Maastricht University Medical Center +, Maastricht, Netherlands; 2. Zuyderland Medical Center, Heerlen, Netherlands; 3. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands; 4. Radboud University Medical Centre, Nijmegen, Netherlands.*

Introduction: The ACOSOG Z0011 trial investigated the safety of omitting axillary lymph node dissection (ALND) in cT1-2N0 breast cancer patients treated with breast conserving therapy (BCT) with 1-2 positive sentinel lymph nodes (SLNs). The BOOG 2013-07 trial investigates whether omission of ALND can be extrapolated to mastectomy patients. In contrast to the Z0011, the BOOG 2013-07 trial includes patients irrespective of the presence of extracapuslar extension (ECE). This study aims to evaluate whether ECE presence in an SLN is associated with nodal tumor burden and its prognostic impact. Methods: All new cT1-2N0 breast cancer patients (BCT and mastectomy) with 1-3 positive SLN(s) who underwent ALND between 2005-2008 were selected from the Netherlands Cancer Registry and Dutch Pathology Registry. Logistic regression analysis was performed to determine the effect of ECE on ≥4 additional lymph nodes. 5-year disease-free survival (DFS) and 10-year overall survival (OS) were computed using Kaplan-Meier survival analysis. Multivariable cox regression analysis was performed to estimate the effect of ECE on survival corrected for other prognostic factors. Results: In total, 3,174 patients were included. Information on ECE was available for 1,884 (59.4%) patients and was present in 654 (34.7%) and absent in 1,230 patients (65.3%). The incidence of ≥4 additional lymph nodes was 104 (15.9%) in the ECE group versus 75 (6.1%) in the group without ECE (p<0.001). Presence of ECE was a predictor of ≥ 4 additional lymph nodes in the ALND (OR 2.6, 95%CI 1.7 - 3.9, p <0.001). 5-year DFS rate was 86.1% in the group with ECE compared to 88.8% in the group without ECE (p=0.08). 10-year OS rate was 83.1% and 79.4% respectively (p=0.041). Multivariable cox-regression analysis showed that ECE is not an independent prognostic factor for both DFS and OS. Conclusions: Presence of ECE was significantly associated with ≥ 4 additional lymph nodes in the ALND. Despite the increased nodal tumor burden, ECE was not an independent prognostic factor for DFS and OS. Therefore it seems justified to include BOOG 2013-07 patients with 1-3 positive SLNs, irrespectively of the presence of ECE.

PT39

The Oncologic Safety and Cosmetic Success of Nipple-Sparing Mastectomy After Neoadjuvant Chemotherapy P. Jadeja,[1]* C. Chin,[1] B. Cantanese,[2] A. Saraf,[2] K. Kalinsky,[1] R. Ha,[1] E. Connolly,[1] M. Chen-Seetoo,[1] S. Feldman,[1] B. Taback.[1] *1. Breast Surgery, Columbia University Medical Center, New York, NY; 2. New York Medical College, Valhalla, NY.*

Background: Nipple-sparing mastectomy (NSM) provides breast cancer patients an opportunity at the best aesthetic outcome. Initially reserved for prophylaxis and small primary tumors, patients with more advanced disease were not offered this surgical option. With the greater utility of neoadjuvant chemotherapy (NAC), patients may become significantly downstaged and be eligible for NSM. We evaluated the outcomes of NSM in high-risk patients treated with NSM after NAC. Methods: A retrospective review of our neoadjuvant database from January 1, 2000 to January 1, 2016 identified 347 patients, of which 31 patients underwent 52 NSM. In this IRB approved study, we evaluated the frequency of flap necrosis, nipple loss, implant loss, pathologic complete response, margin status, tumor type, size, nodal status, molecular subtype, and recurrence. Results: The mean age was 46 years (22-70 years). Pathologically, 96.7% were invasive ductal and 3.3% (n=1) mixed ductal/lobular. Triple negative breast cancer compromised 19.4% (n=6) of the cohort. The mean initial clinical tumor size was 3.5cm (1.3-6.9 cm); the mean final pathologic size was 1.0 cm (0 – 5.5cm), with mean decrease in size of 2.5cm. Of the 31 patients, 54.8% (n=17) of patients were clinically node positive prior to NAC; 41.9% (n=13) were node positive on final pathology. Margins were negative in 93.5% of patients. Of the 31 patients, 29% (n=9) achieved complete pathologic response in the breast and 58% (n=18) a complete pathologic response in the nodes. Fifty-two percent underwent post-mastectomy radiation therapy. The incidence of flap ischemia and/or epidermolysis was 13% (n=4), nipple loss, 10% (n=3), and implant loss 6.4% (n=2). At a median follow-up of 2.1 years (2.5-27 months), there was 1 local skin recurrence and 2 systemic recurrences. Conclusions: In this cohort of high-risk, locally advanced patients, NSM can be performed safely with minimal cosmetic morbidity and excellent local control. Flap ischemia, nipple loss, and implant loss occur in similar rates as low-risk patients undergoing NSM in published studies.

PT40

Trends in Chemotherapy Administration in Breast Cancer Patients with an Intermediate OncotypeDX Recurrence Score: An NCDB Analysis K. Govert,* A. Voci, K.K. Walsh, D. Boselli, L. Hadzikadic-Gusic, T. Sarantou, M. Forster, D. Sarma, R.L. White. *Surgical Oncology, Carolinas Medical Center- Levine Cancer Institute, Charlotte, NC.*

Introduction: The utility of adjuvant chemotherapy in addition to hormonal therapy in patients with an intermediate OncotypeDX (OncoDX) recurrence score (RS) remains under investigation. We examined trends in chemotherapy administration in breast cancer patients with an intermediate RS. Methods: The NCDB was used to query women ages 18 and over from 2004-2013 with primary breast cancer Stages 0-III who had an intermediate OncoDX RS (18-30). Patient demographics, socioeconomic factors, and treatment data were collected. Chi-squared test and multivariate analysis were used for statistical assessment. Results: 25369 patients were identified as stage 0-III primary breast cancer patients with an intermediate OncoDX RS. The median age at diagnosis was 58 [18-90+]; the majority were white (87.0%), Charleson-Deyo score of 0 (86.0%), pathologic T1 (72.6%), pathologic N0 (82.3%), positive ER (99.5%) and PR (86.5%), non-amplified HER2 (93.9%), and underwent partial mastectomy (70.6%). 10515 (41.5%) patients received chemotherapy. 14854 (58.6%) did not receive chemotherapy. Adjuvant chemotherapy was either received or recommended in 14042 (55%). Patients with Medicaid (OR:0.878 95% CI [0.778, 0.989], p=0.0329) or Medicare (OR:0.824 95% CI [0.759, 0.894], p<0.0001) were less likely to receive chemotherapy than patients with private insurance (Table). The odds of chemotherapy administration decreased with year of diagnosis (OR:0.947 95% CI [0.924, 0.969], p<0.0001). Facility characteristics associated with increased odds of chemotherapy administration were increased with hospital case volume (OR:1.028 95% CI [1.018, 1.039], p<0.0001) and treatment in a community versus academic facility (OR:1.200 95% CI [1.075, 1.338], p=0.0011). Conclusion: This study showed that 55% received a recommendation for chemotherapy and 41.5% of breast cancer patients with an intermediate OncoDX RS received chemotherapy. Factors predicting chemotherapy administration in the intermediate RS cohort include

younger age, private insurance, higher hospital case volume, and treatment at a community facility.

Multivariate Logistic Regression Analysis Predicting Chemotherapy Administration (n=25369)

	OR	LB 95% CI	UB 95% CI	p
Age at diagnosis	0.945	0.942	0.948	<0001
Year of diagnosis	0.947	0.924	0.969	<0001
Insurance status (Private Insurance ref.)				
Medicaid	0.878	0.778	0.989	0.0329
Medicare	0.824	0.759	0.894	<0001
Not Insured	0.966	0.782	1.193	0.7467
Other Government	1.051	0.802	1.376	0.72
Facility Type (Academic ref.)				
Community	1.2	1.075	1.338	0.0011
Comprehensive Community	1.016	0.953	1.084	0.6222
Integrated Network	0.935	0.836	1.045	0.2367
Other	1.361	0.85	2.179	0.2001
TNM Pathologic T (T4 ref.)				
0/IS	0.519	0.176	1.529	0.234
1	0.262	0.123	0.558	0.0005
2	0.462	0.217	0.986	0.0457
3	0.563	0.254	1.248	0.1572
TNM Pathologic N (N3 ref.)				
0	0.101	0.041	0.249	<0001
1	0.228	0.093	0.559	0.0012
2	0.815	0.293	2.268	0.6959
ER Status (Positive ref.)				
Negative	1.68	1.104	2.556	0.0154
PR Status (Positive ref.)				
Negative	1.393	1.283	1.511	<0001
Borderline	1.669	0.783	3.557	0.1849
HER2/NEU Status (Non-amplified ref.)				
Borderline/equivocal	1.346	1.106	1.638	0.0031
Amplified	2.356	1.963	2.828	<0001

PT41

Influence of Age on the Presentation, Management and Clinical Outcome of Male Breast Cancer P.A. Cronin,[1]* A.M. Romanoff,[1] M. Stempel,[1] A. Eaton,[2] E. Zabor,[2] L. Smyth,[3] A. Ho,[4] M. Morrow,[1] M. El-Tamer,[1] M. Gemignani.[1] *1. Breast Service, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Biostatistics Service, Memorial Sloan Kettering Cancer Center, New York, NY; 3. Breast Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; 4. Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Male breast cancer (MBC) constitutes <1% of breast cancers. Management is based on the clinical care guidelines of female breast cancer but MBC is under-represented in breast cancer trials. This study evaluates the impact of age on the presentation, management and outcomes of MBC. Methods A database of MBC was retrospectively reviewed from 2000-11. Patients were stratified by age ≤65 and >65. Clinicopathological findings were compared by age using Fisher's exact test. Kaplan-Meier methods were used to compare overall (OS) and breast cancer specific survival (BCSS). Results 152 MBC [128 (84%) invasive breast cancer (IBC) and 24 (16%) ductal carcinoma in situ] were identified. Median age was 64 (range 20-96) and 95% (n=144) presented with a mass or nipple discharge. 75 (49%) had a family history of breast cancer and 48 (31%) had genetic testing. There was 1 BRCA1 and 10 BRCA2 mutations. The median body mass index (BMI) was 28 (range 19-49) and 47% (n=71) had gynecomastia. Patients were stratified by age ≤65 (n=78;51%) versus >65 (n=74;49%). There were no differences in mode of presentation (p=.7), family history (p=.4), gynecomastia (p=.3), proportion of IBC (p=.5) or type of breast/axillary surgery. Patients ≤65 were significantly more overweight compared to those >65 (89% vs 74% overweight/obese, respectively, p=.008). With IBC, median tumor size was 18mm (range 0.4 – 53) and 125 (98%) were ER positive. 7 patients overexpressed Her2. On subset analysis by age there were no differences in nodal metastases (p=.4), ER positivity (p=1) or Her2 overexpression (p=.6). Patients ≤65 were more likely to receive chemotherapy than those >65 (p=.002), but no difference in endocrine therapy (p=.8) or radiation (p=.8) by age group. Median follow-up was 5.8 years (range 0.1-14.4). 5-year OS was 86% (95% confidence interval (CI): 80-93%) whereas 5 year BCSS was 95% (95% CI: 91-99%). OS was significantly better in patients ≤65 (p=.003) but there was no difference in BCSS (p=.833). Conclusions Men ≤65 with MBC were significantly more overweight than their older counterparts but had significantly better OS. The interplay between obesity, age and MBC risk should be further elucidated.

Breast and axillary surgery, overall and by age

Age	Overall, % (n)	≤65, % (n)	>65, % (n)	p
Breast Surgery				0.5
Mastectomy	94.7 (144)	96.2 (75)	93.2 (69)	
Lumpectomy	5.3 (8)	3.8 (3)	6.8 (5)	
Axillary Surgery				1
SLNB alone	53.3 (81)	52.6 (41)	54.1 (40)	
SLNB and ALND	34.9 (53)	35.9 (28)	33.8 (25)	
ALND alone	4.6 (7)	5.1 (4)	4.1 (3)	
No axillary surgery	7.2 (11)	6.4 (5)	8.1 (6)	

SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection

PT42

Novel Prognostic Biomarker Using MicroRNA Signature of Breast Cancer T. KAWAGUCHI,* L. Yan, Q. Qi, S. Liu, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: MicroRNAs (miRNAs) are small non-coding RNAs that exert its functions by regulating expression of their target genes. Dysregulations of miRNAs are related with breast cancer. We hypothesized that the survival of breast cancer can be predicted by representing miRNAs. Methods: Both clinical and miRNA-seq data in The Cancer Genome Atlas (TCGA) dataset were retrieved from the GDC data portal for analyses, and were evaluate by hierarchical clustering based on bioinformatics analysis. We also evaluate clinical relevance including prognostic analysis based on the novel subclasses using the Cox proportional hazard model. Results: Of 1097 cases in TCGA dataset, 1052 cases were used for miRNA expression and survival analysis. We divided the cases into "short" (died within 3 years after diagnosis), "long" (lived longer than 5 years), and the others. We identified that 15 miRNAs were significantly differently expressed between the long and short group. With the expression pattern of these 15 miRNA, the patients were classified into three clusters. Of the 15 miRNAs, we conducted additional feature selection in a multivariate Cox proportional hazard model, and three significant miRNAs remain after model selection (miR-19a located on miR-17-92 cluster; miR-106a on miR-106a-363 cluster; miR-93 on miR-106b-25 cluster). We generated a risk scoring model with the expression of the three miRNAs based on Cox proportional hazard model. We found that the patients with the high score significantly associated with poor outcome, particularly among luminal type breast cancer patients. Moreover, these three significant miRNAs are validated using the other two independent cohorts derived from Gene Expression Omnibus (GEO) datasets. Conclusions: We demonstrated that novel microRNA signature can predict worse survival of breast cancer.

PT43

Benefit of Screening Mammograms for Women Under 45 Years of Age S.P. Cate, A. Bar-Mashiah, V.L. Prowler,* T. Fulop, M. Chadha, S.K. Boolbol. *Surgery, Mount Sinai Beth Israel, New York, NY.*

Introduction: Breast cancer is one of the leading causes of death among women in the United States. There are conflicting guidelines regarding what age to start screening mammograms. The American Cancer Society's (ACS) guidelines for screening women ages 40-44 state that patients in this age group "should have the choice to start annual breast cancer screening with mammograms if they wish to do so." In this study, we sought to determine how many women aged 44 and younger were diagnosed with breast cancer via palpation versus screening mammography at our institution. Methods: In this IRB-approved study, a retrospective chart review was conducted using our breast cancer database. We reviewed 343 patients from 2005-2015. Eighty patients were excluded from our data set due to incomplete medical records resulting in an N of 263. Chi square was used for statistical analysis. Results: One-hundred forty women discovered their cancer via palpation, and 123 were diagnosed via screening. The mean age at diagnosis was 38.7 years old, with 41 patients HER2 positive, 204 patients ER positive, and 30 patients triple negative. Of the women who were diagnosed with breast cancer via screening, 99 (37.5%) patients were stage 0 and 1, versus 54 (20.5%) patients who presented with palpable findings. Sixty-three women (24%) were diagnosed with palpable findings were stage 2, while 17 (6.4%) women diagnosed via screening were stage 2. Of women who were diagnosed with breast cancer

via palpable findings, 23 (8.7%) patients were stage 3 or 4, versus 7 (2.6%) patients who were diagnosed via screening. Conclusion: Women less than 44 years of age diagnosed with pathological stage 0 and 1 breast cancer were more likely to have discovered their malignancy from screening mammogram while stage 3 and 4 cancers were more commonly found via palpation (p<0.001). These findings suggest that women should start screening for breast cancer starting at the age of 40.

Cancer Diagnosis by Method of Detection and Stage

	Palpation	Screening Mammogram
Stage 0-1	54	99
Stage 2	63	17
Stage 3-4	23	7
Total	140	123

P <0.001

PF44

Identifying a Low-risk Group for Residual Disease in Patients with Ductal Carcinoma In Situ B.L. Murphy,* A. Gonzalez, A.L. Conners, T.L. Henrichsen, M.G. Keeney, B. Chen, T.T. Nguyen, H.N. Shah, W. Harmsen, E.B. Habermann, J.W. Jakub. *Mayo Clinic, Rochester, MN.*

Introduction Patients with ductal carcinoma in situ (DCIS) have an excellent overall prognosis. Current randomized controlled trials are investigating the success of non-surgical treatment for select patients with DCIS. We sought to evaluate patient and tumor factors associated with finding no residual disease on final pathology after having a core needle biopsy (CNB) diagnosis of DCIS. Methods After IRB approval, a total of 827 patients with DCIS on CNB underwent 834 operations at our institution between 1/2004-10/2014. We evaluated method of detection and tumor characteristics on CNB to determine the factors associated with finding no residual disease on final pathology after surgical resection of the DCIS lesion using univariate and multivariable analyses. Results Sixty-nine patients (8%) had no residual disease on final pathology. On univariate analysis, patients with a small linear dimension on mammography, no mass lesion seen on imaging, biopsy performed by a technique other than ultrasound, single focus of disease, large gauge CNB (7-12), ≥ 90% of the calcifications removed by CNB, low grade disease, ER positive disease, and no comedonecrosis on biopsy had statistically significant greater likelihoods of finding no residual disease on final pathology. On multivariable analysis, intermediate or low grade lesions, lesions < 1 cm in size on preoperative mammography, and lesions where ≥ 90% of calcifications were removed correlated with finding no residual disease on final pathology, c-statistic 0.84. Of the 14 patients with all 3 low risk factors, only 36% had no residual disease on final pathology (Table). Conclusion Although our multivariable analysis performed well, its clinical utility would be limited as we were unable to identify a subset of patients with DCIS in whom the probability of finding no residual disease is great enough to consider routine use of non-surgical management.

Predicted Probabilities of Factors Associated with No Residual Disease after having a Core Needle Biopsy of Ductal Carcinoma in Situ

Biopsy Grade	Mammography Size	% Lesion Removed	Predicted Probability of No Residual Disease	Total # Patients	# (%) of Patients with No Residual Disease
Intermediate	≥1cm	<50	1.4	85	0 (0.0%)
Intermediate	≥1cm	50-89	4.2	40	0 (0.0%)
High	≥1cm	≥90	4.4	32	0 (0.0%)
Low	≥1cm	<50	2.4	24	0 (0.0%)
High	≥1cm	No Calcifications	1.3	14	0 (0.0%)
High	<1cm	50-89	6.9	14	0 (0.0%)
High	<1cm	<50	2.4	10	0 (0.0%)
Low	<1cm	<50	9.1	5	0 (0.0%)
High	≥1cm	<50	0.6	149	1 (0.7%)
High	≥1cm	50-89	1.8	67	1 (1.5%)
Intermediate	≥1cm	No Calcifications	3.1	18	1 (5.6%)
Low	≥1cm	No Calcifications	5.1	12	1 (8.3%)
Intermediate	<1cm	No Calcifications	11.7	9	1 (11.1%)
Low	<1cm	No Calcifications	18.3	23	3 (13.0%)
Low	≥1cm	50-89	6.8	7	1 (14.3%)
High	<1cm	No Calcifications	5.2	7	1 (14.3%)
Intermediate	≥1cm	≥90	10.1	21	4 (19.0%)
High	<1cm	≥90	16.2	48	10 (20.8%)
Intermediate	<1cm	<50	5.6	12	3 (25.0%)
Intermediate	<1cm	≥90	31.8	58	15 (25.9%)
Intermediate	<1cm	50-89	15.3	15	4 (26.7%)
Low	<1cm	50-89	23.3	6	2 (33.3%)
Low	<1cm	≥90	44	14	5 (35.7%)
Low	≥1cm	≥90	15.9	7	3 (42.9%)

PF45

Does the Utility of Preoperative MRI for IORT Patient Selection Depend on Which Consensus Guideline is Used? R. Ha,[1] N. Consul,[2] P. Jadeja,[1]* E. Kwak,[1] S. Patel,[1] C. Chin,[1] E. Connolly,[1] R. Wynn,[1] S. Feldman.[1] *1. Breast Surgery, Columbia University Medical Center, New York, NY; 2. Columbia University College of Physicians & Surgeons, New York, NY.*

Background: Consensus statements from the ASTRO, ESTRO, ASBS, and ABS each recommend different guidelines for IORT patient selection. The goal of this study is to determine whether the utility of pre-operative MRI varies with the usage of these four guidelines. Methods: An IRB-approved retrospective review from 1/1/12 to 12/31/15 identified 887 breast cancer patients. Of 887 patients, 327 who underwent preoperative MRI were included in this study. The frequency of MRI-detected, mammographically-occult, biopsy-proven multifocal disease or multicentric disease (MFD/MCD) was recorded in 327 patients. Then, the frequency of MFD/MCD was recorded for patients selected by criteria under the four IORT guidelines. Logistic regression analysis was performed to determine which exclusion factors (age, ER, grade, size, N stage) had predictive potential for MFD/MCD. Results: Among all 327 patients who underwent preoperative MRI, 18% patients met criteria based on ASTRO, 43.1% by ESTRO, 45.9% by ABS, and 53.2% by ASBS. Of the 327 patients, 17.7% patients had MFD/MCD, and under the four IORT guidelines, MFD/MCD frequency was: ASTRO (6.8%), ESTRO (7.1%), ABS (6.7%) and ASBS (6.3%). Compared to the non-selected group (17.7%), the reductions in the frequency of MFD/MCD in these four selected groups were all significant (p<0.05). The four IORT selected groups were not significantly different from each other (p>0.05). By logistic regression analysis, only axillary lymph node positivity significantly predicted the presence of MFD/MCD (OR 56.5, p<0.001). Conclusions: The utility of pre-operative MRI is significantly diminished from the non-selected population (17.7%) to the selected population based on the IORT consensus guidelines (6.3-7.1%). While the percent of patients included as possible candidate for IORT based on these selection criteria is highly variable (18% to 53.2%), the utility of pre-operative MRI in these patients is similar in all four groups (6.3%, 6.7%, 6.8%, and 7.1%). This is likely due to exclusion of patients with axillary metastasis in all four selection criteria, which is the most significant predictor of additional MFD/MCD in our study.

PF46

Disparities in Surgical Management of the Axilla in Women with Breast Cancer in North Carolina: The Impact of Socioeconomics & Demographics P.D. Lorimer,* B.M. Motz, R.C. Kirks, K.K. Walsh, Y. Han, T. Sarantou, L. Hadzikadic-Gusic, J.C. Salo, R.L. White, J. Hill. *Surgical Oncology, Levine Cancer Institute, Charlotte, NC.*

Introduction National guidelines advocate for performance of sentinel lymph node biopsy (SLNB) in patients with invasive breast cancer who do not have clinically positive nodes or metastatic disease. The results of SLNB serve as a prognostic indicator and guide additional therapy. Disparities in SLNB rates have been demonstrated on a national level, but few studies examine drivers of these differences. In this study, the North Carolina Cancer Registry (NCCR) was used in conjunction with the Robert Wood Johnson Foundation County Health Rank (RWJF—a composite of health and socioeconomic metrics) to assess factors influencing SLNB. Methods Women with invasive, clinically node-negative breast cancer without metastatic disease who underwent surgery were identified in the NCCR from 2005-2013. Multivariable logistic regression models were used to assess the influence of covariates on the rates of SLNB and axillary lymph node dissection (ALND) after SLNB. The RWJF was used in modeling to assess county-based disparities. Results 21,010 patients were identified, 80.3% White, 17.5% Black and 2.2% Other. Lumpectomy was more common than mastectomy (55% v. 45%). SLNB was performed in 77% and ALND alone was performed in 23%. For those undergoing SLNB, 29% underwent completion ALND, representing 22% of all patients. Blacks and those of Other race were less likely to undergo SLNB than Whites. Patients undergoing lumpectomy were more likely to undergo SLNB than those undergoing mastectomy. Patients with no insurance or Medicaid were less likely to undergo SLNB than those with private insurance, whereas there was no difference between private insurance and Medicare. Patients from a county in the lowest quartile of the RWJF County Health Rank were significantly less likely to undergo SLNB than those in the 1-3rd quartiles. Supporting statistics can be seen in Table 1. Conclusions Racial and socioeconomic disparities exist in management of the axilla in breast cancer patients in North Carolina. Non-White patients from counties with lower RWJF rankings are less likely to receive surgical care which is in compliance with the current standard.

Table 1. Multivariate logistic regression models examining the influence of covariates on likelihood of SLNB and ALND after SLNB.

Comparison	Likelihood of SLNB		Likelihood of ALND after SLNB	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Black v. White Race	0.78	(0.71, 0.85)	1.12	(0.92, 1.37)
Other v. White Race	0.74	(0.59, 0.92)	1.59	(0.93, 2.71)
No insurance v. Private insurance	0.76	(0.62, 0.92)	0.81	(0.53, 1.23)
Medicaid v. Private insurance	0.71	(0.61, 0.84)	1.16	(0.83, 1.62)
Medicare v. Private Insurance	0.92	(0.83, 1.02)	0.95	(0.75, 1.20)
Lumpectomy v. Mastectomy	1.66	(1.55, 1.79)	0.44	(0.38, 0.52)
Highest ranked RWJF quartile v. Lowest ranked RWJF quartile	1.73	(1.57, 1.91)	0.85	(0.66, 1.09)
2nd highest ranked RWJF quartile v. Lowest ranked RWJF quartile	1.82	(1.62, 2.04)	1.03	(0.78, 1.36)
3rd ranked RWJF quartile v. Lowest ranked RWJF quartile	1.16	(1.03, 1.31)	1.23	(0.91, 1.66)

PF47

Survival Outcomes by Racial Differences Among Triple Negative Breast Cancer Patients: A Miami-Population Based Study B. Azab,* D. Yakoub, H. Stuart, F. Moffat, E. Avisar, A.S. Livingstone, D. Franceschi, N. Merchant. *University of Miami, Miami, FL.*

Background: Prior studies have demonstrated the impact of racial difference on breast cancer molecular subtypes. African American (AA) women were found to have a higher incidence of triple negative breast cancer (TNBC) and less favorable outcomes compared to Caucasian (CA) women. The impact of racial differences on survival in Hispanic (H) women with TNBC has not been evaluated, particularly in a Hispanic majority metropolitan area. Methods: 451 TNBC patients of the three most common racial makeups (AA, H and CA) seen at the University of Miami were evaluated. Baseline characteristics, tumor stages, treatment modalities were compared among the three different races. The 5-year overall survival (OS) and disease free survival (DFS) were determined in patients undergoing surgery for TNBC stages I-III. Results: Of the 451 TNBC patients, there were 130 AA, 199 H and 122 CA women. The median follow up was 47 months. CA women had a higher rate of smoking and alcohol use compared to the AA and H women, while AA women had more advanced T stage compared to both CA and H women (T3/T4: 29% AA, 18% H and 15% CA, p=0.03). The three groups had no statistical differences in N stage AJCC stage and treatment modalities. H women had a significant higher 5-year DFS (H – 68%; AA – 55%; CA- 61%; p=0.02) and a trend toward higher OS (H- 87%; AA-79%; CA – 85%; p=0.08), respectively. Cox regression multivariate analysis adjusted for age, T stage, N stage, radiation and chemotherapy showed that the H women had better 5-year DFS than the AA and CA groups (HR was 1.68 for AA and 2.02 for CA, p=0.018 and 0.002), respectively. No difference in OS or DFS between AA and CA were seen. Conclusion: In our Hispanic majority metropolitan area, H women with TNBC stage 1-3 patients, have significantly better DFS compared to AA and CA women. Contrary to prior studies, our results showed no difference in OS or DFS between AA and CA women even when stratified for stage. Further epidemiologic, socio-economic and molecular studies are needed to determine factors contributing to these racial differences in survival in TNBC patients.

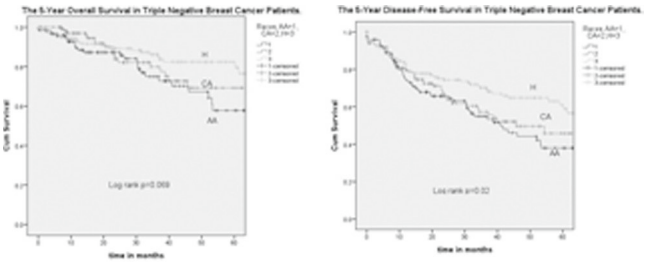


Figure 1. The 5-year overall and disease-free survivals of triple negative breast cancer patients according to the three racial groups (AA= African American, H= Hispanic and CA= Caucasian).

PF48

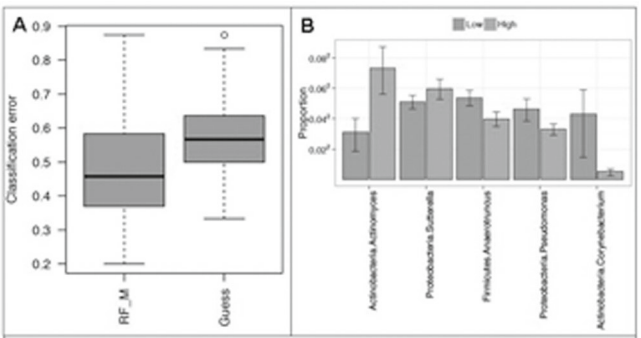
Tamoxifen with Radiotherapy Compared with Tamoxifen Alone in Elderly Women with Early-Stage Breast Cancer Treated with Breast Conserving Surgery: A Systematic Review and Meta-analysis T.R. Chesney,[2]* J.X. Yin,[1] A. Rajaee,[2] A.C. Tricco,[3] S.A. Acuna,[4] A.S. Scheer.[2] *1. Faculty of Medicine, University of Toronto, Toronto, ON, Canada; 2. Division of General Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada; 3. Li Ka Shing Knowledge Institute and Department of Surgery, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada; 4. Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada.*

Purpose. The value of adjuvant radiotherapy in elderly women is unclear. Our objective was to assess the effect of adjuvant radiotherapy on recurrence and survival for elderly women (>70) with early-stage hormone receptor-positive breast cancer treated with breast conserving surgery (BCS) and Tamoxifen. Methods. MEDLINE, EMBASE, and Evidence Based Medicine Reviews were systematically searched through August 12, 2016 to identify randomized controlled trials (RCTs) comparing radiotherapy to no radiotherapy and presenting outcomes for women 70 years or older. Two investigators screened citations, abstracted results, and appraised risk of bias using the Cochrane Risk of Bias tool. Pooled risk ratios (RR) for breast, axillary, and distant recurrence, and overall survival were determined using weights from fixed-effects models. Results. Four RCTs with low risk of bias including 2387 elderly women were identified. Adjuvant Tamoxifen plus radiotherapy reduced breast recurrence compared to Tamoxifen alone from 60 to 10 (95% CI 6-20) per 1000 patients at 5 years (RR 0.18, 95% CI 0.10-0.34; 4 trials, 2387 patients). This effect was maintained at 10 years (RR 0.27, 95% CI 0.13-0.54; 2 trials, 891 patients). Radiotherapy minimally reduced axillary recurrence from 12 to 3 (95% CI 1-10) per 1000 at 5 years (RR 0.28, 95% CI 0.10-0.81; 3 trials, 2287 patients). Radiotherapy did not affect distant recurrence (RR 1.49, 95% CI 0.87-2.54; 3 trials, 2287 patients) or overall survival (RR 0.98, 95% CI 0.79-1.22; 3 trials, 2287 patients). Conclusion. This is the first meta-analysis to evaluate the impact of radiotherapy in women >70. Radiotherapy reduces the risk of breast and axillary recurrence, but does not impact distant recurrence or overall survival in early-stage breast cancer treated with BCS and Tamoxifen. The value of this risk reduction must be weighed by women and their physicians when considering the omission of adjuvant radiotherapy.

PF49

Variations in the Breast Tissue Microbiome with Mammographic Breast Density T.J. Hieken,* J. Chen, C.M. Vachon, T. Hoskin, M.R. Walther-Antonio, S.A. Ramaker, S. Johnson, J.Z. Yao, L.M. Baddour, K.L. Knutson, D.C. Radisky, N. Chia, A. Degnim. *Mayo Clinic, Rochester, MN.*

Introduction Mammographic breast density (MBD) is a well-established breast cancer risk factor. Women with heterogeneously or extremely dense breasts have a 2 to 4-fold elevated risk of breast cancer. MBD has shown consistent associations with stromal changes. Using genomic techniques we recently demonstrated a distinct microbiome within sterile human breast tissues which varied between women with benign disease versus breast cancer. As bacterial communities influence immune-mediated inflammatory changes that affect stroma in ways that may affect breast carcinogenesis, we wished to assess how microbial composition within breast tissue might correlate with MBD. Methods We studied intraoperatively-obtained sterile normal breast tissue samples from 33 women operated on for benign (n=16) or malignant breast disease (n=17) using 16S sequencing and IM-TORNADO bioinformatics pipeline analysis. Microbiome sequencing data were summarized as α and β diversity and taxonomic abundances. We classified MBD as low (BI-RADS a,b) or high (BI-RADS c,d). Statistical associations with β diversity measures were performed with MiRKAT. Random forest was used to assess associations with MBD using genus-level abundances and Boruta feature selection to select genera associated with MBD. Results α diversity appeared lower in high-MBD samples (linear regression P=0.13 for observed OTU number and P=0.23 for Shannon index). β diversity analysis showed a significant association with the microbiome on weighted UniFrac distance (MiRKAT P=0.049) but not unweighted UniFrac distance (MiRKAT P=0.31), indicating MBD associates with community composition (taxa abundance) rather than structure (taxa presence or absence). A random forest-based MBD predictor using genus-level abundances performed better than a predictor without microbiome data (P<0.001, Friedman test). Boruta feature selection identified two genera from the phylum Actinobacteria, Corynebacterium and Actinomyces, as most predictive of MBD. Conclusions We found differences in the breast tissue microbiome associated with MBD. These data suggest the microbiome may be a component of MBD-associated breast cancer risk and provide avenues for further research.



A) Random forest-based predictor using the genus-level abundance (RF_M) or classifier based on the majority class in the training data (Guess).
B) Relative abundance of Boruta selected bacterial genera in association with mammographic breast density (MBD) (red low MBD, blue high MBD).

PF50

The Role of Secreted Frizzled Related Protein 2 Breast Cancer N. Klauber-DeMore,* P. Nassare, W. Da Silveira, G. Hardiman, D. Kim, E. Hilliard, I. Bonillab, Y. Peterson. *Surgery, Medical University of South Carolina, Charleston, SC.*

Introduction: Secreted frizzled-related protein 2 (SFRP2) is a Wnt modulator and angiogenesis factor which activates the calcineurin/NFAT pathway in endothelial cells, but its receptor was unknown, as well as its expression benchmarked to other angiogenesis factors in breast cancer. Methods: TCGA-BRCA gene expression analysis: This study is based upon data from the NCI Genomic Data Commons Portal. We downloaded the mRNA expression data files of TCGA-BRCA dataset. Using information from 877 human samples we evaluated the expression of 119 genes linked with angiogenesis. SFRP2/FZD5 binding studies: The dissociation constant (Kd) between SFRP2 and FZD5 was assessed with a microplate solid phase protein binding assay. For cellular co-localization of SFRP2 ligand and FZD5 receptor, we conducted double immunofluorescence labeling on endothelial cells. Immunostained cells were visualized using a confocal microscope. To evaluate for SFRP2/FZD5 co-immunoprecipitation, protein lysates were prepared from endothelial cells treated with SFRP2 or PBS. Crosslinking was accomplished, and supernatants collected for immunoprecipitation. Immune complexes were eluted and proteins analyzed by Western blotting using antibodies to SFRP2 and FZD5. Functional Assays: To silence FZD5 in endothelial cells, we used HuSH shRNA plasmids to FZD5. The effect of loss of FZD5 compared to sham control was evaluated with Matrigel tube formation assay, and by Western blot for NFATc3 in nuclear fraction of cells. Results: SFRP2 had the highest expression when benchmarked against 119 angiogenesis genes in 877 human TCGA breast cancer samples (Fig. 1). By ELISA binding assays SFRP2 and FZD5 interact with a Kd of 356nM. FZD5 co-immunoprecipitates with SFRP2 in endothelial cells. Immunofluorescence confocal microscopy shows colocalization of SFRP2 and FZD5 at the endothelial cell membrane. In FZD5 knocked-down cells the SFRP2 promoting effect on endothelial tube formation and promotion of effect on NFATC3 activation was lost. Conclusion: These data show that SFRP2 is abundant in human breast cancer and FZD5 is a receptor for SFRP2 in endothelial cells. Blocking SFRP2/FZD5 binding may be a therapeutic target for breast cancer.

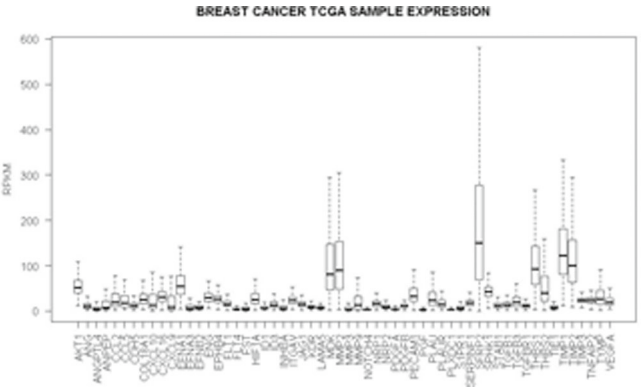


Fig. 1. Expression levels presented as Reads Per Kilobase of transcript per Million mapped reads (RPKM) of the selected angiogenic mRNA in the breast cancer samples present in the TCGA-BRCA data set. Fifty nine of 119 genes were above baseline. SFRP2 has the highest expression of the angiogenesis genes.

PF51

Intraoperative Ultrasound Guidance in Breast-conserving Surgery Shows Superiority in Oncological Outcome, Long-term Cosmetic and Patient-reported Outcomes J. Volders,[1]* M. Haloua,[1] N. Krekel,[1] V. Negenborn,[1] A. Lopes Cardozo,[3] A. Bosch,[5] L. de Widt,[4] h. van der veen,[7] H. Rijna,[6] A. Taets van Amerongen,[1] K. Jozwiak,[2] S. Meijer,[1] P. van den Tol.[1] *1. Surgery, VU Medical Center, Doorn, Netherlands; 2. The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (NKI-AvL), Amsterdam, Netherlands; 3. Northwest Clinics, Alkmaar, Netherlands; 4. Waterland Hospital, Purmerend, Netherlands; 5. Gelderse Vallei Hospital, Ede, Netherlands; 6. Kennemergasthuis, Haarlem, Netherlands; 7. Red Cross Hospital, Beverwijk, Netherlands.*

Background The multicenter randomized controlled COBALT trial demonstrated that ultrasound-guided (USS) breast-conserving surgery results in a significant reduction of margin involvement (3.1% vs 13%) and excision volumes (38cc vs. 53cc) compared to palpation-guided surgery (PGS). The aim of the present study was to determine long term oncological and patient-reported outcomes including quality of life (Qol), together with their progress over time. Methods: 134 patients with T1-T2 invasive breast cancer were randomized to USS (N=65) or PGS (N=69). Cosmetic outcomes were assessed by panel-evaluation, BCCT.core and patient self-evaluation on a 4-point Likert-scale (excellent, good, fair or poor) including a question on patient satisfaction. QoL was measured using the EORTC QLQ-C30/-BR23 questionnaire. Results: No locoregional recurrences were reported after mean

follow-up of 41 months. Seven patients (5%) developed distant metastatic disease (USS 6.3%, PGS 4.4%, p=0.466), of whom six died of disease (95.5% overall survival). USS achieved better cosmetic outcomes compared to PGS, with poor outcomes of 11% and 21% respectively, a result mainly attributable to mastectomies due to involved margins following PGS. There was no significant difference after 1 and 3 years in cosmetic outcome. Dissatisfied patients included those with larger excision volumes, a greater number of additional therapies and worse QoL scores. Patients with poor or fair cosmetic outcomes scored significantly lower on aspects of QoL, including breast-symptoms, body image and sexual enjoyment. In conclusion, USS and PGS did not differ in terms of locoregional recurrence rate, distant metastasis or survival. However, USS clearly improved both short and long-term overall cosmetic outcomes and patient satisfaction. These improvements can be primarily attributed to the smaller excision volumes, fewer positive margins and fewer additional therapies that follow from USS. Cosmetic outcomes after BCS are a major determinant of quality of life, underlining the importance of avoiding poor cosmetic outcomes by improving surgical techniques.

Odds ratios of having a worse cosmetic outcome based on the proportional odds model for ordinal responses.

	Odds Ratio (95% CI)	p-value
Excision method Palpation guided surgery Ultrasound guided surgery	1 (Ref) 0.53 (0.28-0.99)	0.048
Follow-up 3 months 6 months 12 months 36 months	0.39 (0.29-0.54) 0.48 (0.35-0.65) 1.00 (0.74-1.36) 1 (Ref)	<0.001 <0.001 0.988
Evaluation Method BCCT.core Panel-evaluation Self-evaluation	1 (Ref) 0.69 (0.53-0.90) 0.74 (0.57-0.96)	0.005 0.023
T-stage T1 T2	1 (Ref) 2.38 (1.26-4.50)	0.007
BMI	1.08 (1.01-1.15)	0.023

PF52

Impact of Pre-Treatment Axillary Ultrasound on Surgical Axillary Staging in Women Receiving Neoadjuvant Systemic Therapy for Breast Cancer C. Horwood,* N. Ma, J. Hayek, A. Terando, D. Agnese, V. Grignol. *General Surgery, The Ohio State University Wexner Medical Center, Columbus, OH.*

Introduction: The increased use of neoadjuvant chemotherapy (NAC) in women with breast cancer has led to uncertainty regarding the optimal method of surgical axillary staging in this population. The concern with pre-treatment axillary staging beyond physical examination (PE) alone is that patients found to have node positive disease may then be committed to axillary lymph node dissection (ALND), although they may be rendered disease-free after NAC. We sought to evaluate the impact of pre-treatment axillary ultrasound (AUS) on surgical management of the axilla. Methods: A single institution registry was queried to identify patients with T1 or T2 tumors who underwent pre-treatment AUS prior to NAC from 2010 to 2014. Patient demographics, tumor characteristics, AUS/PE findings and total number of positive lymph nodes identified at the time of surgery were examined. Results: Two-hundred fifty-six patients met inclusion criteria. Most patients were stage II (182, 71%), and had invasive ductal carcinoma (230, 90%), with a median tumor size of 2.8cm, (range 0.6-5). Seventy-seven women were clinically node negative by PE, but were found to have abnormal findings on routine AUS. Biopsy confirmed nodal involvement in 54/77 (69%). Forty-seven (87%) patients underwent ALND at the time of surgery; 7 (13%) underwent sentinel lymph node biopsy and completion lymph node dissection only if nodal disease was identified. Twenty-four (44%) had no residual nodal disease identified at the time of surgery. Conclusions: The addition of AUS significantly increases the identification of patients with node positive disease prior to NAC. However, the routine use of pre-treatment AUS may lead to unnecessary ALND. When sentinel lymph node biopsy is performed after NAC, there is no benefit to pre-treatment AUS. Routine use of AUS prior to NAC in the setting of a clinically negative PE may lead to over treatment.

PF53

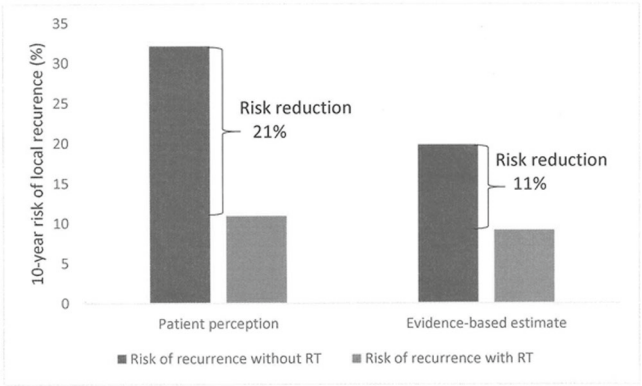
Important 8th Edition Changes for the AJCC Breast Cancer Staging System D.J. Winchester,[1]* S. Edge,[3] A.E. Giuliano,[2] E.A. Mittendorf,[4] J. Connolly,[5] H. Rugo,[6] L. Solin,[7] G. Hortobagyi.[4] *1. Surgery, NorthShore University HealthSystem, Evanston, IL; 2. Cedars-Sinai, Los Angeles, CA; 3. Roswell Park, Buffalo, NY; 4. MD Anderson Cancer Center, Houston, TX; 5. Harvard, Boston, MA; 6. UCSF, San Francisco, CA; 7. Einstein, Philadelphia, PA.*

Introduction: The 7th Edition of the AJCC staging manual for breast cancer is limited to tumor, node, and metastatic (TNM) factors to define stage. Although this system has provided a universally accessible format to stage breast cancers throughout the world, it has limitations in providing useful guidance to determine prognosis and therapy. As a consequence, other prognostic factors have become more relevant. Methods: A multidisciplinary team of pathologists, surgeons, medical oncologists, radiologists, and cancer registrars convened to review the 7th Edition, review current literature, and create an 8th Edition system reflective of current knowledge and practice. Stage groups were created using existing TNM variables, tumor grade, estrogen and progesterone receptor (ER and PR) and Her-2 information. Survival data was calculated with 238,265 patients diagnosed with breast cancer and tracked in the National Cancer Data Base (NCDB). Results: The 8th Edition includes a combination of traditional TNM and biologic variables including grade, ER, PR, Her-2 expression, and genomic assays, creating 170 prognostic groups assigned to stages 0-IV as defined by NCDB survival data. This more comprehensive staging format resulted in reassignment of over 40% of patients using 7th Edition criteria to higher or lower stage groups. Conclusions: The AJCC 8th Edition provides a more comprehensive and accurate staging system with incorporation of biologic variables to define stage and predict survival. This will become effective January 1, 2017.

PF54

Perceptions of Risks and Benefits of Adjuvant Radiation Therapy for Breast Cancer Among Older Women B.K. Killelea,* S. Wang, S. Evans, S. Mougalian, C. Presley, V. Loo, C. Gross. *Surgery, Yale University, New Haven, CT.*

Introduction Although the results of the CALGB 9343 trial revealed that omission of radiotherapy (RT) after lumpectomy can be considered in older women with early stage, estrogen receptor (ER) positive breast cancer, recent analyses demonstrated only a modest decrease in RT. As the decision to omit RT is shared between patients and physicians, who may place different values on risks and benefits, we sought to investigate: 1) factors most important to patients and 2) whether differences in perceived risks and benefits might contribute to continued high rates of RT in practice. Methods Patients aged 65 and over with stage I/II breast cancer who underwent lumpectomy were identified. Patients completed a survey that included items regarding health status, others involved in their decision, perceived risk of recurrence with/without RT, etc. They were also asked about their understanding of RT side effects, impact on survival, costs, etc. Results 93 patients completed the survey; mean age 72.5 years, mean tumor size 1.2 cm. 94.6% were ER positive. 91 patients had sentinel lymph node biopsy; 83 (91.2%) were negative. The most important elements for decision making included the impact of RT on "survival from breast cancer" (91.3%) and "recurrence" (88.0%), "continuing normal activities" (82.6%) and "risk of heart disease" (82.4%). Less important were "changes in breast appearance" (48.9%), "second opinion" (55.1%), "costs" (57.1%), and "transportation" (63.6%). Compared to EBCTCG data, patients overestimated both their 10-year risk of local recurrence without RT (32% vs. 20% p<.001) and the benefit of RT with respect to risk reduction (21% vs. 11%, p<.001). There was no significant difference between perceived risk of recurrence with RT and the EBCTCG estimate (11% vs. 9%, p=.172). Conclusions Older patients consider risk of local recurrence and overall survival greatly when deciding about RT. Many overestimate their risk of breast cancer recurrence without RT and the benefit of RT with respect to local risk reduction. Understanding these risks and benefits in the context of their disease, life expectancy, and comorbidities may help additional patients make informed decisions.

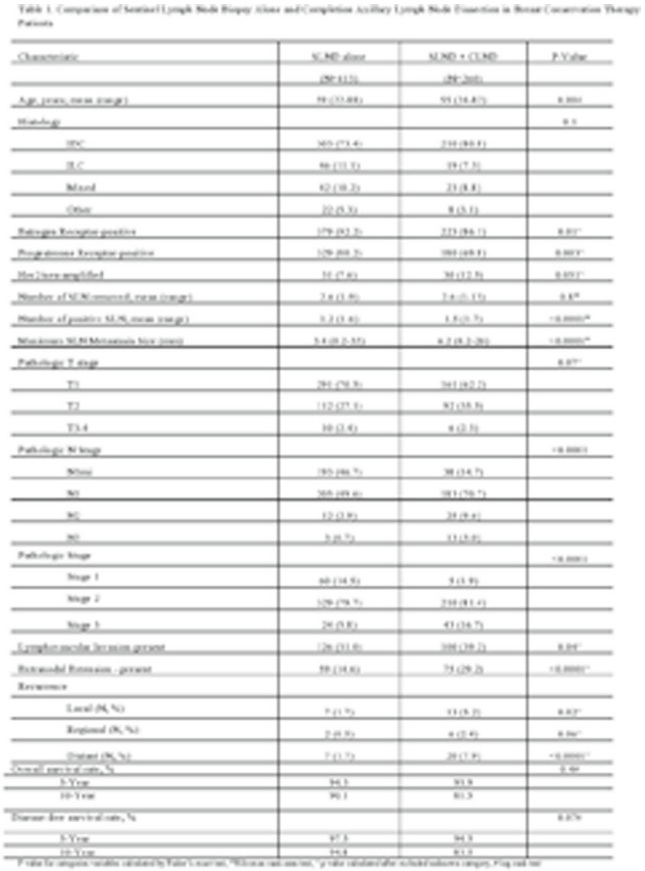


Patients' perceptions of risk of recurrence with and without RT vs. evidence based estimates

PF55

Regional and Survival Outcomes in Patients with Node Positive Disease Based on Axillary Management V. Bea,* M. Yi, H.M. Kuerer, E.A. Mittendorf, E. Fitzsullivan, C. Checka, K.K. Hunt, C. Reyna. *Breast Surgical Oncology, University of Texas, M.D. Anderson Cancer Center, Conroe, TX.*

INTRODUCTION: The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial concluded there was no difference in disease-free survival (DFS) or overall survival (OS) in patients with 1-2 positive sentinel lymph nodes (SLN) undergoing breast conserving therapy (BCT) who were randomized to completion axillary lymph node dissection (cALND) or SLN dissection (SLND) alone. The aim of this study was to examine clinical outcomes of patients undergoing BCT at our institution who were found to have positive SLNs and managed with cALND or SLND alone. METHODS: An IRB approved retrospective review identified female breast cancer patients with node positive disease, ≥18 years old, who underwent BCT between 1993 and 2015. Clinical and pathologic data of patients who underwent SLND alone vs SLND+cALND were analyzed with Fisher's exact test, Wilcoxon rank-sum test and log-rank tests. RESULTS: Of 673 patients, 413 (61.4%) had SLND alone. The median follow-up time was 5.3 years and 7.5 years for SLND and cALND, respectively (p< 0.0001). The SLND alone group had fewer positive SLNs and smaller size of metastasis in the SLNs (p <0.0001). Regional recurrence in the SLN group was 0.5% and 2.4% (p =0.06) in the cALND group which also had more distant metastasis (p< 0.0001). No significant difference was seen in DFS or OS between the groups. In the subset of patients meeting Z0011 eligibility criteria (585 patients), there was no difference in OS between the SLND alone vs cALND groups (94.7% vs 94.3%, p=0.6). There was no difference in regional recurrences but distant recurrence rates were higher in the cALND group (1.6% vs 5.9%, p 0.01). CONCLUSIONS: ACOSOG Z0011 has become an accepted part of clinical practice and is a component of current NCCN guidelines for patients who meet Z0011 eligibility criteria. Our study supports ACOSOG Z0011 findings with no differences in OS in our Z0011 cohort. With the inclusion of additional ineligible Z0011 patients, there was no difference in DFS or OS. Further studies may be beneficial to evaluate expandng criteria and safely omitting cALND in carefully selected patients, previously considered ineligible for Z0011.



PF56

The Optimal Treatment Plan to Avoid Axillary Lymph Node Dissection in Early Stage Breast Cancer Patients Differs by Tumor Subtype M. Pilewskie,* A. Mamtani, A.V. Barrio, E. Zabor, M. Stempel, M. Morrow. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Strategies to reduce the likelihood of axillary lymph node dissection (ALND) among early stage breast cancer patients with nodal metastases include application of Z11 in patients undergoing upfront breast conserving surgery (BCS) or the use of neoadjuvant chemotherapy (NAC). Indications for ALND differ by treatment plan, including ALND for women meeting Z11 criteria with >2 positive sentinel lymph nodes (SLN) and for any positive SLN identified at upfront mastectomy or following NAC. We sought to compare rates of ALND in patients with cT1-2N0 tumors undergoing upfront surgery with mastectomy or a high-risk BCS cohort with a positive SLN to to those treated with NAC. Methods: Patients with cT1-2N0 breast cancer by physical exam were identified. Rates of ALND were compared by subtype among women undergoing upfront surgery to those receiving NAC using Fisher's exact and Wilcoxon rank-sum tests. Multivariable (MV) analysis controlling for age, cT stage, lymphovascular invasion, and stratified by subtype was performed using logistic regression. Results: 1980 cancers in 1943 women who underwent SLN biopsy +/- ALND were identified (669 upfront BCS, 1007 upfront mastectomy, 272 NAC). Women receiving NAC were younger and more likely to have cT2, HER2+ or triple negative (TN) tumors (p<.001). Compared to the NAC group, rates of ALND in the BCS group were lower for ER+/PR+ HER2- tumors (16% vs 35%, p<.001). Rates of ALND in the upfront mastectomy group were higher than the NAC group among HER2+ or TN tumors and similar for ER+/PR+ HER2- tumors (Table). On MV analysis, upfront BCS vs NAC remained significantly associated with lower odds of ALND in the ER+/PR+, HER2- subtype (HR 0.4, p=0.003) while upfront mastectomy vs NAC remained significantly associated with higher odds of ALND in the HER2+ and TN subtypes (HER2+ HR 3.5, p=0.001; TN HR 3.0, p=0.03). Conclusions: Rates of ALND differ according to surgery type and

subtype secondary to differing ALND indications and rates of nodal response to NAC. Breast cancer subtype can be used to personalize treatment planning in order to minimize ALND risk in early stage breast cancer patients.

ALND rates by tumor subtype among women undergoing upfront surgery versus neoadjuvant chemotherapy

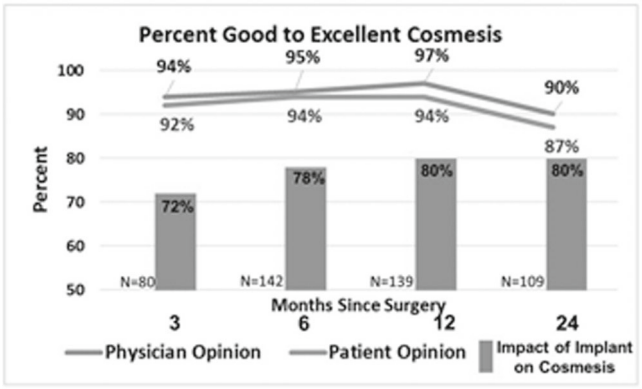
Subtype	Upfront BCS (n=669)	Neoadjuvant chemotherapy (n=272)	P value
ER/PR+, HER2-	91/564 (16%)	26/74 (35%)	<001
ER/PR+, HER2+	7/51 (14%)	11/81 (14%)	1
ER/PR-, HER2+	0/17 (0%)	3/31 (10%)	0.5
ER/PR-, HER2-	8/37 (22%)	7/86 (8%)	0.06
Subtype	Upfront Mastectomy (n=1007)	Neoadjuvant chemotherapy (n=272)	P value
ER/PR+, HER2-	251/724 (35%)	26/74 (35%)	1
ER/PR+, HER2+	35/101 (35%)	11/81 (14%)	0.001
ER/PR-, HER2+	16/44 (36%)	3/31 (10%)	0.01
ER/PR-, HER2-	29/125 (23%)	7/86 (8%)	0.005

PF57

Registry Study of 337 Bio-Absorbable 3-D Implants Marking Lumpectomy Cavity Benefit Cosmesis While Targeting Radiation

C.S. Kaufman,[1]* M.J. Cross,[3] S. Goyal,[2] J. Barone,[4] K. Devisetty,[5] N.S. Dekhne,[6] D. Edmonson,[7] J. Gass,[7] C. Graham,[8] R.L. Hong,[9] B. Patton,[10] R. Phillips,[11] S.M. Schonholz,[12] L.A. Smith,[13] L. Tafra,[14] A. Smith,[15] J. Dilworth.[6] *1. Surgery, University of Washington, Bellingham, WA; 2. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 3. Breast Treatment Associates, Fayetteville, AR; 4. Exempla St. Joseph Hospital, Denver, CO; 5. Karmanos Cancer Institute, Flint, MI; 6. William Beaumont Hospital, Royal Oak, MI; 7. Women's and Infants Hospital, Providence, RI; 8. Georgia Breast Care, Marietta, GA; 9. Virginia Hospital Center, Arlington, VA; 10. Saint Joseph Hospital, Denver, CO; 11. Metro Surgical Associates, Atlanta, GA; 12. Noble Hospital, Springfield, MA; 13. Arizona Breast Cancer Specialists, Albuquerque, NM; 14. Anne Arundel Health System, Baltimore, MD; 15. Highlands Oncology Group, Fayetteville, AR.*

Introduction: Oncoplastic procedures at the time of lumpectomy have become commonplace. A 3-D bioabsorbable implant placed during lumpectomy may deliver solutions to three common problems; providing a dependable tumor bed target for radiation, providing a scaffold for oncoplastic closure resulting in better cosmesis and identifying re-excision sites after tissue rearrangement. An IRB-approved Registry started in 2012 collected 337 cases to assess these issues. Methods: A bioabsorbable 3-D implant was sutured to the tumor excision site during lumpectomy and was utilized for planning and targeting breast irradiation. Data includes patient demographics, breast size, tumor characteristics, surgical and radiotherapy techniques, cosmesis and follow-up. Results: As of September 2016, there are 337 patients from 14 centers involving 17 physicians from 12 States enrolled in the implant registry. Tumor characteristics are similar to other reports involving early breast cancer regarding patient age, size, location, tumor histology, prognostic indicators, node positivity (12%), and location (upper outer 48%). Cancers were T-1 (56%), T-2 (18%) and DCIS (20%). In most cases, implant sizes mirrored the size of the original tumor, 2X2cm (39%) and 2X3cm (33%). The radiation oncologist verified implant as "easily seen" on CT in 92% of cases and 96% found "improved accuracy" in boost targeting and set up. Oncoplastic procedures were used in 90% of patients with 41% using the device as a scaffold for tissue support. Cosmesis was highly rated as "good" or "excellent" at 6, 12, and 24 months by surgeons (94%, 97%, 90%) and by patients (95%, 94%, 87%). The device contributed to the cosmetic benefit for each time period (78%, 80%, and 80%). (See Figure). Conclusion: An IRB approved Registry reports the benefits of a 3-D bioabsorbable implant placed during lumpectomy to provide a dependable target for radiation, a scaffold for oncoplastic tissue rearrangement and to enhance cosmesis over time. This report of 337 patients describes early evidence that this device may achieve multiple goals. Further collection of data over time will validate these early impressions.



Cosmesis as viewed by Surgeon and Patient at post-op, 6, 12, 24 months (lines). 3-D tissue marker contribution to cosmesis in each time interval (blue bars).

PF58

A Novel Fluorescence In Situ Hybridization Assay to Detect 9p24.1 Amplification in Triple Negative Breast Cancer

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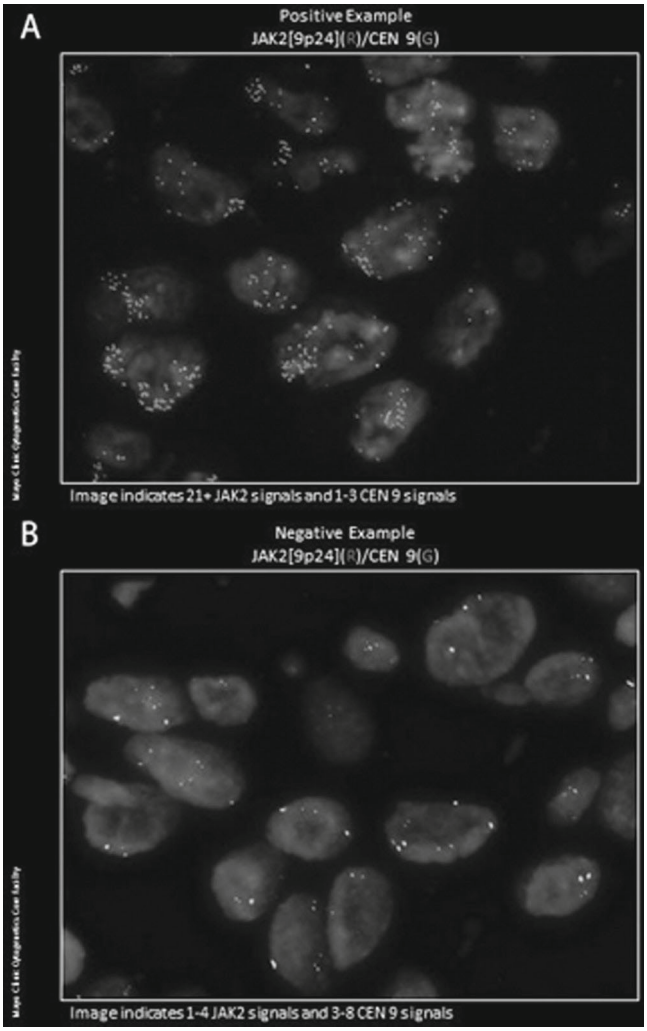
Introduction: Patients with triple negative breast cancer (TNBC) who have amplification of chromosome 9p24.1 encoding PDL1, PDL2, and JAK2 by oligonucleotide CGH arrays (aCGH) have worse survival. We have developed a novel fluorescence in situ hybridization (FISH) for detection of the JAK2/PDL1 copy number gain/amplification (JAK2+). Methods: 38 TNBC tumor samples had prior testing via aCGH to determine the presence of JAK2+, 18 samples as positive for amplification (aCGH log2ratio>0.3) and 20 samples as negative (JAK2-). A FISH probe was developed to map to 9p24.1 with JAK2 DNA labeled with fluorescence dUTP. Chromosome 9 centromere (CEN9) fluorescence probes were combined with JAK2/9p24.1 probe. One hundred events were counted with a fluorescence microscope. The ratio of JAK2 signals to CEN9 signals was used to determine a copy number alteration of JAK2/9p24.1. JAK2+ was defined as a FISH ratio ≥1.1 or average JAK2 signals ≥3. Four samples were excluded due to insufficient tissue. Results: A total of 15 patients were JAK2+ (44%). The FISH ratio ranged from 2.39 to 21.0 (mean 4.65). The highest level amplification sample by aCGH (log2ratio =3.6) correlated by FISH (ratio=8.2). Three JAK2+ samples (aCGH log2ratio=0.38, 0.4, 0.58) were found as neutral by FISH (ratio: 1.04, 1.02, 0.97). In the JAK2- subgroup (n=17), FISH ratios ranged from 0.94 to 2.84 (mean 1.71), the ratio of JAK2 to CEN9 was measured with the range from 0.46 to 1.58 (mean 0.78). One neutral sample by aCGH was detected by FISH as JAK2+. The 9p24.1 copy number gain was detected in 12 out 15 (80%) by FISH. A significant difference in JAK2:CEN9 ratio (p=0.02) was observed between the gain and non-gain subgroups. Clinical data was available for 34 patients: the age, tumor size, and treatment were similar between the two groups. 5-year survival was worse in the JAK2+ compared to JAK- but did not reach statistical significance in this dataset (62 vs 86%) Conclusions: We have developed a novel FISH assay to detect JAK2+ in TNBC. Patients with this biomarker may have worse prognosis and may be suitable candidates for targeted molecular therapies and further study is indicated.

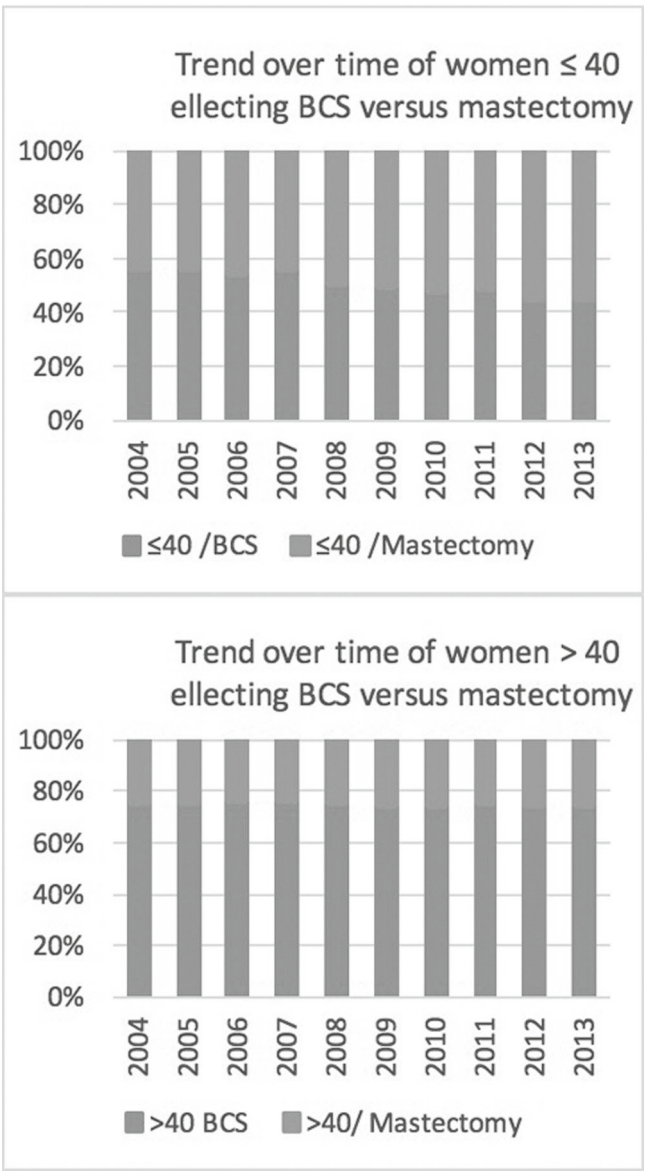


A. Example of tumor sample with signficant JAK2 amplification via fluorescence in situ hybridization. B. Example of tumor sample without JAK 2 amplification.

PF59

Are Race, Socioeconomic Status and Education Associated with Receipt of Adjuvant Radiation for DCIS? H. Alabdulkareem,* T. Pinchinat, A. Landers, X. Wu, P. Christos, H. Nagar, R. Simmons, T. Moo. *Breast Surgery, Weill Cornell Medical Center, New York, NY.*

A recent population-based study showed an association between young age at diagnosis and increased mortality from DCIS. It is unclear whether this is related to biology or socioeconomic factors. We examined the association between race, socioeconomic status and education on receipt of radiation among younger versus older patients undergoing breast conservation for DCIS. Methods The National Cancer Database (NCDB) was used to identify women with DCIS between 2004-2013. Women were then stratified by age > or ≤ 40 years old and by surgical procedure. Chi-square analysis and proportional hazard models were used to examine trends in treatment over time and the impact of race, SES and education on receipt of radiotherapy after BCS. Results 195,447 patients were diagnosed with DCIS. 9198 (4.7%) were ≤ 40 years. Proportions of patients >40 electing BCS remained stable over the study period (median=71.5%). The number of patients ≤40 electing BCS decreased from 53% in 2004 to 42% in 2013 (P<0.001). Among patients ≤40 who underwent BCS, approximately 26% did not receive radiation therapy compared to 27%in patients >40. Among patients ≤40, Hispanic and Asian/Pacific race were associated with no radiation after BCS, 32.7% and 33.5% respectively, compared to non-Hispanic White and Black patients 25.9% and 27%, respectively (p=0.004). In patients >40 Hispanic race was significantly associated with no radiation after BCS (p=0.0001). Among both age groups, patients with higher income levels were less likely to receive radiation therapy after BCS (≤40 p=0.04, >40 p=0.0001). There was no association between education level and receipt of radiation therapy after BCS in patients aged ≤40 (p= 0.79). In women >40 less educated patients were less likely to receive radiation (p=0.0001). Conclusion Over a period of ten years, among patients electing BCS for DCIS, omission of radiation therapy was associated with Hispanic and Asian/Pacific race and higher income levels in patients ≤40. There was no association between education and receipt of radiation in this age group. In patients >40, Hispanic race, high-income and less education were associated with no radiation.

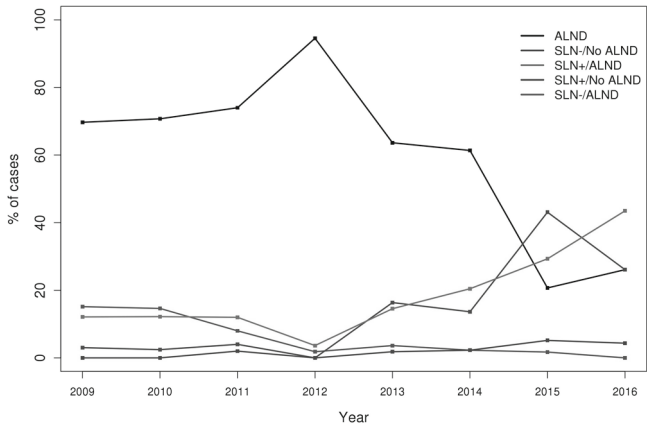


PF60

Evolution of Axillary Surgery for Node Positive Breast Cancer Patients Treated with Neoadjuvant Chemotherapy T.T. Nguyen,[1]* T. Hoskin,[2] C. Day,[2] T.J. Hieken,[1] J.C. Boughey.[1] *1. Mayo Clinic Department of Surgery, Rochester, MN; 2. Mayo Clinic Department of Health Sciences Research, Rochester, MN.*

Background: Neoadjuvant chemotherapy (NAC) may downstage disease in patients (pts) with node-positive breast cancer. Historically, these pts underwent axillary dissection (ALND) following NAC. Several clinical trials now have

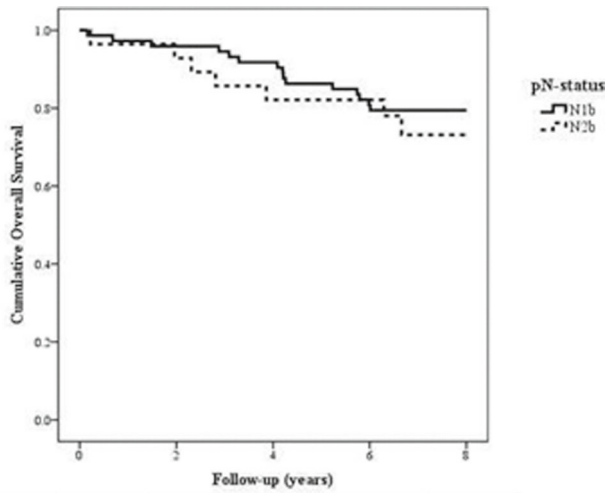
shown that sentinel lymph node (SLN) surgery after NAC is feasible for these pts. We sought to evaluate the use of SLN surgery and ALND in cN1 patients undergoing NAC. Methods: With IRB approval, we identified 359 pts with biopsy proven cN1 breast cancer treated with NAC at our institution between 1/2009 to 7/2016. Pts with recurrent, metastatic or inflammatory breast cancer were excluded. Approximated biologic subtype was determined by estrogen receptor (ER) and HER2 status. Cochran-Armitage trend and chi-square tests were used for statistical analysis. Results: Of 359 pts, 57 (16%) underwent SLN surgery only, 81 (23%) SLN+ALND, and 221 (62%) ALND only. The use of SLN surgery (+/- ALND) increased from 30% in 2009 to 74% in 2016 ($p<0.001$), Figure 1. Omission of ALND for SLN-negative disease increased from 3% in 2009 to 26% in 2016 ($p<0.001$). Among SLN+ pts who underwent ALND, disease was limited to the SLNs in 24 (39%). Overall, the proportion of pts undergoing ALND decreased from 97% to 70% ($p<0.001$). Rate of nodal pathologic complete response was 44% overall and varied by tumor subtype: 75% ER-/Her2+, 64% ER+/Her2+, 50% ER-/Her2-, and 23% ER+/Her2- ($p<0.001$). Among those undergoing SLN surgery, ALND was avoided in 41% overall and this varied by biologic subtype: 52% ER-/Her2+, 52% ER+/Her2+, 58% ER-/Her2-, and 24% ER+/Her2- ($p<0.01$). In 2015-2016 (after the main practice shift), pts more likely to have SLN surgery were those with cT1-cT2 compared to cT3-cT4 (88% vs 64%, $p<0.01$). Use of SLN surgery did not significantly vary by biologic subtype: 79% ER-/HER2+, 91% ER+/HER2+, 77% ER-/HER2-, 69% ER+/HER2- ($p=0.35$). Conclusions:There has been a significant shift in the type of axillary surgery performed for cN1 breast cancer patients treated with NAC with SLN surgery being increasingly used to assess nodal treatment response and guide extent of axillary surgery. Use of ALND has decreased over recent years.



PF61

Does the TNM Classification of Solitary Internal Mammary Lymph Node Metastases in Breast Cancer Still Apply? T. van Nijnatten,[1] V. Habraken,[1] R. Aarnoutse,[1]* L. de Munck,[2] M. Moossdorff,[1] E. Heuts,[1] M. Lobbes,[1] M. Smidt.[1] *1. Maastricht University Medical Center +, Maastricht, Netherlands; 2. Department of Research, Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands.*

Background: TNM-classification of solitary Internal Mammary Lymph Node Metastases (IMLNMs) in breast cancer varies depending on their method of detection: sentinel lymph node biopsy (pN1b) or clinical examination including radiological and/or physical examination (pN2b). This study aimed to evaluate whether there is a difference in prognosis between both groups. Methods: Data of all patients diagnosed with primary invasive epithelial breast cancer between 2005 and 2008 were obtained from the Netherlands Cancer Registry. Groups were defined according to pN1b and pN2b status. The main outcome measures disease-free survival (DFS) after five years and overall survival (OS) after eight years were analysed using Kaplan-Meier survival analysis. Cox regression analysis was used to determine independent predictors for DFS and OS. Results: A total of 101 patients was included for this study, of which 73 patients with pN1b status and 28 patients with pN2b status. DFS rate after 5 years was 75.9% in the pN1b group compared to 90.0% in the pN2b group ($p=0.211$). OS rate after 8 years was 79.5% and 75.0% respectively ($p=0.589$). In multivariable cox regression analysis, nodal status was not statistically significant for DFS (HR 0.29 [95%CI 0.04 – 2.33], $p=0.244$) when corrected for triple negative subtype and administration of endocrine therapy, neither for OS (HR 1.04 [95%CI 0.37 – 2.89], $p=0.947$), when corrected for tumor size, administration of endocrine therapy and trastuzumab. Conclusions: Though TNM-classification regards pN1b and pN2b as distinct prognostic entities, our study found no difference in prognosis between both groups. Therefore, solitary IMLNMs may be regarded as a single category in the future and revision of TNM-classification should be considered.



pN1b	73	70	67	59	34
pN2b	28	26	23	23	12

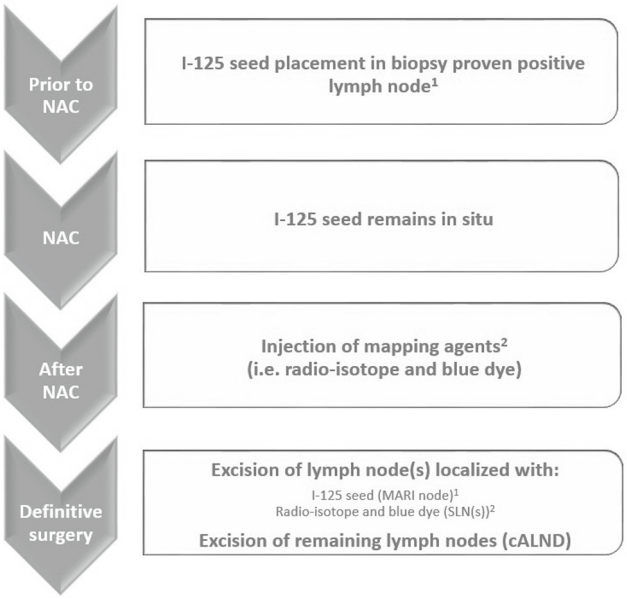
Kaplan Meier Survival curves of overall survival

PF62

A Novel Approach for Axillary Staging After Neoadjuvant Chemotherapy in Axillary Node Positive Breast Cancer Patients by Combining Radioactive Iodine Seed localisation in the Axilla with the Sentinel Node Procedure (RISAS): A Dutch Prospective Multicenter Trial J.M. Simons,[5]* T.J. van Nijnatten,[2] C. van der Pol,[5] M. Smidt,[2] L.B. Koppert,[4] E.J. Luiten.[3] *2. Maastricht University Medical Center, Maastricht, Netherlands; 3. Amphia Hospital, Breda, Netherlands; 4. Erasmus University Medical Center Rotterdam, Rotterdam, Netherlands; 5. University Medical Center Utrecht, The Netherlands, Utrecht, Netherlands.*

Introduction: one out of every 3 patients with initial node positive (cN+) breast cancer converts to axillary pathologic complete response (pCR) as a result of neoadjuvant chemotherapy (NAC). This urges the need for a less invasive axillary staging method. Since recently introduced less invasive procedures are insufficient in accurately identifying pCR we propose RISAS as an axillary staging procedure with potential to safely replace axillary lymph node dissection (ALND). Methods: in this open single arm multicenter intervention study 200 cN+ patients will be enrolled to validate RISAS for predicting axillary response to NAC. RISAS consists of MARI (Marking Axillary lymph nodes with Radioactive Iodine seeds) and SLNB (Sentinel Lymph Node Biopsy)(Figure 1). All patients will undergo completion ALND. RISAS nodes will be compared to ALND specimen lymph nodes. Identification rate (IR), false negative rate (FNR), negative predictive value (NPV) and possible concordance between the MARI node and SLN(s) will be reported. Results: in literature, SLNB and MARI are associated with unacceptable high NPVs and thus miss potentially therapy resistant disease. Targeted axillary dissection (TAD), combining a procedure similar to MARI with SLNB, shows a markedly improved FNR and NPV (2% and 97% respectively). The localized lymph node was not retrieved as an SLN in 23% of patients, indicating added value for combining both techniques. However, we feel that evidence to support TAD is insufficient due to small sample size and single center study design. Furthermore, clips may migrate over time and therefore removal of the biopsied lymph node is not ensured. This is precluded by primary localization with Iodine seeds. Conclusion: RISAS has the potential to safely replace ALND for axillary staging after NAC in initially cN+ patients. When RISAS accurately predicts pCR, ALND and its concomitant morbidity may be rendered only as a management procedure for patients with residual axillary disease.

Figure 1. RISAS, consisting of MARI[1] and SLNB[2].



PF63

Relation Between Pathologic Tumor Response to Neoadjuvant Chemotherapy and Tumor Response Patterns on MRI: Do They Crumble or Shrink? B. Goorts,* K.M.A. Dreuning, J.B. Houwers, L. Kooreman, E.G. Boerma, M. Lobbes, M. Smidt. *Surgery, Maastricht University Medical Centre, Maastricht, Netherlands.*

Purpose – To investigate the correlation between morphological tumor response patterns on breast MRI and tumor response after neoadjuvant chemotherapy (NAC). Methods - In this single center study, all consecutive patients treated with NAC for histologically proven primary invasive breast cancer from 2012-2015 were considered for inclusion. Patients who underwent a breast MRI before and halfway NAC were included. Exclusion criteria were previous ipsilateral breast surgery, previous systemic treatment because of contralateral breast cancer and presence of distant metastasis at diagnosis. All breast carcinomas were reassessed per MRI by an experienced breast radiologist and classified into six shrinkage patterns: Type 0 (complete radiologic response); type 1 (>5mm concentric shrinkage without surrounding lesions); type 2 (concentric shrinkage and crumbling with surrounding lesions); type 3 (crumbling: shrinkage into residual multinodular lesions); type 4 (stable disease, i.e. no increase or decrease of >5mm); type 5 (progressive disease, i.e. increased tumor size or new lesions). The percentage of patients with a good pathologic tumor response (>50% tumor reduction; Pinder 1-2ii) per MRI response pattern was calculated. Furthermore, correlation between response patterns on MRI and pathological tumor response were studied with Pearson's correlation coefficient. Results - A total of 76 patients with 80 primary breast tumors (4 bilateral) were included. Tumors with a type 0, 1 or 3 pattern had significantly higher good pathologic response rates compared to type 2 or 4 ($p<0.001$). All crumbling tumors (type 3, 100%) showed a good pathologic response. Tumors with type 0 or 1 pattern showed a good pathologic response in 80% and 93%. Finally, tumors with type 2 or type 4 pattern only showed 47% and 40% good pathologic response. No tumor showed a type 5 response. Conclusion – Tumor response patterns on MRI are significantly correlated to pathologic tumor response ($p<0.001$). Crumbling tumors (type 3) on MRI have highest good pathologic response rates and tumors that don't show response halfway chemotherapy (type 4) show lowest good response rates.

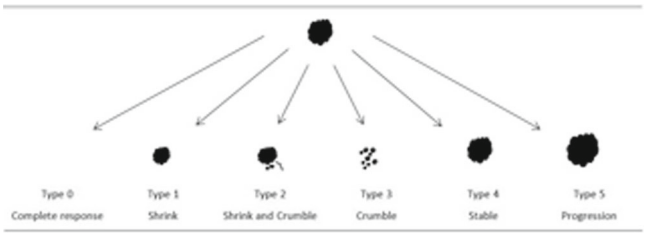


Figure 1. Shrinkage patterns of breast carcinomas on breast MRI halfway NAC treatment.

PF64

Treatment of Elderly cT1-2N0 Breast Cancer Patients: Can Omission of Sentinel Lymph Node Biopsy be Combined with Whole Breast Irradiation? M. Vane,[1]* L. van Roozendaal,[2] S. van Kuijk,[1] S. Siesling,[3] H. de Wilt,[4] M. Smidt.[1] *1. Maastricht University Medical Center +, Maastricht, Netherlands; 2. Zuyderland Medical Center, Heerlen, Netherlands; 3. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands; 4. Radboud University Medical Center, Nijmegen, Netherlands.*

Introduction: Several trials currently investigate whether the sentinel lymph node biopsy (SLNB) can be safely omitted in cT1-2N0 breast cancer patients treated with breast conserving surgery (BCS) and postoperative whole breast irradiation (WBI). Previous randomized trials showed that omission of WBI following BCS could be considered in elderly breast cancer patients. It remains unclear whether SLNB could also be safely omitted in elderly cT1-2N0 breast cancer patients aged 70 years or older in case no WBI is applied. The aim of our study was to investigate the effect of omitting SLNB and WBI in elderly breast cancer patients treated with BCS. Methods: All cT1-2N0 breast cancer patients aged ≥70 years treated with BCS without axillary lymph node staging (SLNB or axillary lymph node dissection (ALND)) were selected from the Dutch National Cancer Registry 2005-2008. Local recurrence (LR), regional recurrence (RR) and disease-free survival (DFS) after five years were analysed using Kaplan Meier curves for WBI or no WBI. Multivariable cox regression analysis was performed to estimate the effect of WBI on DFS corrected for other prognostic factors. Results: Between 2005 and 2008, 24,655 patients were diagnosed with cT1-2N0 breast cancer, of whom 5,926 were 70 years or older. Axillary lymph node staging was not performed in 192 patients (3.2%). BCS was performed in 90 of these patients (46.9%), in whom WBI was performed in 21 patients (23.3%) and omitted in 69 patients (76.7%). Five-year LR was 9.5% (2/21) in WBI group and 2.9% (2/69) in the group without WBI ($p=0.460$), RR after 5 years was 0% (0/21) and 2.9% (2/69) ($p = 0.414$) respectively. Five-year DFS rate was 85.7% (18/21) in the WBI group and 89.9% (62/69) in the group without WBI ($p=0.998$). In multivariable cox regression analysis, WBI was not statistically significant for DFS (HR 0.825 95%CI 0.084 – 8.690, $p=0.892$). Conclusions: There was no significant difference in 5-year LR, RR and DFS between postoperative WBI or no WBI in cT1-2N0 breast cancer patients aged ≥70 years treated with BCS without axillary lymph node staging.

PF65

Disparities Among Fertility Support for Breast Cancer Patients Across the United States A. Vinyard,* E. Avisar, C.M. Bunn. *Surgical Oncology, University of Miami Miller School of Medicine, Miami Beach, FL.*

INTRODUCTION: The incidence of infertility among breast cancer (BC) patients of reproductive age after chemotherapy is approximately 27%. Reportedly, only 23% of women < 40 diagnosed with BC receive proper fertility counseling. Efforts are being made to implement fertility counseling as a part of the multi-disciplinary regimen, however, insurance coverage (IC) for patients who desire fertility preservation and subsequent treatment is not clear. Analysis of IC mandated by each state is indicated to identify possible disparities. METHODS: Data extracted from the National Fertility Association (RESOLVE) and the National Conference of State Legislatures was obtained regarding state laws that mandate IC for infertility treatment. Three areas were analyzed regarding allotted IC, which included infertility workup, fertility preservation procedures, and infertility treatment. Additional information was

collected regarding regional and national programs that provide assistance to patients desiring fertility preservation. RESULTS: In the US, only 15 states currently provide any coverage of infertility workup, fertility preservation, or treatment. There are no current laws in the US that mandate coverage for fertility preservation for cancer patients of reproductive age that may develop chemotherapy induced ovarian failure. Of the 15 states that provide some IC, the definition of infertility varies greatly among each state and cancer patients are not clearly stated as an exception. Local, regional and national programs do exist to provide a portion of financial support for patients seeking fertility preservation. Expenses related to treatment are often tens of thousands of dollars. CONCLUSIONS: As BC treatments continue to improve, women < age 40 are approaching a 92% 5-year survival rate. Patients, who desire fertility preservation prior to treatment, are often denied financial support. Although IC for post-mastectomy reconstruction is mandatory across the U.S., we fail to provide our patients with an opportunity to bear children if our recommended therapies make them infertile. Full coverage for all cancer patients should be mandated.

PF66

Tumor Biology Predicts Pathologic Complete Response to Neoadjuvant Chemotherapy in Patients Presenting with Locally Advanced Breast Cancer L. Gentile,[1]* G. Plitas,[1] E. Zabor,[2] M. Stempel,[1] M. Morrow,[1] A.V. Barrio.[1] *1. Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Neoadjuvant chemotherapy (NAC) is used to downstage the breast and axilla in patients with operable breast cancer. The success of this approach raises the possibility that NAC might allow breast conservation or sentinel node biopsy in locally advanced breast cancer (LABC) patients who are considered ineligible for these procedures. The purpose of this study was to determine rates of pathologic complete response (pCR) in LABC patients and evaluate factors predictive of pCR. Methods: From 2006-2016, 1,522 patients received NAC followed by surgery; 325 had locally advanced disease in the breast defined as cT4 and/or in the nodes defined as cN2 or cN3. 262 had advanced disease in either the breast or axilla, while 63 had advanced disease in both. pCR rates were assessed by T and N stage and receptor subtype. Results: Of 325 LABC patients, 225 were cT4, 79 cN2 and 84 cN3. Median age was 52 yrs and median tumor size was 6cm. 86% had ductal histology, 43% were hormone receptor (HR)+/HER2-, 23% triple-negative and 35% HER2+. All patients had an ALND; 85% had a mastectomy. Overall pCR rates were 25% and differed by receptor subtype (HR+/HER2- 7%; triple-negative 23%; HER2+ 47%; p<0.001). Breast pCR occurred in 27% and was similar in T4 (n = 225) vs. non-T4 (n = 92) disease (29% vs. 23%, p = 0.33). Among cN+ patients (n = 314), nodal pCR was achieved in 38% with similar pCR in cN1 (43%) compared to cN2 (34%) or cN3 (31%) (p = 0.15). Nodal pCR was significantly more common than breast pCR (p= 0.04), across all tumor subtypes. Overall pCR rates in T4d patients were higher than in T4a,b,c (33% vs. 19%, p = 0.02); after adjustment for subtype this association did not retain significance. Receptor subtype was the only predictor of overall pCR; tumor burden was not significantly associated with pCR (Table 1). Conclusion: In patients with LABC, pCR to NAC was seen in 25% of patients, with nodal pCR more frequent than breast pCR. Tumor biology, but not extent of disease, predicts pCR. Studies assessing feasibility of surgical downstaging with NAC in patients with LABC are warranted.

Predictors of Overall Pathologic Complete Response in Patients with Locally Advanced Breast Cancer (n = 325)

Characteristic		n	pCR	No pCR	p value
Age, years, median (range)		325	52 (28-84)	52 (28-81)	0.83
Histology					0.24
	Ductal	280	26%	74%	
	Lobular	22	9%	91%	
	Mixed ductal/lobular	12	17%	83%	
	Other*	11	36%	64%	
cT¥					0.18
	T1	12	17%	83%	
	T2	50	16%	84%	
	T3	30	13%	87%	
	T4	225	27%	73%	
cN§					0.38
	N1	151	28%	72%	
	N2	79	24%	76%	
	N3	84	20%	80%	
Receptor Subtype					<0.001
	HR+/HER2-	138	7%	93%	
	Triple negative	73	23%	77%	
	HER2+	114	47%	53%	

pCR pathologic complete response; cT clinical tumor stage; cN clinical nodal stage; HR hormone receptor
* Includes mammary (n=4), mammary with lobular features (n = 3), metaplastic (n = 2), micropapillary (n=2)
¥Excludes patients with occult cancer (Tx) at presentation (n = 8)
§Excludes patients that were cN0 at presentation (n = 11)

PF67

Mucinous Breast Carcinoma: Incidence of Node Positivity and Comparison with Invasive Ductal Carcinoma, an NCDB Analysis K. Govert,* A. Voci, K.K. Walsh, D. Boselli, L. Hadzikadic-Gusic, T. Sarantou, M. Forster, D. Sarma, R.L. White. *Surgical Oncology, Carolinas Medical Center- Levine Cancer Institute, Charlotte, NC.*

Introduction: Mucinous breast carcinoma (MBC) is a rare type of breast carcinoma that has been associated with a better prognosis and a lower rate of nodal positivity when compared to invasive ductal carcinoma (IDC). We examined the incidence of node positive disease in MBC and IDC in order to identify a population in which a sentinel lymph node biopsy may be necessary. Methods: The NCDB was used to query women between the ages of 18-90+ from 2004-2013 with primary breast cancer Stages 0-III who underwent resection of MBC or IDC. Patient demographics, socioeconomic factors, and treatment data were collected. Chi-squared test and multivariate analysis was used for statistical assessment. Results: 602,864 patients were identified with MBC (14317; 2.4%) or IDC (588547; 97.6%). Patients with MBC were significantly older at diagnosis (p<0.001), had more comorbidities (p<0.001), were more likely to be ER and PR positive (p<0.001), and were more likely to undergo a partial mastectomy (p<0.001). The rate of nodal positivity in IDC patients was 32.72% and 9.67% in MBC patients (p<0.001). In a multivariate analysis of MBC, surgery type and over amplification of Her2neu influenced nodal positivity (Table). Conclusion: This study shows that MBC has a significantly lower rate of nodal positivity and more favorable tumor biology when compared to IDC. A cohort may be identified in which a sentinel lymph node biopsy may not be of benefit.

Multivariate Analysis Predicting Lymph Node Positivity in MBC patients (n=14317)

	OR [95% CI]	p
Age at diagnosis	0.971 [0.965, 0.978]	<0.0001
Race		
Black	1.254 [0.967, 1.625]	0.0876
Other	0.544 [0.362, 0.817]	0.0034
White	ref.	
TNM Pathologic T		
0	0.146 [0.042, 0.502]	0.0023
IS	unestimable	0.9586
1	0.036 [0.018, 0.072]	<0.0001
2	0.143 [0.072, 0.286]	<0.0001
3	0.413 [0.199, 0.855]	0.0172
4	ref.	
HER2/NEU Status		
Non-amplified	ref.	
Borderline/equivocal	2.495 [1.384, 4.497]	0.0024
Amplified	2.224 [1.630, 3.035]	<0.0001
Surgery Type		
Partial mastectomy	ref.	
Mastectomy	2.634 [2.163, 3.207]	<0.0001

PF68

DCIS on Core-Needle Biopsy with No Residual Disease at Surgery N. Gerber, S. Lowe, A. Brodsky, E. Kurz, M. Marmer, J. Chun, S. Schwartz, R. Shapiro, D. Axelrod, A. Guth,* F. Schnabel. *Surgery, NYU Langone Medical Center, New York, NY.*

Introduction: The treatment of ductal carcinoma in situ (DCIS) remains controversial, and treatment approaches include surgery, post-lumpectomy radiation therapy (RT), and/or hormonal therapy for prevention of recurrent disease. These decisions may be particularly difficult for patients with minimal disease. There is a dearth of information regarding patients who have been diagnosed with DCIS on core-needle biopsy (CNB) who have no residual disease in the area at surgery. The purpose of this study was to explore the frequency of this presentation and short-term outcomes in these patients. Methods: Our institutional Breast Cancer Database was queried for all women who were diagnosed with pure DCIS from 2010-2016. Variables included age, method of presentation, risk factors, tumor characteristics and outcomes. Statistical analyses included Pearson's Chi Square and Fisher's Exact Tests. Results: Out of a total of 548 patients with pure DCIS, 55 (10%) had DCIS on CNB alone with no residual in the surgical specimen. The median age was 55 years (range 36-83). Of the patients with DCIS on CNB alone, 6 (11%) were treated with mastectomies. 14 (25%) had lumpectomy and RT, while 35 (64%) had lumpectomy without RT. The median follow up was 4 years. There were three ipsilateral recurrences in women who were treated by lumpectomy alone. One of these recurrences was invasive carcinoma, and the other two were recurrent pure DCIS. None of the patients who recurred had taken hormonal therapy. There were no contralateral second primaries detected in the study period in this cohort. Conclusions: Despite the minimal extent of disease exhibited in these cases, 3 of 35 patients with DCIS on CNB with no residual disease at surgery and no RT had ipsilateral recurrence at a median follow up of 4 years. These data suggest that even minimal DCIS represents a significant risk of recurrence to the patient. Additional information provided by genomic analysis may better stratify the risk for recurrence in this group and help identify the population that would most benefit from post-lumpectomy RT.

PF69

Socioeconomic Disparities in Breast Cancer Treatment and Outcomes: A Population-Based Analysis A. Kong,* A. Nattinger, L. Pezzin. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Breast cancer survival is dependent on patient, tumor and treatment characteristics. However, the relationship between these variables and socioeconomic status is complex. The purpose of this study was to examine the relationship between patterns of breast cancer care and 5-year mortality among a population-based cohort of elderly women with incident breast cancer, with a special focus on identifying sources of socioeconomic (SES) disparities in survival outcomes. Methods: We identified women with newly diagnosed breast cancer in 2006-2009 from the Surveillance and Epidemiology End Result study linked with Medicare claims (SEER-Medicare). A Classification and Regression Tree (CART) model was applied to 15 individual indicators of neo-adjuvant and adjuvant breast cancer treatment, tumor characteristics, and patient sociodemographic variables to identify patterns (i.e. combinations of variables) with the greatest discriminant value in predicting 5-year survival. We subsequently examined the extent to which these patterns varied by the patient SES. Results: Eighteen unique patterns were identified as best discriminating 5-year survival probability. Survival probabilities associated with these patterns ranged from 87% to 22%. CART identified the number of positive nodes as the best single discriminator between high and lower survival outcomes. The most common discriminant factor among patterns with poor (< 25%) survival was absence of radiation treatment, followed by the presence of comorbidities, tumor size >2cm and no breast surgery. Relative to high SES women, poor women were nearly 4 times (24.2% vs. 8.5%) as likely to be classified in the pattern associated with worse survival, and less than half as likely (8% vs. 17.8%) to receive the pattern associated with greatest survival. Conclusions: Greater adoption of certain patterns of care could improve survival of elderly women with incident breast cancer overall, and reduce SES disparities therein.

PF70

Contralateral Prophylactic Mastectomy: Does More Surgery Imply More Risk of Complications or Delay in Treatment? P. George,* C. Valente, R. Couri, C. Pasick, C. Weltz, E. Port, H. Schmidt. *Surgery, Icahn School of Medicine at Mount Sinai, New York, NY.*

A significant number of patients continue to choose contralateral prophylactic mastectomy (CPM) for treatment of unilateral breast cancer in spite of a lack of benefit in terms of cancer outcomes. This study aims to determine and quantify increased risk of adverse outcomes in the postoperative setting. Methods: A prospectively maintained database allowed identification of patients with unilateral breast cancer undergoing either unilateral or bilateral mastectomy. Medical records were reviewed to determine outcomes within 30 days of surgery. Patients with bilateral breast cancer, metastatic disease, or breast conserving therapy were excluded. Results: A total of 229 patients were identified meeting study criteria, 47% having unilateral and 53% having bilateral mastectomy. These two groups had similar distribution of demographic variables, disease stage, BMI, and other risk factors with the exception of slightly more diabetes in the unilateral group (9% vs 2.4%, p=.03). Of the total population 70% had prosthetic reconstruction vs 30% autologous. Overall complication rates were not significantly different in unilateral vs bilateral mastectomy groups (29% vs 24%, p=.33). No difference was observed in time to adjuvant chemotherapy (unilateral 44.1 days vs bilateral 42.4 days, p=.33). Type of reconstruction was evenly distributed between unilateral vs bilateral procedures, however complication requiring intervention was 21% for autologous and 11% for prosthetic reconstruction (p=.07). Conclusion: Choice of CPM did not lead to higher complication rate or delay in adjuvant chemotherapy.

PF71

Second Primaries in Men with Breast Cancer P.A. Cronin,[1]* A.M. Romanoff,[1] M. Stempel,[1] A. Eaton,[2] E. Zabor,[2] M. Morrow,[1] M. El-Tamer,[1] M. Gemignani.[1] *1. Breast Service, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Biostatistics Service, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Male breast cancer (MBC) is rare, it accounts for <1% of all breast malignancies and <1% of all cancers in men. BRCA1 and BRCA2 mutations account for ~10%. Aim This study assesses the rate and type of non-breast second primary cancer (SPC) on MBC and its effect on survival. Methods A database of MBC was retrospectively reviewed from 2000 to 2011. All SPC prior and/or after diagnosis of MBC were recorded. Kaplan-Meier methods were used to estimate overall (OS) and breast cancer specific survival (BCSS). Competing risk methods were used to analyze time to SPC with death from any cause treated as a competing risk. Results 128 invasive MBCs were identified with a median age of 65 (range 20-96). 64 (50%) had a family history of breast cancer and 44 (34%) had genetic testing. Mutations were detected in 9 patients: 7 with BRCA2, 1 with both BRCA1 and BRCA2, and 1 patient with a BRCA1 mutation of unknown significance. Median follow-up among survivors was 5.8 years (range 0.1-14.4). 5-year OS was 86% (95% confidence interval (CI): 80-93%) whereas 5-year BCSS was 95% (95% CI: 91-99%). SPC was identified in 41(32%) patients; 27 presented with a prior history and 14 developed it later. The most common prior SPC site was prostate 7.8% (n=10), followed by bladder 3.1% (n=4), melanoma 3.1% (n=4) and Hodgkin's lymphoma 1.6% (n=2). The cumulative incidence of subsequent

SPC at 5 years was 8.4% (95% CI: 3.4-13.4%) with prostate being the most common site (n=6), followed by bladder (n=2), esophageal (n=2), melanoma (n=1), lung (n=1), renal (n=1) and acute myeloid leukemia (n=1). Patients were stratified by age ≤65 (n=64; 50%) vs. >65 (n=64; 50%). The rate of history of SPC was significantly higher in patients >65, (n=20; 31%) compared to those ≤65, (n=7; 11%) (p=0.008). The cumulative incidence of SPC subsequent to the diagnosis of MBC was not different by age group (p=0.3). In addition a history of contralateral breast cancer was noted in 2 (1.6%) men and 3 (2.3%) patients developed contralateral breast cancer. Conclusions Men with breast cancer have a high rate of SPC (32%), either at presentation or subsequently that may impact their survival. The prostate is the most common site of SPC; appropriate screening should be considered.

PF72

Predictors of Axillary Response to Neoadjuvant Therapy in Patients with Positive Axillary Lymph Node Core Biopsy at Time of Diagnosis K. Pisapati,* A. Nayak, C. Weltz, E. Port, H. Schmidt. *Surgery, Icahn School of Medicine at Mount Sinai, New York, NY.*

Patients presenting with positive axillary lymph nodes at time of breast cancer diagnosis may avoid complete axillary node dissection in the setting of significant response to neoadjuvant chemotherapy. This study reviews characteristics of these cases in an attempt to predict complete pathologic response in the axilla. Methods: A retrospective search of preoperative axillary node core biopsy positive patients was performed. Patients not treated with neoadjuvant therapy were excluded. Results: One hundred nineteen patients were identified with a positive axillary lymph node on core biopsy. Sixty two patients (52%) were treated with neoadjuvant chemotherapy. Upon completion of chemotherapy 47% underwent sentinel node biopsy and 53% had axillary node dissection only. In patients who had axillary node dissection alone, one-third had negative nodes. In SLNB patients 52% had negative sentinel nodes. Among multiple variables tested regarding preoperative pathology, imaging, and treatment, only Her2+(p=.01) and triple negative (p=.04)phenotypes predicted complete pathologic response in the axilla by regression analysis. Response rates in breast vs axilla were consistent for Her2+ and Triple negative patients; however, hormone receptor positive patients demonstrated a modest advantage in axillary lymph node response vs in breast (29% vs 13%, p=.15). Conclusion: Patients with triple negative and Her2+ node positive breast cancer have high rates of response in the axilla with neoadjuvant chemotherapy and often may avoid complete node dissection. Neoadjuvant therapy should also be considered for hormone receptor positive patients presenting with disease in the axilla at time of diagnosis.

PF73

Reducing the Re-excision Rate in DCIS: How Does the Use (or Not) of Cavity Shave Margins and Preoperative MRI with Partial Mastectomy Patients Impact Outcomes A. So,[1]* L. De la cruz,[1] M.T. McMillan,[2] A.D. Williams,[1] C.S. Fisher,[1] J. Tchou.[1] *1. Hospital of the University of Pennsylvania, Philadelphia, PA; 2. University of Michigan Medical School, Ann Arbor, MI.*

Introduction: This study compares the use of cavity shave margins (CSM) and preoperative magnetic resonance imaging (pMRI) with either procedure alone on the final surgical margin (SM) status and on re-excision rates (RR) of patients with ductal carcinoma in situ (DCIS) who underwent breast conservation therapy (BCT). Methods: This is a retrospective review of patients with a new diagnosis of DCIS who underwent BCT between 2010 and 2013 at our institution. We excluded patients who had mastectomy on initial treatment and those without available pathology data. We divided patients in 4 groups: I) BCT alone (n=44), II) BCT with CSM (n=57), III) BCT with pMRI (n=55), and IV) BCT with CSM and pMRI (n=63). Data analyzed included conversion to mastectomy rate (MR), RR, conversion to negative margins due to CSM and residual disease on re-excision (RD). Results: We identified 219 patients with a mean age of 60.1. A total of 61 (27.9%) underwent re-excision for positive SM (<0.2mm). There was no difference in RR (I: 29.5%; II: 22.8%; III: 32.7%; IV: 23.8%) or MR among groups. Of all who underwent re-excision, 36 (62.1%) had residual disease, but there was no difference among groups. Of all who underwent CSM, 5 (4.2%) converted to negative on SM due to CSM, avoiding a re-excision. There were differences among patients who had MRI versus no MRI in age (mean age 57.3 versus 63.3), surgical specimen size (mean size 8.5cm versus 6cm), and sentinel lymph node biopsies (29.4% versus 5%) (p<0.0001). LR remained low (1.8%) and did not differ between patients with or without CSM (p=0.952) nor MRI (p=0.496). Conclusion: Neither CSM nor MRI was associated with decreased RR, LR, or MR in women undergoing BCT for DCIS. Further, CSM with MRI did not reduce RR compared to either procedure alone. The lack of association between CSM and re-excision contrasts previous studies that evaluated the association of CSM with RR for invasive disease (IBC). Given that guidelines for re-excision for IBC and DCIS have recently changed, our findings encourage further research into the utility of CSM and MRI in women undergoing BCT for DCIS.

Table 1. Results of Statistical Analysis

	Cavity Shave Margins				
	No (n, %)		Yes (n, %)		p-value
MR	4 (4.0)		3 (2.5)		0.518
RR	31 (31.3)		28 (23.3)		0.185
LR	2 (2.0)		2 (2.0)		0.952
	MRI				
	No (n, %)		Yes (n, %)		p-value
MR	3 (3.0)		4 (3.4)		0.860
RR	26 (25.7)		26 (25.7)		0.639
LR	2 (2.0)		2 (2.0)		0.496
	BCT alone (n, %)	BCT+CSM (n, %)	BCT+MRI (n, %)	BCT+MRI+CSM (n, %)	
RR	13 (29.5)	13 (22.8)	18 (32.7)	15 (23.8)	
	BCT alone		BCT+CSM		p-value
RR	13 (29.5)		13 (22.8)		0.448
	BCT alone		BCT+MRI		p-value
RR	13 (29.5)		18 (32.7)		0.738
	BCT alone		BCT+MRI+CSM		p-value
RR	13 (29.5)		15 (23.8)		0.604

MR: Mastectomy Rate; RR: Re-Excision Rate; LR: Local Recurrence; BCT: Breast Conservation Therapy;
MRI: Magnetic Resonance Imaging; CSM: Cavity Shave Margin

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Prognostic Relevance of Tumor Suppressive MicroRNA for Breast Cancer T. KAWAGUCHI,* L. Yan, Q. Qi, S. Liu, J. Young, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: MicroRNAs (miRNAs) are noncoding RNAs with 19-25 nucleotides that exert its function by either degradation of coding mRNA or inhibition of mRNA translation. Some miRNAs, such as miR-31, miR-126, miR-146b, miR-206, miR-335, have been reported as tumor suppressive miRNAs targeting oncogenes. However, clinical relevance of those reports has not yet been validated using common large cohort study, which provides sufficient statistical power with proved high quality genetic samples. In this study we took advantage of the high-throughput data from The Cancer Genome Atlas (TCGA) as a validation cohort to evaluate the clinical relevance of well-known nine suppressive miRNAs. Methods: All data were obtained from The Cancer Genome Atlas (TCGA). Expression of five suppressive miRNAs in BrCa, miR-31, miR-126, miR-146b, miR-206, miR-335, were retrieved from the GDC data portal and were analyzed using microRNA-Seq dataset. Overall survival was compared using the Cox proportional hazard model between the high and low expression groups determined by each miRNA-specific thresholds. Results: Among the 1097 patient breast cancer samples logged in TCGA, 1053 samples were found to contain both microRNA-seq datasets and survival data. High expression levels of miR-31 and miR-146b demonstrated significantly better survival ($p = 0.032$ and $p = 0.025$, respectively), while high expression levels of miR-206 tend to show worse prognosis ($p = 0.091$). The other miRNAs of interest, miR-126 and miR-335 have no significant difference between high and low expression groups. All of the miRNAs examined did not show any significant difference between high and low expression groups in clinicopathological factors such as staging, tumor size (T category), nodal metastasis (N category), distant metastasis (M category), and intrinsic subtype (ER, PR, and HER2 status), except for miR-126 that demonstrated significant association with PR and HER2 status ($p = 0.003$ and $p < 0.001$, respectively). Conclusions: We conclude that it is essential to validate the survival impact of reported miRNAs using a large publically available data base such as TCGA.

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Management of the Axilla in Clinical T1-2N0 Patients Undergoing Mastectomy: What Can We Learn from AMAROS?

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Background: The AMAROS trial demonstrated that axillary radiation (AxRT) provides equivalent local control to axillary dissection (ALND) in patients with cT1-2N0 disease found to have 1-2 positive sentinel lymph nodes (SLN). In clinical practice, the extent to which post-mastectomy radiation therapy (PMRT) decisions are influenced by the performance of ALND in this setting remains uncertain. Here we evaluate how the application of AMAROS findings may impact clinical practice and examine factors that predict for use of PMRT in this population. Methods: Patients with cT1-2N0 breast cancer treated with primary mastectomy (TM) and found to have 1-2 positive SLN were identified from institutional databases (2005-2015). Patients with prior chest wall radiation and > 3 positive SLN were excluded. Clinical factors and outcomes were abstracted from the medical record. Comparisons were made by receipt of PMRT. Results: Among 2594 patients with cT1-2N0 breast cancer undergoing TM, 192 (7.4%) had 1-2 positive SLN and met all study criteria. Median patient age, 50 yrs (22-83); median cT size, 2.4cm (2.0-3.1) and median number of SLN, 2 (0-8). 167 (87%) patients underwent ALND, of whom 75 (45%) had additional positive nodes. Among 24 patients not having ALND, 20 (83%) had SLN micromets only. Overall, 65 (34%) patients received ALND alone, 11 (6%) received PMRT alone, 102 (53%) received both and 14 (7%) received neither. Factors predictive of PMRT were younger age ($p<0.0001$), larger tumor size ($p=0.037$), LVI ($p<0.0001$), SLN macromets ($p<0.0001$) and 2 positive SN ($p=0.0089$). Tumor grade, subtype and multifocal/centric disease were not associated with PMRT. At a median follow-up of 46mos (0.3-133) there was no difference in LRR by use of PMRT. Conclusions: These data suggest that 53% of patients with cT1-2N0 breast cancer having TM and found to have 1-2 positive SLN could have been spared intraop SLN evaluation and ALND in favor of PMRT plus AxRT. Clinical factors such as young age, LVI and tumor size are associated with use of PMRT. Additional work to define pre-op selection criteria for PMRT are needed to determine the true impact of AMAROS on clinical practice.

Clinicopathologic characteristics of patients who did and did not receive PMRT

Variable	No PMRT (n=79)	PMRT (n=113)	p-value
Median patient age, years	56 (22-83)	47 (25-76)	<0.0001
US tumor size, cm (median, IQR)	1.7 (1.0-2.1)	1.7 (1.2-2.3)	0.037
Presence of LVI	30 (38%)	89 (79%)	<0.0001
2 positive SLN	6 (8%)	25 (22%)	0.009
SLN macromets	45 (57%)	93 (82%)	<0.0001
Chest wall recurrence	2 (3%)	0	NS
Regional recurrence	0	1 (0.8%)	NS
Distant recurrence	3 (4%)	10 (9%)	NS

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Impact of 2,009 Screening Guidelines on the Clinical Presentation of Breast Cancer: A National Cancer Data Base (NCDB) Analysis

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Background: Following release of the 2009 U.S. Preventative Service Task Force (USPSTF) updated breast cancer screening guidelines, numerous studies have evaluated the rate of mammography and screening in at-risk women. Very little literature exists regarding the impact of these guidelines on stage of presentation of women with breast cancer. We hypothesized that due to reduced rates of screening, more patients would present with advanced disease. Methods: The American College of Surgeons National Cancer Database (NCB) was queried for patients diagnosed with breast cancer (n=1,467,443) from 2004 – 2013. Patients were grouped according to date of diagnosis, either between the years 2004 – 2009 (n=677518) or between 2010 – 2013 (n=789925). These two groups were compared with regard to patient demographics, disease characteristics, and stage at presentation. Results: Patients diagnosed with breast cancer between 2004 – 2009 compared to those diagnosed between 2010 – 2013 were of similar race, income level, insurance status, and socioeconomic status. In both groups, a majority of patients were white (79% vs. 78%) and treated at nonacademic centers (67% vs. 67%). The percentage of patients receiving treatment at urban as opposed to rural centers were also similar (86.3% vs. 86.5%). Following the release of the 2009 USPSTF screening guidelines, patients diagnosed with breast cancer appear to present at clinically similar stages as those diagnosed in years prior. In both groups, a majority of patients were diagnosed with Stage 1 disease (40.1% and 44.72% respectively). The percentage of patients diagnosed with Stage 3 (7.3% vs. 5.9%) or Stage 4 (5.4% vs. 4.5%) disease decreased slightly. Conclusion: Despite theorized reduced rates of mammography and screening in certain populations following the 2009 USPSTF guidelines, patients diagnosed with breast cancer in 2010 – 2013 were not more likely to present with advanced disease. Further research is needed to assess the longitudinal impact of these guidelines on presentation and outcomes from breast cancer.

Characteristic	*2004-2009 (n = 677518)*	*2010-2013 (n = 789925)*	*P value*
Clinical Stage			<0.0001
Stage 0	23.96%	21.79%	
Stage 1	40.60%	44.72%	
Stage 2	22.8%	23.1%	
Stage 3	7.29%	5.92%	
Stage 4	5.36%	4.47%	

PF77

Correlating the Preoperative Axillary Ultrasound and MRI Findings of Abnormal Axillary Lymph Nodes in Women with Breast Cancer

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Introduction: Debate exists regarding the role of axillary ultrasound (AxUS) for preoperative lymph node (LN) staging in women with breast cancer. Simultaneously, the use of preoperative breast MRI is ubiquitous yet evaluation of the axillary LNs by breast MRI is inconsistently reported. We sought to evaluate the correlation between LN findings on AxUS and breast MRI and determine the value of AxUS in the setting of a negative MRI. Methods: We performed a retrospective review of 222 women with Stage I-III breast cancer who planned neoadjuvant chemotherapy and underwent both AxUS and MRI. Two breast radiologists blinded to clinical, pathological, and AxUS findings re-reviewed the breast MRIs specifically focusing on the axillary LNs. We correlated the descriptive characteristics as well as the qualitative and quantitative axillary assessments for each imaging modality. Results: Median patient and tumor characteristics included: age 52yo, BMI 27.6, cT2, cN1. Overall, more patients had abnormal axillary LN findings by breast MRI (AxMRI) than AxUS [151/222 (68%) vs 133/222 (60%), $p=0.008$] and AxMRI found more LN abnormalities in all descriptive categories than AxUS (table 1). Although, AxUS and AxMRI findings agreed in 81% patients [both abnormal 121/222 (54%), both normal/negative 59/222 (27%)], McNemar's test found statistically significant discordance ($p=0.008$) between the modalities as 30/222 (14%) women had abnormal AxMRI and negative AxUS and 12/222 (5%) women had a negative AxMRI and an abnormal AxUS. Preoperative needle biopsy of abnormal LNs was performed in 132 women resulting in AxUS: sensitivity 87%, specificity 25%, PPV 95%, NPV 11% and AxMRI: sensitivity 92%, specificity 50%, PPV 97%, and NPV 29%. When correlating axillary imaging and biopsy results, MRI was 89.4% accurate compared to 82.6% accuracy of US. Conclusion: In this high risk patient cohort, axillary assessment by MRI is feasible and accurate. A minority of patients have a negative AxMRI and positive AxUS. Obtaining additional AxUS for dedicated axillary assessment when high quality breast MRI imaging exists may be futile.

Table 1. Comparison of abnormal LN characteristics according to imaging modality

	Abnormal AxMRI 151/222 (68%)	Abnormal AxUS 133/222 (60%)
# abnormal LN per patient 1 2 3 >4	 28 (18.5%) 29 (19.2%) 23 (15.2%) 71 (47%)	 51 (38.3%) 12 (9%) 4 (3%) 66 (49.6%)
Frequencies LN described as:		
>1cm	146/151 (96.7%)	115/133 (86.5%)
Having cortical thickness >3mm	141/151 (93.4%)	52/133 (39.1%)
Abnormal shape	94/151 (62.3%)	3/133 (2.3%)
Replaced hilum	92/151 (60.9%)	13/133 (9.8%)

PF78

Can Post Neoadjuvant Treatment Imaging and Tumor Biology Predict Axillary Downstaging in Breast Cancer Patients?
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Introduction: Neoadjuvant systemic treatment (NAT) for breast cancer can downstage the axilla. This study aims to assess how well post treatment MRI (ptMRI) and tumor biology can help predict axillary downstaging in patients who have had biopsy confirmed axillary lymph node (cN+) metastasis prior to NAT. Methods: A retrospective chart review was conducted on breast cancer patients who underwent NAT followed by surgery at an academic institution between 9/2013 and 5/2016. Patients that had biopsy confirmed cN+ disease prior to NAT and surgery with axillary staging were included for further evaluation (n=44). When performing a sentinel lymph node biopsy (SLNB)/targeted axillary lymph node dissection (tALND), it was ensured that the biopsied/clipped node was removed. Fisher 's Exact Test was used for statistical analyses. Results: (see Table) Of the 44 cN+ patients, 20 (44%) converted to node negative disease (ypN0). Of these, 10 had SLNB/tALND and 10 had a formal ALND. Fifteen (75%) had complete pathologic response (CPR) of the primary tumor, 10 (50%) were Her2+, 7 (35%) were triple negative (TN), and 3 (15%) were hormone receptor (HR)+/Her2-. Of the cN+ patients, 24 (54%) remained with node positive disease (ypN+) post NAT. Of these, only 3 (13%) had CPR of their primary tumor; 5 (21%) were Her2+, 2 (8%) were TN and 16 (67%) were HR+/Her2-. The ypN+ patients were more likely to be HR+/Her2- than the ypN0 patients ($p< 0.01$). Of the 44 cN+ patients, 39 had pre and post NAT breast MRI, 19 of which were ypN0 and 20 that were ypN+. Of the 19 ypN0 patients, 7 (37%) had complete clinical response (CCR) of their axilla on MRI, and 11 (58%) had CCR of the primary tumor on MRI. Of the 20 ypN0 patients, only 2 (10%) had complete clinical response (CCR) of their axilla on MRI, and 5 (25%) had CCR of the primary tumor on MRI. Downstaged axillary disease was more likely to exhibit CCR of the axilla ($p=0.06$) and/or primary tumor ($p=0.05$) on ptMRI than ypN+ disease. Conclusion: Axillary downstaging in NAT patients can be suspected based on ptMRI results and tumor biology and can facilitate the decision to proceed with SLNB/tALND during surgery.

	Patients with Biopsy Proven Axillary Nodal Metastasis (cN+) Prior to Neoadjuvant Treatment (n=44)		
	ypN0 patients (n = 20)	ypN+ patients (n = 24)	p value
# with Complete Pathologic Response (CPR) of Primary Tumor on Final Pathology	15/20 (75%)	3/24 (13%)	0.000039
Tumor Biology			
Her 2+	10 /20 (50%)	5/24 (21%)	0.058
Triple Negative (TN)	7/20 (35%)	2/24 (8%)	0.057
Hormone Receptor (HR)+/Her2-	3/20 (15%)	16/24 (67%)	0.000768
MRI Evaluation			
# with Pre and Post Neoadjuvant Treatment MRI	19/20	20/24	
# with Some Response of Axilla noted on MRI	18/19 (95%)	16/20 (80%)	Not Significant
# with Complete Clinical Response (CCR) of Axilla on MRI	7/19 (37%)	2/20 (10%)	0.064
# with Complete Clinical Response (CCR) of Primary Tumor on MRI	11/19 (58%)	5/20 (25%)	0.053

PF79

Axillary Reverse Lymphatic Mapping Does Not Increase the Incidence of Axillary Recurrence J.L. Pasko,[1]* N. Johnson,[2] J.R. Garreau.[2] *1. General Surgery, OHSU, Portland, OR; 2. Legacy Good Samaritan Hospital, Portland, OR.*

Introduction: Axillary reverse mapping (ARM) is a technique which allows identification of the lymphatics from the arm during axillary dissection. Early studies suggest that protection of the lymphatics with this technique will decrease the incidence of lymphedema. There has been some concern regarding the oncologic safety of this technique.. Method: Patients who underwent axillary dissection between 2009 -2012 were identified from the hospital tumor registry. During this time ARM was implemented during axillary dissection. Outcomes and incidence of axillary recurrence in this group was reviewed. Results : 142 patients were identified and 119 (83. 8%) had positive nodes at initial dissection. There were 20 recurrences (14%) within the cohort. Ninety women underwent ARM. Of the women with ARM 10 women (11%) had recurrence, while another 10 (19.2%) recurred after traditional axillary dissection. Recurrence data can be seen in Table 1. There was no statistical difference between recurrence and use of ARM ($p= <0.18$). Recurrence was most notable in triple negative tumors (30%) and patients who did not receive adjuvant radiation (35%). Conclusion : ARM was not associated with a higher incidence of local, regional or distal recurrence. ARM does not compromise oncologic outcome.

Recurrence data

	# patients	# recurred	Local recurrence (breast only)	Regional recurrence (axillary recurrence)	Distal recurrence	# Received radiation (%)
ARM	90	10	2	2	6	64 (71.1)
Traditional	52	10	1	2	7	31 (59.6)

PF80

Selective Shave Margin Technique for Lumpectomy: Can We Decrease Re-excision and Mastectomy Rates without Increasing Defect Size? C. Donovan,* N. Manguso, H. Vora, A. Harit, A.P. Chung, A.E. Giuliano, F. Amersi. *Surgery, Cedars-Sinai Medical Center, Los Angeles, CA.*

Introduction: Previous "shave" techniques used in margin assessment for lumpectomy have involved near total re-excision of the lumpectomy cavity. This approach results in lower re-excision rates, but significantly larger excision volumes than standard lumpectomy techniques. Given that many re-excisions yield no evidence of tumor, targeted systematic and smaller cavity sampling may result in lower re-excision rates and lower mastectomy rates with smaller lumpectomy defects. Methods: Patients who underwent lumpectomy for invasive breast cancer between 2006-2014 were identified in a prospectively maintained database. Tumor and operative factors were compared between groups who underwent a selective shave margin (SSM) technique confirmed by pathology report and those who had conventional lumpectomy (CL) excision. SSM technique involves taking 1x1x2 cm specimens from six sides of the lumpectomy cavity. Factors predicting re-excision and mastectomy rates were identified and compared. Results: Of the 1190 patients identified who underwent lumpectomy, 409 operations involved SSM and 781 the CL approach. Patients who underwent SSM more frequently had tumors with DCIS and were slightly older, but otherwise had tumors that were similar to patients who underwent CL approach with respect to tumor size, grade and hormone receptor status (Table 1). Patients who had the SSM approach had a lower re-operative rate than patients who had the CL approach ($p=0.04$). They also had significantly lower mastectomy rates compared to patients with CL (5.4% vs. 0.1% $p<0.01$). With a median follow-up of 50 months, local recurrence rate was not different between the groups ($p=0.84$). Re-excision was associated with lobular and mixed histology, associated DCIS, LVI and CL excision on multi-variable analysis (MVA). Higher mastectomy rates were related to lobular histology, associated DCIS, larger tumor size, younger age and CL approach. Conclusions: Patients undergoing SSM excision during lumpectomy had lower volume segments, lower re-excision rates, and significantly lower mastectomy rates than the CL approach without increasing local recurrence rate.

Selective Shave Margin vs. Conventional Lumpectomy: Tumor and Operative Characteristics

Characteristic	Selective Shave Margins N=409	Conventional Lumpectomy N=781	P-value
Age (Range)	62 (29-89)	65 (29-98)	<0.01
Median Tumor Size [IQR]	1.5 [0.9-2.4]	1.6 [1.0-2.5]	0.58
Grade 1 (%)	106 (26)	179 (5.4)	0.49
Grade 2 (%)	184 (45)	373 (5.4)	
Grade 3 (%)	118 (29)	225 (29)	
ER+ (%)	359 (88)	669 (86)	0.47
HER2+(%)	46 (11.2)	81 (10)	0.69
Triple Negative (%)	36 (8.8)	77 (9.9)	0.60
Associated DCIS	326 (79.7)	556 (72.8)	0.01
Median segment volume in grams [IQR]	24.7 [15-39]	35.0 [20-58]	<0.01
Margin Length [IQR]	2.75 [1.8-3.5]	3.3 [2.5-4.5]	<0.01
% Mastectomy	22 (5.4)	79 (10.1)	<0.01

IQR=Interquartile Range

PF81

Patterns of Practice for the Management of the Axilla in Patients with Breast Cancer and a Positive Sentinel Node Following the ACOSOG Z0011 Trial Results J.R. Asturias, A. Gleisner,* C. Finlayson, N. Kounalakis. *GI, Endocrine Surgery, University of Colorado Health, Denver, CO.*

Background: Results from The American College of Surgeons Oncology Group Z0011 trial (Z11) showed comparable survival and recurrence rates between completion axillary lymph node dissection (cALND) and observation only (OBS) in patients with T1/T2 tumors < 3 positive sentinel lymph nodes (pSLN) treated with lumpectomy and radiation. The aim of this study is to determine the current patterns of practice for axillary management in patients with breast cancer and a pSLN. Methods: The National Cancer Database from 2012-2013 was used to identify women who underwent resection of the primary tumor and sentinel node biopsy (SNB). Patients with inflammatory breast cancer, neoadjuvant chemotherapy or incomplete data were excluded. Institution, patient and tumor characteristics were compared between groups with a pSLN who underwent cALND versus OBS. Multivariable regression analysis assessed factors independently associated with cALND. Results: A total of 108,353 women underwent SNB for axillary staging in 2012-2013 at 1272 institutions; 29,345(27%) had at least one pSLN. Most patients (17,515, 59.7%) underwent cALND. Of those under OBS, 54.5% met Z11 inclusion criteria. Factors associated with higher rates of cALND included black race ([OR] 1.22; [95%CI]1.10-1.36), larger tumor sizes (OR 2.14;95%CI1.84-2.49 for tumors >5cm), mastectomy (OR 3.73;95%CI3.39-4.11) and ER/PR negative tumors (OR1.30;95%CI 1.13-1.52) in the multivariate model; age, insurance, income, education, radiation treatment, institution and surgical volume were not associated with cALND. Institutions with higher rates of cALND (>75%) had a larger proportion of patients that underwent OBS outside the Z11 inclusion criteria (51.2% vs 43.8% institutions with lowest rates [<45%], p<0.001). Conclusions: Women with pSLN were more likely to undergo cALND when Z11 inclusion criteria was not met (mastectomy and tumors >5 cm) but race and receptor status were also significant factors. Rates of cALND by institution is not explained by the type of institution or surgical volume or by the Z11 inclusion criteria adherence.

PF82

High BCI Adherence Impacts Shared Decision Making for Extended Endocrine Therapy in Early Stage Breast Cancer V.L. Prowler,* S.P. Cate, L. Lee, N. Berger, J. Rescigno, A. Gillego, C. Mills, S. Malamud, M. Chadha, D. Kwon, S.K. Boolbol. *Surgery, Mount Sinai Beth Israel, New York, NY.*

Introduction: The breast cancer index (BCI) is a PCR-based assay used to determine the benefit of extending antiestrogen therapy beyond 5 years for women with hormone receptive node negative breast cancer. We sought to evaluate the clinical utility of the BCI assay in a single institution study. Methods: Patients with node negative, HER2-neu negative, estrogen receptor positive invasive breast cancer who had the BCI assay between May 2014 and August 2016 were evaluated (n=106). The primary endpoint was patient acceptance of BCI-based decision making in the use of extended hormonal therapy based on BCI predicted benefit (high vs. low). A secondary endpoint was assessment of clinicopathologic features, including age at diagnosis, tumor pathology, T stage, tumor grade, and Oncotype DX result, that were associated with BCI predicted risk of recurrence and BCI predicted benefit of extended hormonal therapy. Results: Median age at diagnosis was 54. Low risk and low benefit BCI result was found in 45% of patients and 19% were found to have high risk and low benefit, so 64% of patients were not recommended additional anti-estrogen therapy beyond 5 years. BCI risk of recurrence was associated with intermediate/high grade histology (p=0.009), Oncotype DX score (p=0.003), and T stage (p=0.001). However, BCI extended hormonal benefit category was not associated with any clinicopathologic factors. Of 87 patients who were near the 5 year time point to decide whether to proceed with extended adjuvant therapy, 27 of 29 with high predicted benefit chose to remain on anti-estrogen therapy, and none of 58 patients with low predicted benefit did (p<0.001). Conclusion: Adherence to BCI-based recommendation for antiestrogen therapy beyond 5 years is high. The BCI assay contributes to shared clinical decision making and adds to personalization of the duration of anti-estrogen therapy, beyond standard clinical and pathologic factors.

BCI recurrence risk and benefit

BCI	Low benefit	High benefit
Low recurrence risk	48	14
Intermediate recurrence risk	7	5
High recurrence risk	13	19
Total	68/106 (64%)	38/106 (36%)

PF83

Breast Cancer Surgery Decision Making: Comparison of Attitudes, Treatment Goals and Outcomes of Patients in a Collaborative Clinical Research Network I. Lizarraga,[1]* M. Schroeder,[1] S.L. Sugg,[1] I. Jatoi,[2] L. Hoeth,[1] A. Trentham-Dietz,[3] E. Chrischilles.[1] *1. General Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA; 2. University of Texas - San Antonio, San Antonio, TX; 3. University of Wisconsin, Madison, WI.*

Introduction: Little is known about how priorities differ for women who elect CPM over unilateral mastectomy (UM) or lumpectomy (BCS), and whether these affect subsequent worry. The Great Plains Collaborative (GPC) Breast Cancer group conducted a multi-site survey with linked tumor registry data to examine these factors. Methods:Our cohort contained 777 women: 457 (58.9%) BCS, 135 UM (17.4%) and 184 CPM (23.7%), aged ≥18 years with Stage 0-3 breast cancer, diagnosed January 2013 to May 2014. Women with bilateral or recurrent breast cancer or unknown type of surgery were excluded. Patient demographics, attitudes, and outcomes were compared in univariate and multivariate regression models. Results: Mean time since diagnosis was 1.8yrs. All 3 groups reported similar preferences for their decision making role (active/ collaborative/passive), but more CPM than BCS patients described a more active role than preferred (p=0.001) (fig 1). CPM patients were more likely to state prevention of recurrence as an important goal of therapy than BCS patients (83.7% vs 67.6%, p<0.001). CPM patients had lower mean worry scores (worry about ipsilateral + contralateral recurrence + spread of breast cancer) than UM (2.1 vs 2.4, p=0.035) and BCS patients (2.1 vs 2.5, p<0.001). Expressing reduction of worry as an important goal of therapy was predictive of increased worry for patients with BCS but not CPM or UM (β = -0.2, p =0.011). Additional oncologic surgery (such as re-excision) predicted increased worry among all patients and was 3 times more common in the BCS group (p<0.001). UM and CPM patients were >20 times more likely to need unplanned surgery for complications or to improve cosmetic outcome than BCS patients (p<0.001), but this did not increase worry. Decisional conflict scores were low in all groups. Conclusions: Treatment goals and decision making roles differ for patients undergoing CPM, BCS and UM in the GPC, but overall satisfaction with surgery choice is high. At 2 years post diagnosis, patients who chose CPM are significantly less worried than those who had UM or BCS.

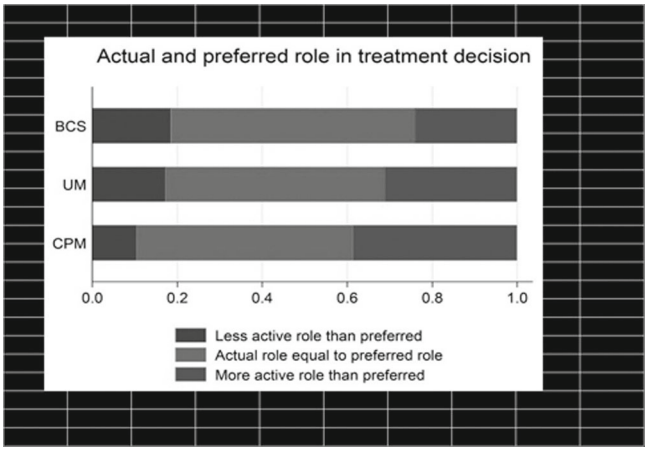


Fig 1. Actual and preferred role in treatment decision by surgery type

PF84

Are Cavity Shave Margins Necessary? Targeted Resection of Additional Margins for Patients Undergoing Lumpectomy Can Lower Re-excision Rates K. Gray,* C. Dauphine, J. Ozao-Choy. *Harbor UCLA, Torrance, CA.*

Background: Margin re-excision rates for breast cancer patients who undergo lumpectomy can be as high as 47%. Taking cavity-shave margins (CSM) at the initial surgery has been shown to reduce the rate of re-excision by up to half. We examined whether selective intraoperative margin resection guided by the detailed labeling of the specimen in combination with intraoperative imaging can produce low rates of margin re-excision and be a viable alternative to CSM. Methods: A retrospective analysis of women with invasive breast cancer or ductal carcinoma in-situ (DCIS) who underwent lumpectomy from March 2013 through July 2016. All specimens were labeled on 6 sides using a radio-opaque marker device and either radiographed in 2 views with 90-degree rotation or evaluated over all labeled margins using ultrasound. The surgeon then selectively chose which additional margins to resect. Margins were definitively evaluated using standard anatomic pathology protocols and current clinical definitions. Results: Of 111 women who underwent lumpectomy (20.7% DCIS, 80.3% invasive cancer), 58 (52.3%) underwent selective intraoperative resection of additional margins based on the images that were reviewed by the surgeon. Intraoperative specimen radiographs were used to guide additional margin resection in 75.7% of cases, ultrasound in 18.9% of cases, and both were used in 5.4% of cases. There were no patient's that required a second surgery for margin re-excision when ultrasound was used. Overall, 12 (10.8%) patients had positive margins on the specimen and 7 patients (6.3%) required a second surgery for re-excision of margins. Of the 58 patients that underwent selective margin resection, re-excision was prevented in 11 patients (9.9%), thus taking a potential re-excision rate of 16.2% and reducing by more than half to 6.3%. Conclusion: Detailed labeling of the specimen using a radio opaque marking device in combination with intraoperative imaging can help direct selective margin resection. This technique may be a successful alternative to CSM for lowering rates of positive margins and re-excision.

PF85

Surgery in the Treatment of Breast Cancer Metastatic to Ipsilateral Supraclavicular Lymph Nodes G. Winter,* K. Hessel, B. Spornitz, J.M. Mammen. *Surgery, University of Kansas, Kansas City, KS.*

Introduction : Metastatic breast cancer (BC) to ipsilateral supraclavicular lymph nodes (SCLN) is present in 1-4% of all BC patients. With the 2003 AJCC staging manual moving the disease to Stage IIIC from Stage IV, there has been a shift to intent to cure rather than the previous recommendation of palliative treatment. A standard of care has yet to be established regarding the use of surgery or radiation for locoregional treatment. In this study, we seek to better understand the role of surgery and radiation in the tretament of BC metastatic to SCLNs. Methods: 1798 patients were identified in the NCDB from 2004-2011 with TXN3CM0 disease. Patients were then stratified based upon treatment. Key demographic information, tumor characteristics, and survival information was evaluated. Statistical analysis performed with p value of 0.05 denoting significance. Results Of the 1798 patients in the database, 816 had adequate information for further evaluation. Median age of patients was 55 and 98.6% were women. 77% of patients are white and 18% were black. Most patients (59.2%) received radiation as their sole form of treatment of ipsilateral supraclavicular lymph nodes with 5.2% of patients undergoing surgical resection of supraclavicular lymph nodes. After eliminating patients in whom vital status is not available. 29.3% of patients had neither surgery or radiation. Median follow up was 59 months. No median survival difference was identified between patients treated with radiation only (77.7 months) versus those treated with surgery (69.7 months), but both treatments had significant greater survival than patients who did not receive treatment of their lymph nodes with surgery or radiation (62 months) (p = 00006). Conclusion The most common locoregional strategy for BC metastatic to SCLN is radiation. A review of the NCDB suggest that radiation is the most common treatment of the disease, but a significant minorityunderwent lymphadenectomy. No difference in survival was found between the two strategies, but survival was greater than those patients who had neither radiation or surgery.

PF86

A Natural History of DCIS in Active Surveillance Patients at UCSF M. Fischer-Colbrie,[3]* R.A. Mukhtar,[1] E. Hwang,[2] N. Hylton,[1] S. Eder,[1] L.J. Esserman.[1] *1. Surgery, University of California, San Francisco, San Francisco, CA; 2. Duke University, Durham, NC; 3. University of California, San Diego, San Diego, CA.*

Background: Controversy surrounds the management of ductal carcinoma in situ (DCIS), yet there is a dearth of information regarding its natural history. Over the last several years we have developed surveillance protocols for women thought to have low risk disease, and for those who declined recommended surgical excision. We sought to determine outcomes in a group of patients with DCIS enrolled in these protocols who had more than 6 months of observation without surgical intervention. Methods: We performed chart reviews for patients with DCIS enrolled in prospective imaging surveillance studies at UCSF from 1997-2016. All patients were enrolled in one of several institutional review board approved surveillance trials. We gathered outcomes including treatment, follow up time, and survival. Results: Of 88 patients with DCIS enrolled in imaging protocols at UCSF, we identified 25 with a minimum of 6 months follow up and no surgical intervention. Average age was 57 (range 42-87), 76% were ER positive, 72% were PR positive, and 70% were non-high grade (1 or 2). 48% of cases had comedonecrosis. Hormone therapy was given in 84% of cases, with aromatase inhibitors (62%) or tamoxifen (38%), for a mean duration of 26 months (range 2-110 months). With average follow up time of 41 months (6-102 months), no patients had breast surgery, diagnosis of invasive breast cancer, or death. One patient with multifocal DCIS developed an enlarging mass on MRI at 2 year follow up, with a repeat core biopsy showing grade 3 ER positive PR positive DCIS, and remained on hormonal treatment only with 6 months of follow-up. Overall survival is 100% in the entire cohort of 88 patients. Conclusion: Of the 88 patients enrolled in active surveillance for DCIS, 28% chose extended active surveillance and have been able to safely avoid surgical excision with a mean of 41 month follow up time. Future analyses of imaging results will help identify predictors for who will go on to require surgical treatment, but these data support the need for ongoing investigation into how we can reduce overtreatment of a largely non-lethal condition.

PF87

Is Breast Reconstruction Worth the Wait? Neoadjuvant Versus Adjuvant Chemotherapy May Improve Timing of Breast Cancer Treatment J.E. Millien,* A. Mackey, A. Rivere, G. Hayek, J. Bruggers, G. Fuhrman, R. Corsetti. *Surgery, Ochsner Clinic Foundation, River Ridge, LA.*

Background: The usage of neoadjuvant chemotherapy (NACT) is on the rise in the treatment of breast cancer. Data suggests the timing and delivery of adjuvant chemotherapy (ADJ) impacts outcomes. We performed this study to determine if type of surgery impacts the time from diagnosis to surgery and chemotherapy. Methods: An IRB approved, prospective review of a retrospective database identified patients treated with chemotherapy for invasive breast cancer from 2006-2014. Patients were divided into 4 groups depending on the type of surgery used to treat their breast cancer: lumpectomy (lump), mastectomy alone (mast), mastectomy with implant reconstruction (mast+IR),

and mastectomy with flap reconstruction (mast+flap). We had 2 subsets of patients: neoadjuvant vs. adjuvant chemotherapy. We compared time from diagnosis to surgery and time from surgery to ADJ with time from diagnosis to NACT and time from last chemotherapy to surgery. Results: A total of 707 patients were noted: 206 had NACT and 499 had surgery followed by ADJ. We further divided these into subgroups according to surgery type with 204 ADJ lump, 69 NACT lump, 134 ADJ mast, 84 NACT mast, 84 ADJ mast+IR, 26 NACT mast+IR, 69 ADJ mast+flap, and 22 NACT mast+flap. In the ADJ group, the average time to surgery was 25.9 and 48.6 days (lump vs mast+flap, respectively). The average time from surgery to chemo in the ADJ group for mast+flap was 62 days. The NACT group revealed significantly shorter times from time of diagnosis to chemo and time of last chemo to surgery (28 and 45 days, respectively). Conclusion: We observed minimal variability in time from diagnosis to chemotherapy and in time from chemotherapy to surgery in the NACT group regardless of surgery performed; however, the ADJ group had significantly longer times to intervention both in the time from diagnosis to surgery and from surgery to chemo in those undergoing reconstruction, most notably flap reconstruction. Prior literature demonstrated that delays in surgery and systemic therapy impact outcomes, therefore NACT should be considered in patients undergoing flap reconstruction who meet criteria for adjuvant chemotherapy.

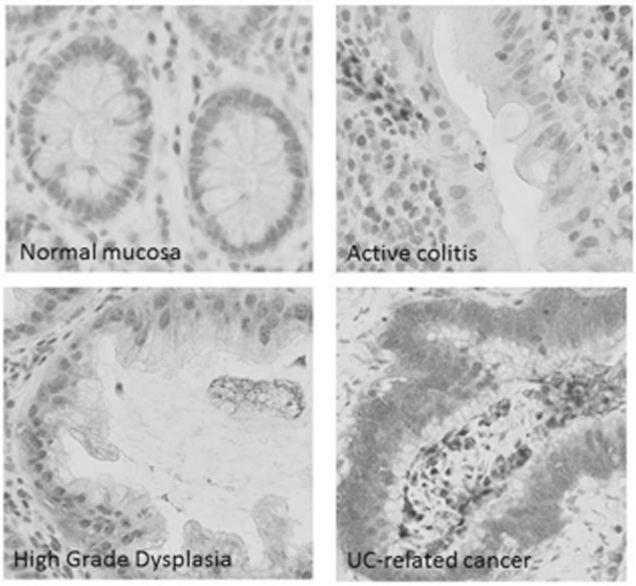
		Lumpectomy	Mastectomy (No Recon)	Mastectomy + Implant	Mastectomy + Flap
Adjuvant	Time from Dx to Surgery (days)	25.9	32.9	38.7	48.6
	Time from Surgery to chemo (days)	48.9	45.9	57.0	62.2
Neoadjuvant	Time from Dx to chemo (days)	29.6	26.7	33.0	22.8
	Time from chemo to surgery (days)	41.4	49.4	41.1	49.8

Timing Differences of Treatment of NACT vs ADJ groups

PT88

ATF6, a UPR Related Gene, Expression in Malignant Conversion and Progression of Ulcerative Colitis (UC)-Associated and Non-UC-Associated Colorectal Cancer M. Hanaoka,* T. Ishikawa, M. Ishiguro, M. Tokura, S. Yamauchi, A. Kikuchi, S. Okazaki, M. Yasuno, H. Uetake, T. Kawano. *Colorectal Surgery, Tokyo Medical and Dental University, Tokyo, Japan.*

Background: Unfolded protein response (UPR) is reported to be associated with development of several malignancies including colorectal cancer (CRC). In addition, recent data show that UPR leads to enterocolitis in ulcerative colitis (UC), and UPR may play an important role in development of UC-associated CRC. Purpose: We investigated the expression of UPR-related gene and relation to the development and progression of CRC, especially of UC-associated CRC. Materials and Methods: 1) From our gene expression database of genome-wide microarray analysis of 115 CRCs resected at our hospital from 2005 to 2009, we extracted 3280 genes whose expression was elevated in CRC (1.5-fold of normal mucosa). Among them, we extracted ATF6, the only UPR-related gene, as a candidate gene. 2) The expression of ATF6 protein was evaluated by immunohistochemistry (IHC) using following specimens. [A] 48 adenoma, 44 Tis CRC and 65 ^T1 CRC which were resected endoscopically or surgically from non-UC patients. [B] 50 active colitis, 9 dysplasia and 13 CRC which were surgically resected from UC patients. The reasons for surgery were development of malignant transformation (n=16) or uncontrollable inflammation (n=17). P53 expression was also analyzed by IHC. Result: [A] ATF6 protein expression was higher in adenoma than in normal mucosa ($p<0.001$), and higher in CRC than in adenoma ($p<0.001$). When 65 surgically resected ^T1 CRC were divided to high (n=30) and low (n=35) ATF6 expression, ^T3, venous invasion, moderate and poorly differentiation, and lymph node metastasis were associated with high ATF6 expression. [B] ATF6 protein expression was higher in UC-related CRC and dysplasia than in inflammatory mucosa ($p=0.002$). Expression of ATF6 and P53 had positive correlation with correlation coefficient of 0.43 ($p<0.001$). Conclusion: ATF6 may contribute to malignant conversion and progression of both non-UC and UC-associated CRC.



PT89

Comparison of Two Novel Staging Systems with the TNM System in Predicting Stage III Colon Cancer Survival R. Walker,[1]* E. Le Souder,[1] T. Wood,[1] M. Maganti,[2] S. Chadi,[1] T. Jackson,[1] A. Okrainec,[1] F.A. Quereshy.[1] *1. Division of General Surgery, Toronto Western Hospital, University Health Network, Toronto, ON, Canada; 2. Department of Biostatistics, Princess Margaret Cancer Centre, Toronto, ON, Canada.*

INTRODUCTION: The Lymph Node Ratio (LNR) has demonstrated superior prognostic ability when compared to pN stage for patients with stage III colon cancer. Two adaptations of the TNM staging system that incorporate LNR have been proposed for stage III patients. The goal of this study was to compare the concordance of the two novel staging systems and the TNM classification system with the observed survival outcomes in stage III colon cancer patients. METHODS: A retrospective review of patients who underwent surgery for stage III colon cancer between January 2002 and April 2015 at a tertiary care centre was performed. The Kaplan-Meier method was used to estimate the 5-year overall (OS) and disease free survival (DFS) rates, and the concordance probability was calculated to evaluate the discriminatory power of the three staging systems. RESULTS: 261 patients were identified with a mean of 21.1 lymph nodes retrieved. The mean number of positive nodes was 3.6, and the mean LNR was 0.2. Kaplan-Meier estimates of OS according to each staging system are shown in Figure 1. For TNM stages IIIA, IIIB, and IIIC, 5-year OS was 83.4%, 67.6%, and 38.3%, respectively ($p<0.001$), and 5-year DFS was 80.1%, 53.1%, and 30.2%, respectively ($p<0.001$). Multivariate analysis revealed that chemotherapy and all three staging systems were independently predictive of OS and DFS ($p<0.001$). However, the novel staging system by Sugimoto et al. was the most favourable prognostic tool, with a concordance of 0.646 for DFS and 0.659 for OS. The TNM system achieved concordances of 0.624 for DFS and 0.623 for OS, and the staging system by Wang et al. achieved concordances of 0.601 for DFS and 0.598 for OS. CONCLUSIONS: The novel staging system by Sugimoto et al. was superior to the current TNM system. Incorporating LNR into staging models for node positive colon cancers may improve survival information available to patients and potentially aid treatment decisions. However not all applications of LNR may improve model discriminatory power, and further validation studies are necessary to define the optimal LNR and its utility in prognostication.

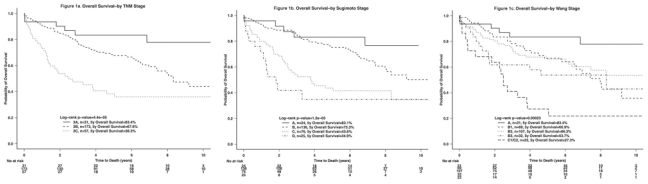


Figure 1. Kaplan-Meier curves for OS according to each staging system. a TNM. b Sugimoto. c Wang.

PT90

Neoadjuvant Pelvic Perfusion May Facilitate Resection of Pelvic Recurrent Rectal Cancer H. Wanebo,* G. Begossi, J. Belliveau, E. Gustafson. *Landmark Medical Center, Woonsocket, RI.*

Introduction: Pelvic recurrence of rectal cancer is a persisting therapeutic challenge in spite of common use of adjuvant/neoadjuvant chemo radiation and wide resection. Isolated pelvic perfusion (IPP) may facilitate pelvic resection in selected high-risk patients. Patients: IPP was done in 42 patients with locally advanced previously irradiated rectal cancer, 26 as a preoperative therapy and 16 for palliation. A comparative larger non perfused group included 63 patients having pelvic resection alone. Method: Isolated pelvic perfusion (IPP)(60 min) using pump oxygenation (Temp>41c), chemo agents – 5 FU 1500mg/m^2, Cisplatin/Oxaliplatin 150mg/m^2, and Mitomycin as 10mg/m^2, was done in 42 patients. Results (follow up surgery): Palliative IPP in 16 advanced rectal cancer patients induced significant relief (1-4 months) of narcotic resistant pain (in 70%). Preoperative IPP in 26 locally advanced rectal cancer achieved a clinical path (CR) in 2 patients, and significant regression in 11 patients rendering them resectable. Seven had R0 pelvic resections; of 6 other patients, 4 refused surgery, 2 were medically excluded. Median survival was 24 months in 12 resectable and 30 months in the 7 resected pts (2 pts were 5 year survivors). This is compared to outcome in 63 patients amenable to having pelvic resection alone: 57% had R0 resection (median OS 36 mos), 28% had R1 resection (med OS = 15 mos) and 15% had R2 resection (med OS 21 mos). Conclusion: Neoaduvant IPP may facilitate selection of recurrent rectal cancer by identifying therapeutic responders likely to benefit from major pelvic resection and excluding non-responders most likely to benefit from non-surgical therapy. The potential to induce regression and facilitate R0 resection merits further exploration. Synopsis: Neoadjuvant pelvic perfusion appears to induce significant regression potentiating resection in over 50% of patients with locally advanced rectal cancer recurrence.

PT91

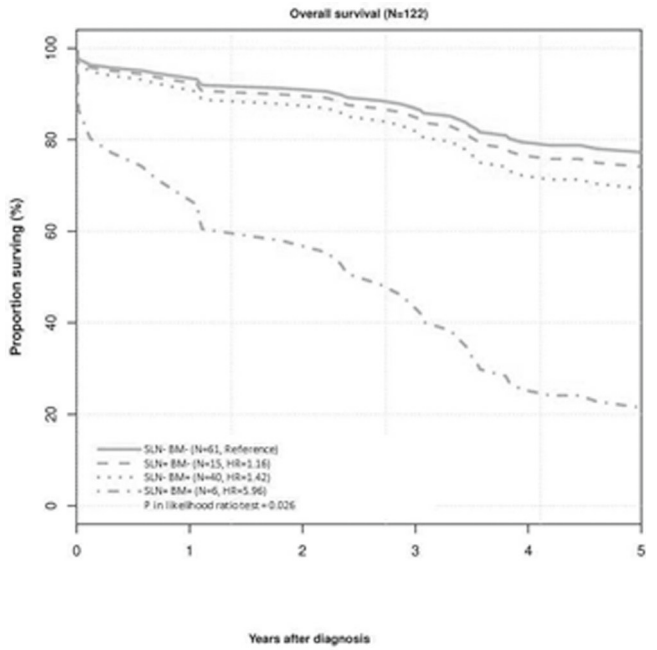
Comprehensive Genomic Research to Identify the Treatment Resistance-Related Gene, ASCL2, in Colorectal Cancer T. Tanaka,* K. Yamashita, S. Ishii, N. Nishizawa, K. Yokoi, H. Katoh, T. Sato, T. Nakamura, M. Watanabe. *Surgery, Kitasato University School of Medicine, Sagamihara, Japan.*

Background: In our laboratory, ZEB1, epithelial-mesenchymal transition (EMT)-related gene, have been identified to be associated with Phenylbutyrate (PB) resistance in breast cancer (Kikuchi M, Oncotarget 2015). The treatment-resistant factors to a variety of anti-cancer therapy have not been well elucidated in colorectal cancer (CRC), here in, we investigated gene expression profiles by comprehensive genomic research to identify biomarkers predictive of treatment-resistant in CRC. Materials and Methods: 1)Six CRC cell lines were treated by 1 to 20-fold PB solution (1-fold = 0.5mM) for the purpose of sensitivity classification. 2)Gene profiles between PB-sensitive and PB–resistant strains were compared using microarrays (harboring 54675 genes) to identify the PB resistance-related gene. 3)EMT related genes were selected from among the PB resistance-related genes and observed to change of their expression by demethylating treatments. 4)The plasmid and small-interfering RNA (siRNA) targeting the EMT related genes were transfected into the PB-sensitive and PB-resistant strains, respectively, to evaluate the relationship between treatment-resistant and expression of the each genes. Results: 1) HCT116 cells were significantly identified as PB-sensitive (p=0.005), while DLD1 and HCT15 cells were PB-resistant. 2)In microarray analysis,26 genes were identified as PB resistance-related gene. 3)Among the 26 genes, ASCL2, LEF1, and TSPAN8 gene had been reported to be associated with EMT, and had no changes in each gene expression after the demethylation treatments. 4)Cells transfected with the respective 3 genes significantly received the resistance to PB (ASCL2: p<0.001, TSPAN8: p<0.001, LEF1: p<0.001, respectively). Therefore, the transfection of ASCL2 induced the expression of LEF1 and TSPAN8. 5)Cells inhibited ASCL2 by siRNA significantly received the sensitivity to not only PB but also 5-FU and radiation therapy (PB: p<0.005, 5-FU: p<0.001, radiation: p<0.001, respectively). Conclusions: ASCL2 gene may associated with resistance to PB, 5-FU, and radiation therapy in CRC cell lines and serve as a critical biomarker for predicting resistance to CRC treatments.

PT92

Correlation of Bone Marrow Micrometastases and Micrometastatic Lymph Node Deposits in Stage I-III Colon Cancer Patients: A Prospective Multicenter Study B. Weixler,[1]* R. Warschkow,[2] C.T. Viehl,[3] U. Güller,[4] M. Zuber,[5] T. Eberlein.[6] *1. University Hospital Basel, Basel, Switzerland; 2. Department of Surgery, Cantonal Hospital St. Gallen, St. Gallen, Switzerland; 3. Department of Surgery, Hospital Center Biel, Biel/Bienne, Biel/Bienne, Switzerland; 4. Divsion of Oncology & Hematology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland; 5. Department of Surgery, Cantonal Hospital Olten, Olten, Switzerland; 6. Not author but sponsor of the abstract; Department of Surgery, Washington University Medical School and Siteman Cancer Center, St. Louis, MO.*

Background: Bone marrow micrometastases (BMM) and small nodal tumor infiltrates (SNTI; isolated tumor cells and micrometastases) in sentinel lymph nodes (SLN) each have been described as negative prognostic factors in patients with colon cancer. This study examines the relationship of BMM and SNTI in patients with colon cancer. Methods: In a total of 122 patients with stage I-III colon cancer, bone marrow (BM) was aspirated from both iliac crests immediately preoperative after induction of general anesthesia and in vivo SLN mapping was performed during open standard oncological resection. Bone marrow aspirates were stained with the pancytokeratin marker A45-B/B3. All SLN underwent multilevel sectioning and were stained with H&E and with the pancytokeratin marker AE1/AE3. The correlation between the occurrence of BMM and SNTI in SLN as well as their impact on survival was assessed using Cox regression analyses. Results: A total of 46 (37.7%) patients showed BMM, and 21 (17.2%) SNTI. BMM were not associated with the presence of SNTI in univariate (Odds ratio [OR]=0.64, 95% confidence interval [95%CI]=0.22-1.69, p=0.377) and multivariate (OR=1.08, 95%CI=0.33-3.37, p=0.897) analysis. Both, BMM and SNTI were independent negative prognostic factors for overall survival (OS) (hazard ratio [HR]=2.68, 95%CI=1.26-5.70, p=0.011, and HR=4.04, 95%CI=1.56-10.45, p=0.005, respectively) and disease free survival (DFS) (HR=2.07, 95%CI=1.06-4.06, p=0.037, and HR=2.93, 95%CI=1.24-6.93, p=0.016, respectively). Combined detection of BMM and SNTI demonstrated the poorest OS (HR=5.96, p=0.026) and DFS (HR=6.73, p=0.006). Conclusions: This study demonstrates that BMM and SNTI are not associated with each other in stage I-III colon cancer, therefore suggesting independent metastatic pathways. These results furthermore identify BMM and SNTI as negative prognostic factors for cancer recurrence and death. Future trials will have to evaluate if standard lymph node evaluation is truly sufficient for the identification of patients at risk of disease recurrence or has to be supplemented by additional and/or more in-depths analyses.



Kaplan Meier curve for overall survival

PT93

Pathologic Complete Response and Adjuvant Therapy in Rectal Cancer: An Analysis of Long-term Survival J.V. Gahagan,* M.D. Whealon, M.J. Phelan, S. Mills, M.J. Stamos, J.C. Carmichael, J.A. Zell, A. Pigazzi. *UC Irvine Health, Orange, CA.*

Objective: The aim of this study is to examine the effect of postoperative (adjuvant) chemotherapy on survival in patients with stage II or III rectal adenocarcinoma who undergo neoadjuvant chemoradiation (CRT) and surgical resection. Methods: A retrospective review of the National Cancer Database (NCDB) from 2006 to 2013 was performed to identify patients with clinical stage II or III rectal adenocarcinoma who underwent CRT and surgical resection. Cases were analyzed based on pathologic complete response (pCR) status and use of adjuvant therapy. The non-pCR group was further stratified by pathologic node status. The Kaplan-Meier method was used to estimate overall survival probabilities. Results: 23,045 cases were identified, of which 5,832 (25.31%) achieved pCR. In the pCR group, 1,513 (25.9%) received adjuvant chemotherapy, and in the non-pCR group, 5,966 (34.7%) received adjuvant therapy. Demographic characteristics were similar between those who achieved pCR and those who did not, as well as between those who received adjuvant therapy and those who did not. In the pCR group, five-year survival probability was 87% (95% CI 84%-89%) with adjuvant therapy and 81% (95% CI 79%-82%) without adjuvant therapy. In the non-pCR group, five-year survival probability was 78% (95% CI 76%-79%) with adjuvant therapy and 70% (95% CI 69%-71%) without adjuvant therapy. In the non-pCR and node-negative subgroup (ypN-), five-year survival probability was 86% (95% CI 84%-88%) with adjuvant therapy and 76% (95% CI 74%-77%) without adjuvant therapy. In the non-pCR and node-positive subgroup (ypN+), five-year survival probability was 67% (95% CI 65%-70%) with adjuvant therapy and 60% (95% CI 58%-63%) without adjuvant therapy. Conclusions: The use of adjuvant chemotherapy in stage II or III rectal adenocarcinoma is associated with increased five-year survival probability regardless of pCR status. We observed similar survival outcomes among non-pCR ypN- treated with adjuvant chemotherapy compared with patients achieving pCR treated with adjuvant chemotherapy. Regardless of postoperative chemotherapy use, ypN+ disease was associated with poor survival in rectal cancer.

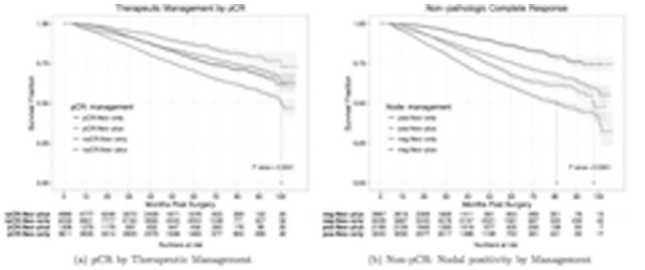


Figure 1: Kaplan-Meier Estimates of the fraction survived over months post surgery. Left panel: Survival based on pathologic response and therapeutic management. Right panel: Survival based on nodal positivity and therapeutic management. Groups labeled as follows: pathologic complete response (pCR), non-complete response (npCR), neoadjuvant-only therapy (Neo-only), and neoadjuvant-plus-adjuvant therapy (Neo-plus), nodal positive (pos), nodal negative (neg). Two-sided P-values shown for the log-rank test of equality of survival.

PT94

The Influence of Clinicopathologic and Molecular Markers on Stage Specific Survival of Right Versus Left Colon Cancer S. Narayanan,* E. Gabriel, K. Attwood, S. Nurkin. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: Previous studies have identified variability in pathologic molecular markers as well as poorer survival outcomes in patients with right sided colon cancer compared to left. However, several studies have shown conflicting results when examined stage for stage. We examined different stages of right and left sided colon cancer to assess for differences in histopathologic features and overall survival (OS). Methods: The National Cancer Database was used to identify patients with colonic adenocarcinomas from 2004 to 2013. Right sided colon cancers (RCC) were those from the cecum to the hepatic flexure (excluding transverse) and left sided cancers (LCC) were found within the splenic flexure, descending colon and sigmoid. A propensity adjusted analysis evaluating association between primary site and outcomes was performed. Results: Of the 422,443 patients identified 54.7% had RCC and 45.3% had LCC. In all stages, patients with RCC were older (71.7% over age 65 vs. 55.2%, $p < 0.001$), had more poorly differentiated tumors (22.5% vs. 13.1%, $p < 0.001$) and a higher degree of microsatellite instability than left (31.4% vs. 16.7%, $p < 0.001$). Patients with RCC also had higher incidence of KRAS mutations than LCC (45.0% vs. 33.7%, $p < 0.001$). RCC patients had poorer three-year and five-year survival at all stages, especially at Stage 3 (62% vs. 73% and 50% vs. 62% respectively, $p < 0.001$). Median OS was 77.5 months for LCC compared to 62.3 months for RCC ($p < 0.001$) with the largest difference at Stage 3 (94.3 vs. 60.8 months, $p < 0.001$). Conclusion: In this study, we were further able to demonstrate that right and left sided colon cancer are likely different biological entities. RCC had significantly higher rates of microsatellite instability in all stages which has been previously shown to be prognostically advantageous. However, this study showed poorer OS at every stage of disease for RCC over LCC. This is likely due to later presentation, poorer tumor differentiation and higher rates of mutated KRAS. These factors may have important implications for the further use of targeted therapies in the treatment of advanced colon cancer.

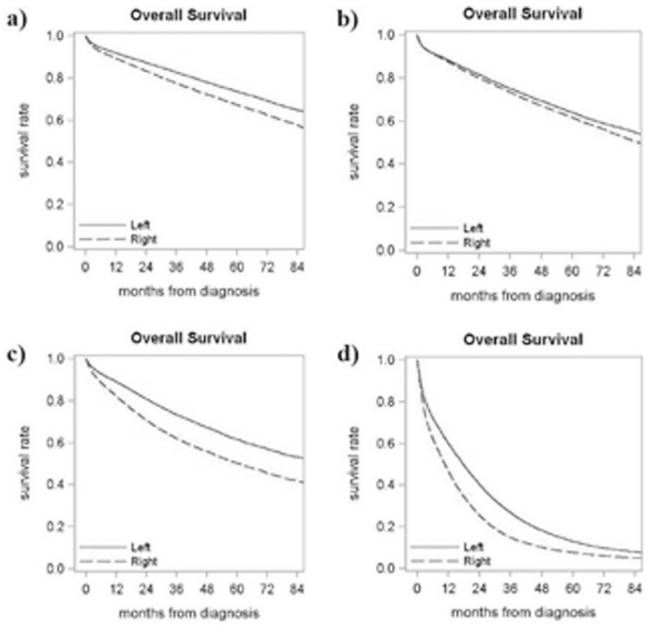


Figure 1- Kaplan Meier curves demonstrating poorer overall survival of right compared to left colon cancer at a) Stage 1 (median OS 101.2 vs. 129.3 months, p < 0.001), b) Stage 2 (median OS 85.5 vs. 98.9 months, p < 0.001), c) Stage 3 (median OS 60.8 vs. 94.3 months, p < 0.001) and d) Stage 4 (median OS 10.7 vs. 17.8 months, p < 0.001).

PT95

Interest and Intent to Take Aspirin As Chemoprevention in Colorectal Cancer Survivors A. Greenbaum,* R. Ruckman, M. Murillo, K. Flores, A. Rajput, A. Kinney. *Surgery, University of New Mexico, Albuquerque, NM.*

Introduction: An estimated 1.2 million colorectal cancer (CRC) survivors currently live in the United States. Daily, low-dose administration of aspirin (ASA) reduces recurrence and prolongs survival in CRC patients. In this study we aimed to identify patient-level factors affecting interest and intent to take ASA or other chemopreventive agents. Methods: CRC survivors were identified through the New Mexico Tumor Registry, a population-based cancer registry participating in the Surveillance, Epidemiology and End Results (SEER) program. A mailed survey was distributed with a 62% cooperation rate. Statistical analysis was performed using chi-square and logistic regression analysis (crude odds ratios (OR) and 95% confidence intervals (CI)) and significance was considered for p-values ≤ 0.05. Results: Three-hundred and five CRC survivors responded to the survey. Hispanics compromised 42% of the cohort, while 59% were Non-hispanic White. The median age was 64 (± 7.7) years and 52% were male. Overall, 51% of patients reported they were currently taking ASA or another NSAID daily. Most respondents (86%) stated they would take ASA on a regular basis if the drug would decrease their risk of recurrent cancer. There were no differences in current ASA use, intent or interest when comparing, ethnicity, place of residence and annual income. However, non-English speakers took ASA significantly less often (34% vs. 52% in English speakers; p=0.02), and were less likely to indicate interest (p=0.0002) or intent (p=0.03) to take ASA for chemoprevention. Survivors with a high school degree or less were more interested in learning about the chemopreventive benefits of ASA (OR 3.08, CI 1.35-7.07; p=0.01); however, those with more advanced education levels demonstrated higher intent to take ASA (OR 2.11, CI 1.06-4.18; p=0.048). Conclusions: Only half of CRC survivors currently take ASA daily, although high interest and intent was observed. Disparities in current ASA use, interest and intent may exist in non-English speakers and populations with a high school education or less. Interventions aimed at educating cancer survivors about ASA for CRC prevention will aid patients in informed decision-making.

PT96

Does the Addition of Biologic Agents to Chemotherapy in Patients with Unresectable Colorectal Cancer Metastases Result in a Higher Proportion of Patients Undergoing Complete Resection? A Systematic Review and Meta-analysis J. Bogach, O. Levine, L. Ruo, P. Serrano.* *General Surgery, McMaster University, Hamilton, ON, Canada.*

Background The likelihood of converting unresectable colorectal cancer (CRC) metastases to operable disease with systemic therapy is unknown. The purpose of this study was to determine the proportion of patients with unresectable CRC metastases that become resectable on combination systemic therapy, and whether biologic agents (antiantiogenics, anti-EGFR and multitargeted agents) improve the rate of resection (primary outcome). Methods We searched Medline, Embase, CENTRAL and PubMed for randomized controlled trials comparing chemotherapy and biologics (intervention) vs. combination chemotherapy alone (control) in patients with unresectable CRC metastases. Study selection, data abstraction, risk of bias and quality of evidence assessment were carried out in duplicate. Secondary outcomes included overall survival (OS) and progression free survival (PFS). Risk of bias was assessed using the Cochrane tool. Statistical heterogeneity was calculated using chi-squared and I^2. Clinical heterogeneity was explored via subgroup analyses. The quality of the evidence was assessed using GRADE. Protocol was published in PROSPERO. Results Of 7954 abstracts retrieved, 12 studies were analyzed and 8 reported the primary outcome, with 2604 intervention and 2661 control patients. The proportion of patients resected was higher in the intervention group, Relative Risk 1.36, 95% confidence interval (CI) 1.08-1.69, p=0.008. The absolute risk of undergoing resection was 48 per 1000 (control); vs. 65 per 1000 (intervention). There was no difference in OS, Hazard Ratio (HR) 0.91, 95% CI 0.82-1.01. PFS was better in the intervention group (HR 0.83, 95% CI 0.74-0.92). The risk of bias for the included studies was low. Statistical test for heterogeneity was low (I^2 was 0%, p=0.72). There was significant clinical heterogeneity, which was not explained with subgroup analyses. The quality of the evidence (GRADE) was moderate. Conclusion The addition of biologic agents to systemic chemotherapy in patients with unresectable CRC metastases improves resectability and PFS but not OS.

PT97

Practice Patterns of Molecular Profiling in Colorectal Cancer N. Nweze,* A. Nadler, S.S. Reddy, B. Luo, E.R. Sigurdson, C.S. Denlinger, W.S. El-Deiry, M. Hall, J.M. Farma. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Colorectal cancer (CRC) is a genetically heterogeneous disease. Molecular profiling (MP) using next-generation sequencing is increasingly used to personalize therapy. No guidelines currently exist regarding patient selection and optimal timing. Our goal was to describe our experience at a tertiary cancer center using MP in CRC patients. Methods: This is an IRB-approved, retrospective study in patients with CRC who underwent MP between March 2007 and August 2016. Tissue samples were sent for analysis in the following MP platforms: Foundation One, Caris and FCCC Targeted Cancer Panel (FTCP), which tests for the 50 most common mutations. Data regarding patient demographics, mutations and clinical outcomes were analyzed. Kaplan Meier methods were used for survival analysis using SPSS. Results: We evaluated 248 patients with CRC. 60.1% were male and 80.1% were white. The median age was 59.5 years. 66.5% had colon and 33.5% had rectal CA. Initial stages: stage 1 (2.8%), stage 2 (14.1%), stage 3 (22.9%), stage 4 (59.2%). 82.2% were tested via FTCP, 8.9% via Foundation One and 9.3% via Caris. 60.9% had the primary tumor tested. 5.2% had no mutations, 19% had 1 mutation, 28.6% had 2 mutations, 27% had 3 mutations and 20.2% had >4 mutations. The most common mutation guiding targeted therapy was KRAS (43.5%). 50% of patients had R0 resection and 19.3% went on to targeted therapy. 76.2% of resectable patients had a metastatic recurrence. 51.9% had targeted therapy for recurrence and/or stage 4 disease. The median time from diagnosis to MP was 9.9 months overall and 2.7 months for stage 4 patients. The median time from date of recurrence to MP was 7.7 months. Median length of follow up was 1.7 years. 14.9% had no evidence of disease at last follow up, 73% were alive with disease and 10.9% had died of the disease. Median overall survival was 55.8 months (CI 41.9 - 69.7). Conclusions: MP is utilized commonly in patients with stage 4 and recurrent CRC and occurs within 2.7 months and 7.7 months respectively. Further research is underway to evaluate if the information provided by MP improves outcomes in CRC, provides novel targets and will lead to increased clinical trial accrual.

PT98

Fluid Administration and Morbidity in Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy O.S. Eng,* S. Dumitra, M. O'Leary, M. Raoof, M. Wakabayashi, T.D. Dellinger, E. Han, S. Lee, I.B. Paz, B. Lee. *Surgery, City of Hope National Medical Center, Duarte, CA.*

Background Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal malignancies can be associated with significant complications. Randomized trials have demonstrated increased morbidity with liberal fluid regimens in abdominal surgery. We sought to investigate the association of fluid administration and morbidity in CRS/HIPEC patients at our institution. Methods Patients who underwent CRS/HIPEC from 2009-2016 were identified retrospectively from a prospectively collected institutional database. Patient demographics including perioperative fluid rates (ml/kg/h) were recorded. The comprehensive complication index (CCI) was calculated for each patient to assess perioperative morbidity. Adjusting for interacting variables, stepwise linear regression analyses were performed with CCI as the outcome variable. Results A total of 133 CRS/HIPEC patients were identified, with 38% and 37% having diagnoses of metastatic appendiceal and colorectal malignancies respectively. Mean age was 54 (IQR 47-64), and mean peritoneal cancer index was 13 (IQR 7-18). Mitomycin C and platinum-based chemotherapeutic agents were used in 72% and 28% of patients respectively. Mean intraoperative fluid (IOF) rate was 15.7 ml/kg/h (IQR 11.3-18.7). Mean CCI was 26.0 (IQR 8.7-36.2). On univariate analyses, blood loss (ml, $p<0.001$), urine output (ml, $p=0.022$), IOF rate ($p<0.001$), and PCI ($p<0.001$) were significantly associated with CCI, while age, ASA classification, and gender were not. On multivariate analysis, age (coef 0.32, CI 0.01-0.63, $p=0.043$), IOF rate (coef 1.02, CI 0.26-1.78, $p=0.009$) and blood loss (coef 0.02, CI 0.01-0.03, $p=0.003$) were independent predictors of increased CCI. In particular, patients who received greater than the mean IOF rate were associated with a 43% increase in CCI compared to patients below the mean IOF rate (31.5 vs. 22.0, $p=0.019$). Conclusion Excessive intraoperative fluid administration is associated with a significant increase in perioperative morbidity in patients undergoing CRS/HIPEC. Standardized restrictive fluid rates and protocols can potentially help mitigate morbidity in CRS/HIPEC patients.

PT99

Targeting Radiation Resistance in Colorectal Cancer Using a CD133-Targeted Oncolytic Adenovirus J. Huang,* M. Sato-Dahlman, Y. Miura, K. Jacobsen, A. Salzwedel, R.D. Madoff, J. Davydova, M. Yamamoto. *Surgery, University of Minnesota, Minneapolis, MN.*

Background: Mortality from colorectal cancer (CRC) remains high due to recurrent disease and distant metastasis. CRC stem cells overexpressing the cell surface marker CD133 contribute to therapeutic resistance, tumor initiation, and decreased survival in patients. The oncolytic adenovirus (OAd) is a promising modality of targeted therapy with selective cancer killing ability. In this study, we investigate the efficacy of targeting radiation-resistant CRC cells using a novel OAd specific for CD133. Methods: Using high-throughput screening with a recombinant adenovirus library, the CD133-targeted OAd was isolated. To establish radiation-resistant cells, two CRC cell lines (LS174T and SW480) were exposed to serial doses of fractionated ionizing radiation. The extent of radiation resistance was quantitated and flow cytometry was used to analyze CD133 expression. After treatment with OAd, cell viability of radiation-resistant cells and viral replication were evaluated. The tumor initiating capability of radiation-resistant CRC cells after OAd treatment was assessed by subcutaneous tumor formation assay in nude mice. Results: Fractionated radiation increased the surface expression of CD133 by 20-fold for LS174T cells and 4-fold for SW480 cells. In both cell lines, dose-dependent cytotoxicity was observed after the treatment of radiation-resistant CRC cells with CD133-targeted OAd, compared to non-irradiated cells (Figure 1). In addition, replication of CD133-targeted OAd increased by 2 log-folds in irradiated compared to non-irradiated cells ($p<0.05$). In vivo, treatment of radiation-resistant cells with CD133-targeted OAd abolished their tumor-forming capacity, compared to non-irradiated cells (0% vs 100% respectively, $p<0.05$). CD133-targeted OAd also decreased the tumorigenic potential of radiation-resistant CRC cells, compared to no treatment ($p<0.05$). Conclusions: CD133-targeted OAd is effective for cytotoxic killing and reduction of tumor formation in radiation-resistant CRC cells established by fractionated radiation. This targeted OAd therapy may be applicable in the adjuvant setting to address therapeutic resistance and prevent the establishment of metastasis.

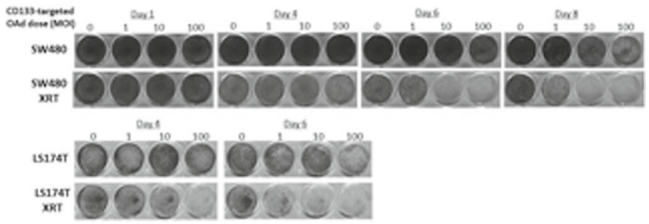
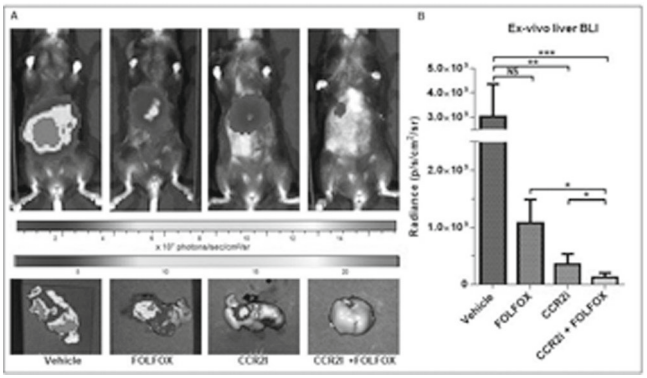


Figure 1: After treatment with CD133-targeted OAd, the cell viability of two CRC cell lines was evaluated and compared to their radiation-resistant counterparts (SW480 XRT and LS174T XRT). Cells were fixed and stained with 1% crystal violet to evaluate cell viability at the indicated time points. Compared to non-irradiated cell, dose-dependent cytotoxicity of radiation-resistant CRC cells with CD133-targeted OAd treatment is demonstrated, as indicated by increasingly white wells at all MOI with passage of time. The experiments were repeated three times and representative plates are shown. MOI, multiplicity of infection as indicated by dose of infectious viral particles per cell.

PT100

Targeting Inflammatory Monocytes in Human Metastatic Colorectal Cancer J.g. Grossman,[1]* T.M. Nywening,[1] B.A. Belt,[2] M. Ahlers,[1] W. Hawkins,[1] S.M. Strasberg,[1] P. Goedegebuure,[1] D.C. Linehan,[2] R. Fields.[1] *1. Surgery, Washington University School of Medicine, St. Louis, St. Louis, MO; 2. University of Rochester, Rochester, NY.*

Intro: Colorectal cancer (CRC) is the most common gastrointestinal malignancy. 60% of CRC patients are diagnosed with metastatic CRC (mCRC) and the 5-year survival is <20%. CCR2+ inflammatory monocytes (IM) are recruited from the bone marrow to the tumor microenvironment by the CCL2/CCR2 chemokine axis. At the tumor, they become tumor associated macrophages (TAM) and play a crucial role in promoting tumor progression, metastasis, and chemoresistance. While the importance of IM has been shown in other malignancies, little is known about their role in mCRC. Methods: Flow cytometry was performed on human and murine PBMCs, adjacent normal tissue, and tumors. Qualitative RT-PCR, ELISA, and confocal microscopy were performed for CCL2 expression. T-cell suppression assays were performed using CD14+ IM isolated from patient PBMCs and liver metastasis (LM). A murine model of CRC LM was created by hemispleen injection of luciferase-labelled MC38 CRC cells. Mice were treated with a CCR2 inhibitor and/or FOLFOX. Results: Prior to liver resection, mCRC patients have a higher percentage of IM in the peripheral blood compared to healthy donors ($p<0.0001$), and on multivariate analysis elevated monocytes were prognostic of poor survival. We also found higher levels of CCL2 in the serum of mCRC patients ($p<0.01$). Additionally, there was increased expression of CCL2 in LM compared to uninvolved tissue ($p<0.01$), with the production of CCL2 localized to mCRC cells. FACS analysis showed CCR2+ TAM were elevated in LM compared to adjacent normal liver ($p<0.05$) with a paucity of effector T-cells. CD14+ TAMs isolated from mCRC inhibited T-cell proliferation, illustrating the immune suppressive phenotype of these cells. In a murine model of CRC LM, treating mice with a CCR2 inhibitor alone or in combination with FOLFOX chemotherapy resulted in decreased tumor burden. FACS analysis of treated tumors showed increased effector T-cells in mice treated with CCR2 inhibitor. Conclusion: IM are involved in the progression of mCRC. Targeting these immunosuppressive cells with a CCR2 inhibitor decreases tumor burden in a murine model. This represents a potential novel treatment for mCRC.

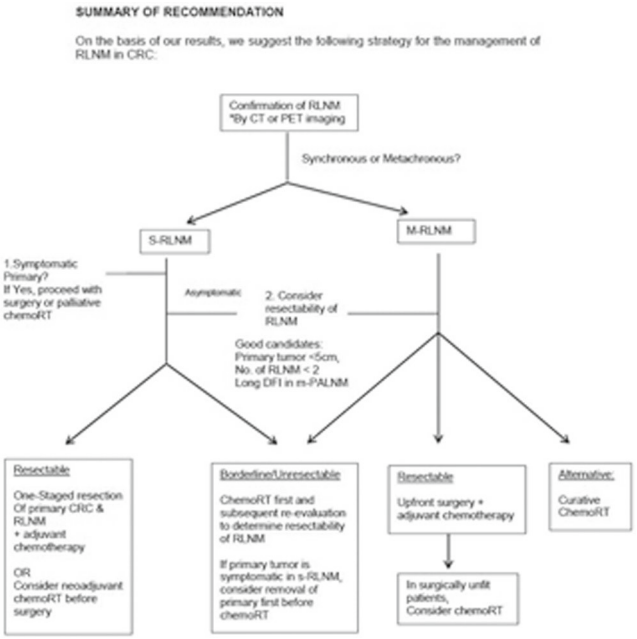


Reduction of tumor burden by CCR2-blockade in a murine liver metastasis model. (A)Representative in-vivo(above) and ex-vivo (below) BLI images of MC38 liver metastasis mice treated with CCR2i, FOLFOX, CCR2i + FOLFOX, or vehicle (n=15 mice/group). (B) Quantification of ex-vivo liver BLI. (*p<0.05, **p<0.01, ***p<0.001)

PT101

Management of Extra-regional Retroperitoneal Lymph Node Metastasis in Colorectal Patients: A Systemic Review J. Wong,* G.H. Tan, M. Teo. *Surgical Oncology, National Cancer Centre, Singapore, Singapore.*

Introduction Retro-peritoneal lymph node (RLN) involvement occurs in up to 2% of colorectal cancer (CRC) patients. While resection for isolated hepatic and pulmonary metastases in CRC is standard practice, the role of RLN dissection (RLND) has not been established and remains a controversy. Given the lack of randomised trials and high quality evidence, we aim to perform a systemic review of the current literature to evaluate evidence for or against surgery in the management of RLN metastasis (RLNM) in CRC. We also hope to define a management strategy for both synchronous and metachronous RLNM (s- and m-RLNM) based on the reported survival and morbidity outcomes. Methodology A literature search of PubMed, Ovid MEDLINE, and EMBASE databases was conducted for studies reporting on the management of RLNM in CRC. Studies including patients with s- and m-RPLN were included, and studies with patients with other sites of metastases were excluded. The study was conducted in accordance to the PRISMA guidelines Results Eighteen retrospective, single-centre studies were included. The reported incidence of isolated RLNM ranged from 1.3 to 1.7%. A total of 370 patients with RLNM were evaluated, of which 145 had synchronous, and 225 had metachronous RLNM. For s-RLNM, the 5-year overall survival (OS) after metastatectomy ranged from 22.7% to 33.9%. For m-RLNM, the 5-year OS ranged from 15 to 60%; median OS was 34 to 40 months in the RLND group versus 3 to 14 months in patients who did not undergo RLND. A longer disease free interval (DFI), tumour size < 5cm, infra-renal location of RLNM and R0 resection were predictors of a favourable OS. Overall surgical morbidity was 7.8 to 33%. In m-RLNM patients who received curative chemoradiation therapy, median OS was 37 to 41 months with the largest study reporting a 5-year OS of 36.4%; no high grade toxicity was reported. Conclusion Upfront surgery for resectable RLNM in CRC confers acceptable survival and morbidity outcomes. Patients with long DFI, low volume infra-renal RLNM should be considered for surgical resection in a multi-disciplinary setting. Chemoradiation therapy may be considered in borderline or unresectable cases.



PT102

Multidisciplinary Tumor Conference Changes Clinical Management of Rectal Cancer G. Karagkounis,* L. Stocchi, I. Lavery, D. Liska, E. Gorgun, S. Amarnath, A. Khorana, M. Kalady. *Cleveland Clinic, Cleveland, OH.*

Background: Presentation of rectal cancer cases at a multidisciplinary tumor conference (MTC) is a required standard for the newly formed National Accreditation Program for Rectal Cancer. However, its impact on clinical decision-making remains incompletely defined. Our aim was to determine the frequency and manner in which MTC changed the management of patients with rectal cancer at a tertiary academic center. Methods: All rectal cancer cases presented at the weekly Colorectal Cancer MTC between July 2015 and June 2016 were prospectively included. Patient demographics and clinical information were recorded. The presenting physician completed a uniform written questionnaire outlining their plan before and after the MTC discussion, and any changes in management as a result of the discussion. Imaging and pathology were reviewed for each case at MTC and consistency with prior interpretation was recorded. Results: 234 unique initial rectal cancer cases were included. Survey responses were obtained for 212 cases (91%). The mean patient age was 58.3 years. 37 patients (16%) had Stage IV disease and 20 (9%) had locally recurrent cancer. There was a documented change in plan as a result of the MTC discussion in 70 of 212 (33%) cases surveyed, including 22 cases (10%) in which the presenting physician had a “definitive plan” prior to the MTC. Changes in management included a change in therapy or change in therapy sequence in 45 cases (64%), and recommendation of further evaluation in 26 cases (37%). Change in management following MTC did not vary by surgeon experience: it occurred in 31.4%, 37.2% and 29.8% of cases presented by surgeons with <10, 10-20, and ≥20 years of experience respectively (Chi-square p=0.71). The imaging or pathology review at MTC resulted in a different interpretation than previously reported in 23% and 12% of cases, respectively. Conclusions: MTC changes clinical management for a significant portion of rectal cancer patients at a tertiary center, independent of the presenting surgeons’ years of clinical experience. Our results highlight the utility of multidisciplinary rectal cancer care and support the MTC standard for the National Accreditation Program for Rectal Cancer.

PT103

Peritoneal Metastases are Underrepresented in Published Clinical Trials of Metastatic Colorectal Cancer J. Tseng,* D.S. Bryan, E. Poli, M.R. Sharma, B. Polite, K.K. Turaga. *University of Chicago, Chicago, IL.*

Introduction Peritoneal metastases occur in 6-15% of patients with metastatic colorectal cancer. Non-invasive detection of peritoneal metastases is difficult given limitations in discrimination of cross sectional imaging. We hypothesized that patients with peritoneal metastases are underrepresented in clinical trials. Methods Randomized controlled trials of systemic chemotherapy for metastatic colorectal cancer between 2003-16 were included after a PubMed search. Articles were restricted to those published in leading oncology journals and with ≥100 patients (total). Protocol designs were hand searched to identify whether clinical trials explicitly included or reported on patients with peritoneal metastases. Results Of 72 clinical trials identified, 7 (10%) studies specifically reported inclusion of peritoneal disease (Table 1). Of 45,783 patients enrolled in all trials, 670 patients (1.5%) specifically had peritoneal metastases. Response for peritoneal disease was measured using Response Evaluation Criteria in Solid Tumors (RECIST) criteria in 6 (of 7, 86%) and modified World Health Organization (WHO) criteria in 1 but not reported in the final manuscript or supplementary material. Peritoneal specific outcomes were not reported in any study. No studies included metastatic colorectal cancer patients with peritoneal metastases alone. Conclusions Patients with peritoneal metastases are underrepresented in published clinical trials. Specific efforts to include patients, measure burden of disease and response to therapy and report peritoneal specific outcomes are essential to draw generalizable inferences.

Table 1

Author Journal/Year	Treatment Arms	Measurement of Response	# Patients in Treatment Arms	# Patients with Peritoneal Disease	% Patients with Peritoneal Disease
Ducreux et al. Lancet Oncology 2011	5FU + LV vs. FOLFOX vs. FOLFIRI vs. FOLFOX or FOLFIRI	Modified WHO criteria	410	63	15.4%
Hong et al. Lancet Oncology 2012	Capecitabine + Oxaliplatin vs. S-1 + Oxaliplatin	RECIST	340	73	21.5%
Jonker et al. NEJM 2007	Cetuximab + Best Supportive Care vs. Best Supportive Care	RECIST	572	45	7.9%
Seymour et al. Lancet 2007	5FU/Irinotecan vs. 5FU then 5FU/Irinotecan vs. Oxaliplatin vs. 5FU/Irinotecan	RECIST	2135	288	13.5%
Seymour et al. Lancet Oncology 2013	Panitumumab + Irinotecan vs. Irinotecan	RECIST	460	99	21.5%
Tournigand et al. Lancet Oncology 2015	Avastin vs. Avastin + Erlotinib	RECIST	700	83	11.9%
Yoshino et al. Lancet Oncology 2012	TAS-102 vs. Placebo	RECIST	169	28	16.6%

PT104

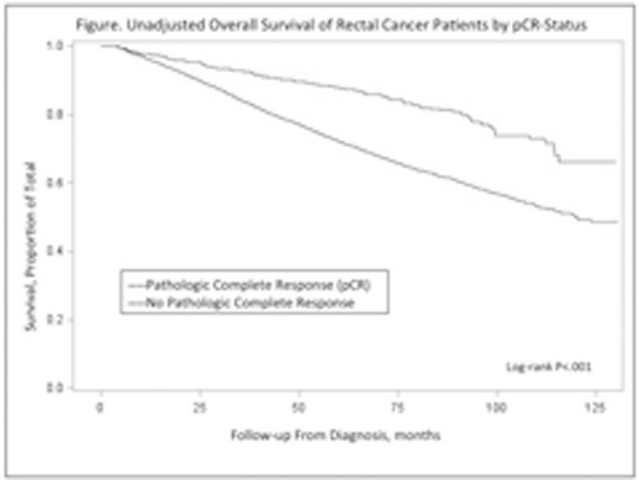
Evaluation of the Macroscopic Quality of the Mesorectum in Patients Undergoing Open, Laparoscopic, or Robotic Rectal Cancer Surgery S. Tsukamoto,* H. Ochiai, D. Shida, J. Mazaki, Y. Kanemitsu. *Colorectal Surgery, National Cancer Center, Tokyo, Japan.*

Background: Macroscopic completeness of mesorectal fascia integrity may serve as a factor for surgery-related prognosis or an indicator of the quality of total mesorectal excision (TME). Patients who had an incomplete mesorectal resection after surgery in curative intent reportedly have an increased risk of local recurrence, as compared with patients who had a complete resection. Aim: This study aimed to evaluate the macroscopic completeness of mesorectal resection after open, laparoscopic, or robotic TME. Methods: 106 patients who underwent radical surgery for rectal cancer between 2014 and 2016 were considered eligible. The patients were classified into three groups, open, laparoscopic, and robotic surgery groups. A pathologist retrospectively examined mesorectal grade (MG) based on three pictures taken postoperatively. The quality of the mesorectum was graded as poor, moderate, or good according to the Dutch TME trial, and the mesorectal fascia was evaluated as rough or smooth. Results: The open surgery group included more pathologically advanced cases than laparoscopic and robotic surgery groups, according to tumor depth (open surgery: T1 in 5, T2 in 8, T3 in 16, T4 in 1; laparoscopic surgery: T1 in 32, T2 in 6, T3 in 5; robotic surgery: T1 in 24, T2 in 2, T3 in 7). In the open surgery group, 3 specimens were classified as poor, 5 as moderate, and 22 as good. In the laparoscopic surgery group, no specimen was classified as poor, 8 as moderate, and 35 as good. In the robotic surgery group, 1 specimen was classified as poor, 0 as moderate, and 32 as good. The rate of good MG was significantly higher in the robotic surgery group (73.3% vs. 81.4% vs. 97.0%; p=0.03). The mesorectal fascia was evaluated as smooth in 10 (33%) specimens in the open surgery group, 22 (51.2%) in the laparoscopic surgery group, and 20 (60.1%) in the robotic surgery group. Conclusion: The quality of specimens was higher in the robotic surgery group compared to the laparoscopic surgery group, although they had similar tumor stage profiles. These results are likely attributed to superior wrist-like movements of robotic instruments that allow for fine dissection.

PT105

Long-term Survival in Patients with a Pathological Complete Response After Chemoradiotherapy for Rectal Cancer: A National Study C. Ellis,* C. Samuel, K. Stitzenberg. *Department of Surgery, University of North Carolina, Chapel Hill, NC.*

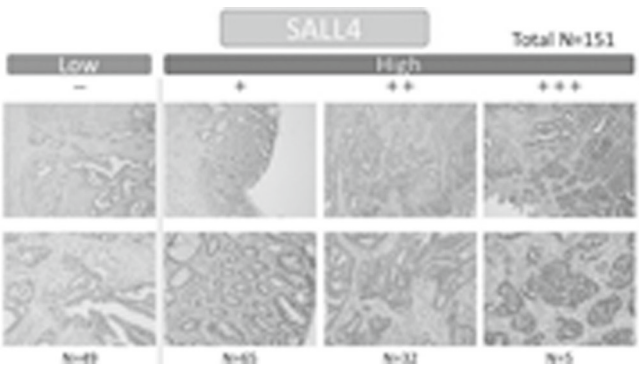
Background: Pathological complete response (pCR) rates after neoadjuvant chemoradiotherapy (nCRT) for rectal cancer are reported between 11.4-27% and are associated with improved survival for compared to survival after incomplete response to nCRT. However, these data come from clinical trials and small series, which limits generalizability. Objective: We sought to determine the association between pCR-status and long-term overall survival (OS) on a population level for clinical stage II/III rectal cancer patients. Methods: Using the National Cancer Database, our study included individuals with clinical stage II/III rectal adenocarcinoma treated with nCRT (≥ 4500 cGy) plus proctectomy from 2004-2008. OS was compared by pCR-status using Kaplan-Meier Analysis and an Adjusted Cox proportional hazards model, controlling for patient-, tumor-, and facility-factors. We also examined characteristics associated with pCR-status using logistic regession models, OS. Results: Overall, 9.3% (n=760) of the cohort had a pCR. Individuals with Medicaid/uninsured (aOR 0.57 95% CI 0.42 to 0.77) or treated at low-volume centers (aOR 0.61, 95% CI 0.50 to 0.74) were less likely to have a pCR compared to those with Private/Medicare insurance and those treated at high-volume centers, respectively. At 5 years post-diagnosis, 87% of the pCR-group were alive compared to 72% of the non-pCR-group, Figure. On adjusted analyses, pCR was associated with improved OS, HR 0.50, 95%CI 0.42-0.59. Conclusion: In a national sample of rectal cancer patients, the proportion of individuals with a pCR was lower than reported in other series. Social determinants, such as insurance status and facility volume, were associated with lower pCR rates even when limiting our cohort for long-course radiation. This suggests there may have been interruptions or other limitations to the nCRt for these patients. pCR was associated with similar improved OS as previously reported. Efforts that address care received by individuals with low-socioeconomic status, who are less prone to achieving a pCR, could narrow the disparities gap in long-term survival of rectal cancer patients.



PT106

Histopathological Significance of Sal-like Protein 4 Expression in Colorectal Cancer H. Takahashi,* N. Haraguchi, J. Nishimura, T. Hata, C. Matsuda, H. Yamamoto, T. Mizushima, Y. Doki, M. Mori. *Gastroenterological Surgery, Osaka University, Suita, Japan.*

Background Sal-like protein 4 (SALL4), a homolog of the Drosophila homeotic gene spalt, is a zinc finger transcription factor required for proliferation and maintenance of pluripotency through interactions with OCT3/4, SOX2, and NANOG. SALL4 is indispensable for generation of organs and play important role in self-renewal and pluripotency of embryonic stem cells. However, the relationship between SALL4 and colorectal cancer have not been well studied. Materials and Methods All experimental protocols described in this study were approved by the Institutional Ethical Review Committee. This retrospective study consecutively enrolled 151 patients. The associations between SALL4 expression in colorectal cancer specimens and clinicopathological features including prognosis were assessed by immunohistochemistry using Mouse monoclonal anbibody (SALL4 monoclonal antibody (M03), clone 6E3) was obtained from Abnova (Taiwan). Results High expression of Sall4 was observed in 107 patients. SALL4 expression levels were positively correlated to serum CEA levels, distant metastasis, worse recurrence free survival, and overall survival. Using cox proportional hazards models for recurrence free survival which is factor of importance for decision for performing adjuvant chemotherapy, depth of tumor invasion (hazard ratio (HR) = 4.29, 95% confidence interval (CI): 1.75-5.68), lymph node metastasis (3.43, 1.54-8.43), lymphatic invasion (5.48, 1.62-34.10), venous invasion (3.43, 1.56-7.44), serum CEA levels (2.88, 1.31-6.76), and SALL4 (4.48, 1.55-18.91) were significant factor in univariate analysis, and only SALL4 expression was remained in multivariate analysis (HR = 4.10, 95%CI = 1.36-17.67, P < 0.01). Cox proportional hazards models for overall survival also indicated that SALL4 expression levels were independent factor for worse prognosis as well as depth of tumor invasion. Conclusions Although this is single institutional study on limited number of patients, Sall4 expression levels in resected specimens were novel prognostic factor for colorectal caner.



PT107

The Ovary as a Biological Sanctuary for Wasmannian Mimicry of Colorectal Metastasis C. Ong,[1]* N. Shannon,[1] Q. Xuan,[1] W. Ng,[1] J. Hendrikson,[1] C. Chia,[1] G.H. Tan,[1] T.K. Lim,[2] O. Kon,[1] K. Soo,[1] M. Teo.[1] *1. National Cancer Centre, Singapore, Singapore; 2. Singapore General Hospital, Singapore, Singapore.*

Introduction The last 2 decades have seen a paradigm shift in the prognosis of patients with colorectal metastasis. However, the conundrum in managing metastatic disease lies in the deficiency in understanding metastatic tumour biology. Focusing on transcoelomic metastasis of colorectal origin, we aim to elucidate the signalling pathways dictating biological behaviour in different metastatic sites. Methods Tissue samples were collected from cytoreductive surgery, enabling matching of primary tumours, peritoneal or ovarian metastases from 4 patients. After pathologic review, laser capture microdissection was performed to separate tumour and stroma components. An optimized genomic library generation pipeline was performed to generate RNA sequencing data (n=26). Gene set enrichment analysis (GSEA) was used to compare dysregulation of molecular pathways in ovarian metastasis (Krukenberg tumours) versus peritoneal metastases. Separate profiles were generated for tumour and stroma. Results RNA sequencing of stroma and epithelial cancer cells uncovered multiple differentially expressed genes. qPCR verification confirmed the high fidelity of the sequencing process. GSEA revealed a hyperproliferative transcriptomic signature in Krukenberg tumours relative to peritoneal metastasis. Consistent with the known biology of colorectal tumours and peritoneal metastasis, the KRAS signalling pathway was significantly upregulated (Normalised enrichment score 1.56, P<0.01). Intriguingly, Krukenberg metastasis exhibited a divergent transcriptomic signature, relying on estrogen and mTOR signalling (Normalised enrichment score 1.37 (P<0.01) and 1.32 (p<0.05) respectively). Moreover, stroma derived from the ovary harbouring Krukenberg metastasis was enriched in NOTCH signalling relative to peritoneal metastasis. Conclusion It is well known that NOTCH signalling regulates normal follicular development in the ovary. Our study demonstrates that colorectal cancer cells harnesses the potential of normal ovarian physiology to enhance its own survival via additional and unique signalling stimuli. This finding provides potential avenues for novel therapeutic strategies in synchronous transcoelomic metastasis.

PT108

A Novel Approach For Continence Preservation with Intersphincteric Resection in Ultra-Low Rectal Cancer M.M. Khafagy,* W. Gawad. *National Cancer Institute, Cairo, Egypt.*

Introduction:The aim of this study was evaluation of oncolgic & functional outcome of this approach for Intersphincteric Resection with continence preservation through saving part of the anal canal followed by coloanal anastomosis for carcinoma of the distal rectum and the Ano-rectal junction. Methods:From January 2008 to June 2016, 50 patients were prospectively enrolled in this study. All patients had an infiltrating adenocarcinoma 5cm or less from the anal verge.6 patients (12%) were stage I,24 patients (48%) stage II and 20 patients (40%) stage III. Long Course neo-adjuvant chemo-radiation was applied for 32 patients (65%) with locally advanced lesions stages IIb &III. Post-operative chemoradiation was given to 18 patients (35%). All patients underwent Intersphincteric resection through a combined abdominal and a peri-anal approach with preservation of anal sensation by sparing nearly half of the anal canal with the pectinate line on the contralateral side of the tumour with a safety margin of at least 1cm on both sides of the lesion and (1-2)cm distal margin. Results M: F Ratio was 1.8:1. Tumors were located between 2.5 -4.5 (mean 3.6) cm from the anal verge. one case of postoperative mortality from anaerobic pelvic sepsis. Surgical morbidity occurred in 3 patients with anastomotic leakage, one healed spontaneously, the other 2 patients underwent temporary colostomy. After 72 months follow up (range: 24-120), local recurrenceate was documented in 9 % of patients. One patient developed left inguinal node recurrence 3 years after surgery & underwent ilio-inguinal nodal dissection. One patient died of distant metastasis. The 5 years actuarial survival rate was 79% (Kaplan-Meier). Circumferential margin involvement CRM was evident in 21%of stage II & 35% in stage III. Continence was assessed subjectively according to Kirwan scale, 80 % of patients were continent (Kirwan scale:1) while four patients suffered from minor soiling. Conclusion:The preliminary results indicates that the suggested technique may be considered a valid option to abdomino-perineal resection for selected rectal tumors situated at the distal rectum and the Ano-rectal junction.

PT109

Salvage Therapy for Recurrent Mucinous Appendiceal Adenocarcinoma Following Complete Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy T.E. Grotz,* R. Royal, P.F. Mansfield, M.J. Overman, G.N. Mann, D.m. Cox, K. Beaty, S. Rafeeq, A. Matamoros, M.W. Taggart, K.F. Fournier. *MD Anderson Cancer Center, Houston, TX.*

Background: Mucinous appendiceal adenocarcinoma has a propensity for recurrence despite complete cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Outcomes, prognostic factors and optimal salvage therapies after recurrence need to be better defined. Methods: Single institution review of a prospectively maintained database of 231 patients with mucinous appendiceal adenocarcinoma undergoing complete CRS and HIPEC. Results: After a median follow up of 54 months 94 (41%) patients developed recurrence. The median time to recurrence was 19 (13.5-29.5) months. Recurrences were unifocal in 47 (50%) patients and multifocal in 47. The most frequent unifocal recurrences were to the pelvis (21, 45%) and abdominal wall (10, 21%). Twenty four (25%) patients were treated with chemotherapy alone, 25 (27%) underwent repeat CRS and HIPEC, 31(33%) underwent CRS alone, 5 (5%) underwent palliative bypass and 9 (10%) patients received supportive therapy alone. The median OS for those treated with systemic chemotherapy, CRS and HIPEC, CRS without HIPEC, palliative bypass and supportive care were 46, 72, 96, 15 and 14 months respectively. In univariate analysis well and moderate grade tumor, absence of signet ring cells, ECOG status 0-1, focal recurrence and treatment with CRS +/- HIPEC were associated with improved OS. In multivariate analysis CRS +/- HIPEC was the only independent predictor of improved OS (Figure 1). Patients who underwent CRS +/- HIPEC were more likely to have well and moderate grade tumors (p=0.002) without signet ring cells (p<0.001) and unifocal disease (p=0.006) than those managed non-surgically. Patients undergoing CRS alone were more likely to have unifocal recurrences compared to those treated with CRS and HIPEC (p< 0.001). However, the DFS and OS were comparable for patients treated with CRS with and without HIPEC. Conclusion: Repeat CRS +/- HIPEC confers a survival benefit for patients who relapse following previous CRS and HIPEC. This benefit may be most pronounced for those with preserved functional status, low grade histology, absence of signet ring cells and unifocal recurrence.

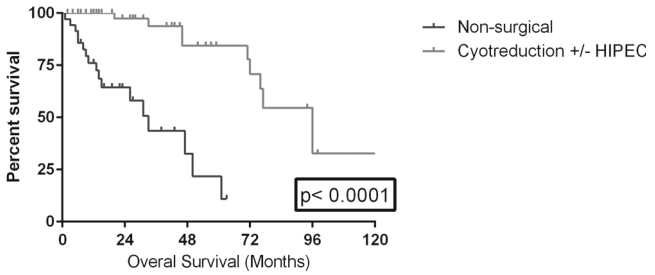


Figure 1: Kaplan Meier curve demonstrating signficant improvement in overall survival (OS) for patients with recurrent mucinous appendiceal adenocarcinoma treated with cytoreductive surgery (CRS) with or without hyperthermic intraperitoneal chemotherapy (HIPEC) compared to non-operative therapy. (Log rank test p < 0.001)

PT110

Preoperative Predictive Score (PROPS) for Unresectability in Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Colorectal Cancer Peritoneal Metastases: A Comparison with Current Selection Tools Z. Yong,[1] G.H. Tan,[2]* N. Shannon,[2] M. Teo.[2] *1. Singapore General Hospital, Singapore, Singapore, Singapore; 2. Division of Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore, Singapore.*

Introduction Presently, 20-30% of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS and HIPEC) result in open-and-close laparotomy. Current selection tools such as the peritoneal surface disease severity score (PSDSS) and the prognostic score (PS) are established from studies that excluded unresectable cases and included intraoperative findings. This results in difficulty to exclude unresectable cases in the preoperative setting. We conducted our study by including all patients who underwent CRS and HIPEC regardless of outcome and developed a preoperative predictive score (PROPS) for unresectability and compared it with PSDSS and PS. Methods Between April 2004 to May 2014, 56 patients with colorectal cancer peritoneal metastases were eligible for CRS and HIPEC, of which 7 patients (13%) underwent open-and-close laparotomy. The first 31 patients (discovery set) were used to generate the model and the subsequent 25 patients were used to validate it (validation set). Using the discovery set, univariate analysis identified significant variables (p<0.1) and PROPS was developed from the approximated beta-coefficient values from multivariate analysis. PROPS, PSDSS and PS were applied to the validation set to generate a receiver operating characteristic curve to calculate its accuracy. Results PROPS have 9 variables: (i) poor tumour biology (1 point each): previous inadequate resection, underwent multiple lines of chemotherapy, and poorly differentiated or signet cell histology; (ii) heavy tumour burden (2 points each): abdominal distension, palpable abdominal mass, and computed tomography findings of ascites, small bowel disease and omental thickening and (iii) active tumour proliferation (2 points): elevated tumour markers. Using the validation set for unresectability prediction, PROPS achieved 86% accuracy, PSDSS 85% and PS 73%. Conclusion PROPS is equally effective in predicting unresectability as PSDSS but has the added advantage of using solely preoperative factors which may help guide selection in the preoperative setting.

PT111

A Comparison of Outcomes After Surgical Treatment of Colorectal Liver and Colorectal Peritoneal Metastases Over a 12-Year Period W. Wang,* G.H. Tan, C. Chia, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Approximately 50% of patients with colorectal cancer(CRC) develop colorectal liver metastases(CLM), while 10-25% develop colorectal peritoneal metastases(CPM). In CLM, hepatectomy is the treatment of choice while in CPM, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) benefit a selected group of patients. Survival outcomes after hepatectomy in CLM patients and CRS and HIPEC in CPM patients treated over a 12-year period were compared in this study. Methods: Patients with CLM and CPM who underwent hepatectomy and CRS/HIPEC respectively between Jan 2003 and Sep 2015 were included in this study. Demographic and clinicopathological data were retrospectively collected from clinical charts and electronic records. Overall (OS) and disease-free survivals (DFS) were compared between the 2 groups. Results: 280 CLM patients who underwent hepatectomy and 57 CPM patients who underwent CRS/HIPEC were followed up for a median of 45 and 30.5 months respectively. There were no differences in age, sex and race but CPM patients underwent a longer surgery(460min vs 300min, p<0.001), had more intraoperative blood loss(800ml vs 300ml, p<0.001) and a longer hospital stay(12 vs 6 days; p<0.001). We achieved R0 resection in 79.3% (222 of 280) in the CLM group and completeness of cytoreduction (CC) score 0 or 1 in 98.3% (56 out of 57) in the CPM group. Median OS was not reached in the CPM group but median DFS was 15 months. Median OS and DFS for the CLM patients were 70 and 19 months respectively. Kaplan-Meier curves showed a shorter DFS in CPM patients (p=0.011) but no difference in OS (p=0.531)(Figure 1). 32 out of 43(74.4%) CPM patients who recurred had distant metastases while the remaining recurred intraperitoneally. Discussion: There continued to be no significant differences in OS between CLM and CPM patients after hepatectomy and CRS/HIPEC respectively, as was reported in our initial experience. CPM patients had shorter DFS and this could be improved with better preoperative selection for patients with a lower risk of distant failure.

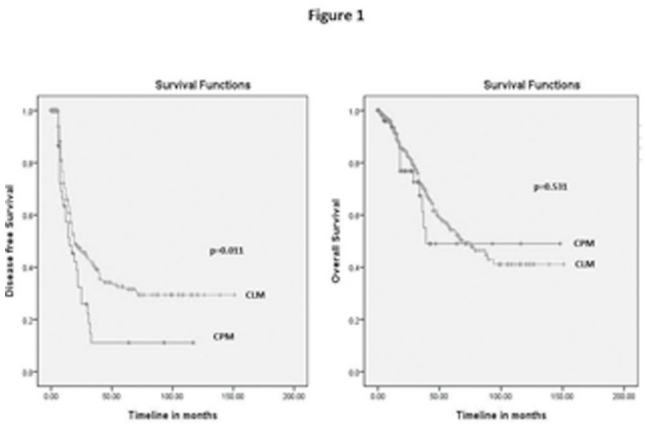
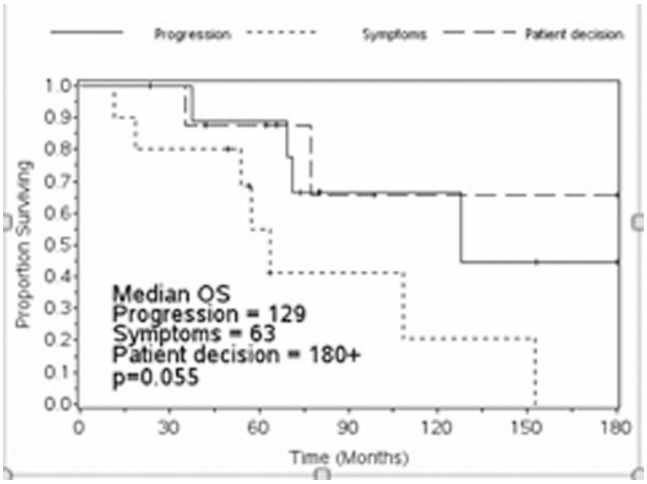


Figure 1: Kaplan-Meier curves comparing DFS and OS between CPM patients and CLM patients



PT112

Role of Expectant Management in Patients with Recurrent Peritoneal Surface Disease After Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy for Low-Grade Appendiceal Neoplasms M. Garland,* G. Russell, K. Cummins, E.A. Levine, K. Votanopoulos, P. Shen. *surgery, Wake Forest University School of Medicin, Winston Salem, NC.*

Cytoreduction (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is the treatment of choice for patients with peritoneal surface disease from low-grade appendiceal neoplasms. Though repeat surgery has been shown to be beneficial when disease recurs, the timing of intervention is not well-defined. A prospectively maintained database of patients undergoing CRS/HIPEC from 1991-2016 was used to identify patients with low-grade appendiceal tumors and recurrence of disease. They were divided into 3 groups: 1) Immediate repeat CRS/HIPEC within 3 months of recurrence, 2) Delayed repeat CRS/HIPEC greater than 3 months from recurrence, and 3) Patients who did not undergo repeat CRS/HIPEC. Factors associated with immediate surgery were analyzed, as well as reasons for delayed intervention. There were142 patients with recurrence of which 46 (32.4%) were R0/R1, 57 (40.1%) were R2a, and 39 (27.5%) were R2b resections. The median time to recurrence was 13.9 months (range, 1.1 - 152.4). Forty-five (31.7%) patients had a repeat CRS/HIPEC, with 17 (38%) immediate and 28 (62%) delayed. Median time to surgery from recurrence in the immediate and delayed groups were 1.3 (range, 0 - 2.5) and 6.1(range, 3.02 - 70.8) months, respectively. Median overall survival (OS) from first CRS/HIPEC for the immediate, delayed, and no surgery groups were 136, 108, and 49 months, respectively (p=0.0001). Significant predictors for immediate repeat surgery versus observation were younger age (p=0.001), prior R0/R1 resection status (p<0.0001), and lower rate of complications after first surgery (p=0.042). Factors that led to delayed repeat surgery were symptoms (36%), radiologic progression (36%), and patient decision (29%). Patients with symptoms trended towards worse OS (Figure). Younger patients who had a complete cytoreduction and good postoperative recovery after their first CRS/HIPEC can undergo immediate repeat surgery for recurrent disease with long-term OS. Other patients can be observed and undergo delayed repeat surgery with similar OS, unless they become symptomatic.

PT113

Adjuvant Chemotherapy Following Pathologic Complete Response Improves Long-term Survival in Rectal Cancer: A Propensity Score Matched Analysis A.A. Mokdad,* S. Huerta, R. Minter, J.C. Mansour, M.A. Choti, P.M. Polanco. *Surgery, University of Texas Southwestern, Dallas, TX.*

Introduction: The role of adjuvant chemotherapy following resection in patients with rectal cancer that achieve pathologic complete response (pCR) after neoadjuvant therapy is unclear. Current data have been limited by small sample size series. This study examined the impact of adjuvant chemotherapy following pCR on overall survival in a national cohort of patients. Methods: Patients with rectal adenocarcinoma were identified in the National Cancer Data Base between 2006 and 2012. Those with locally advanced tumor (clinical stage II or III) that achieved pCR (defined as ypT0N0 in surgical specimens) after neoadjuvant chemoradiotherapy (nCRT) were included in the study. We matched by propensity score patients that received adjuvant chemotherapy (ACT) and patients that did not receive postoperative treatment (no-ACT) controlling for demographic as well as perioperative patient and tumor characteristics. Overall survival was compared using a Cox proportional hazards model. Results: We identified 2,543 patients (ACT: 732, no-ACT: 1,811 patients) with resected locally advanced rectal adenocarcinoma that achieved pCR after nCRT. Among patients that received ACT, 711 were matched with 711 patients in the no-ACT group. Adjuvant chemotherapy was associated with improved overall survival compared to no-ACT (hazard ratio[HR] = 0.46, 95% confidence interval [CI] = 0.29 – 0.75, Figure 1). Overall survivals at 1, 3, and 5 years in the ACT and no-ACT groups were 100% vs 98% (P=0.1), 98% vs 94% (P<0.01), and 94% vs 89% (P<0.01), respectively. In subgroup analyses, adjuvant chemotherapy improved overall survival in patients with clinical stage II (HR = 0.43, 95% CI = 0.22 – 0.85) as well as stage III tumor (OR = 0.50, 95% CI = 0.26 – 0.98). Among patients that received adjuvant chemotherapy, there was no difference in overall survival between single agent and multiagent regimens (HR = 1.37, 95% CI = 0.57 – 3.29). Conclusions: Adjuvant chemotherapy may provide a small long-term survival benefit in patients with resected locally advanced rectal cancer and pCR after nCRT.

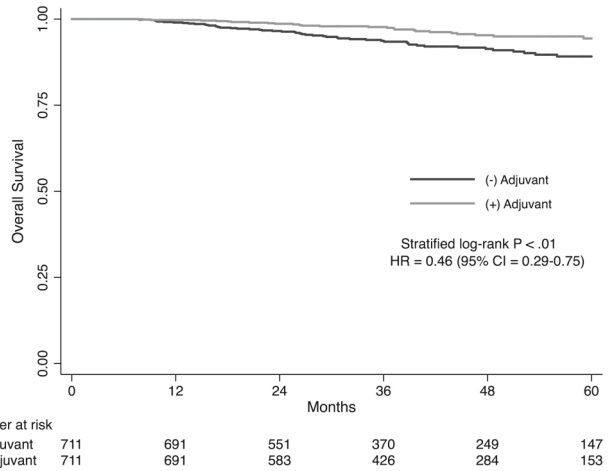


Figure 1. Kaplan-Meier curve for overall survival according to receipt of adjuvant therapy in a propensity score matched dataset. HR, Hazard ratio.

PT114

Utilization of Primary Chemoradiotherapy for Anal Squamous Cell Carcinoma in the Elderly: An Analysis of the NCDB B.M. Motz,* P.D. Lorimer, K.K. Walsh, I.N. Perry, D. Boselli, R.L. White, J.C. Salo, J. Hill. *Department of Surgery, Levine Cancer Institute, Charlotte, NC.*

Introduction: Definitive chemoradiotherapy (CHEMORT) is the treatment of choice for anal squamous cell carcinoma (SCC), while surgery is typically reserved for salvage therapy. Patients who are frail due to advanced age or medical comorbidities often have difficulty completing therapy. The National Cancer Database (NCDB) was used to evaluate trends in the utilization and completion of definitive CHEMORT for anal SCC. Methods: The NCDB was queried for patients with anal SCC (2004-2012). Patients younger than 50 and those with in situ or metastatic disease were excluded, as were those with incomplete chemotherapy (CHEMO) or radiation (RT) treatment data. The primary outcome was defined as completion of CHEMORT. Secondary outcomes, such as requirement of salvage surgical therapy were also assessed. Statistical analyses include Chi-square, univariate and multivariable logistic regression. Results: 11918 patients were identified. 5907 patients (49.5%) did not complete recommended CHEMORT. 9862 (82.8%) received CHEMO, 6011 (61.0%) of whom completed RT with dosage >45Gy. 2056 patients (17.3%) failed to receive CHEMO, of whom 1387 (67.6%) did not receive RT and only 377 (18.3%) completed RT. Factors significantly associated with failure to complete therapy on multivariable analysis include: older age at diagnosis, higher Charlson-Deyo score, earlier year of diagnosis, male gender, and earlier clinical T and N stages (Table 1). 41.7% of patients who did not complete CHEMORT ultimately required salvage surgical therapy, versus 25.1% of patients completing CHEMORT (OR: 2.14 95% CI [1.97, 2.31], p<0.01). Conclusions: Approximately half of patients older than 50 years of age with anal SCC failed to complete definitive CHEMORT, and 11.6% were not treated with CHEMORT at all. This study highlights the negative impact of patient frailty on the ability of patients to receive optimal therapy, which in this case resulted in more operative interventions. Medical optimization of older patients with more comorbidities in order to improve utilization of CHEMORT is one possible area of improvement in the management of anal SCC.

Table 1: Multivariable analysis of covariate influence on failure to complete chemoradiotherapy (p<0.05 in each instance)

	Multivariable Logistic Regression	
Covariate	Odds Ratio	95% Confidence Interval
Age at Diagnosis	1.023	[1.018, 1.027]
Year of Diagnosis	0.91	[0.894, 0.925]
Gender		
Female	0.89	[0.811, 0.978]
Male	referent	
Charlson-Deyo Score		
0	0.72	[0.595, 0.872]
1	0.749	[0.602, 0.932]
2	referent	
Clinical T Classification		
T1	referent	
T2	0.604	[0.542, 0.674]
T3	0.638	[0.558, 0.729]
T4	0.649	[0.542, 0.778]
Clinical N Classification		
N0	referent	
N1	0.636	[0.547, 0.74]
N2	0.632	[0.548, 0.729]
N3	0.734	[0.617, 0.872]

PT115

Minimally Invasive Surgery Improves Time to Chemotherapy in Colon Cancer: Compliance to the American College of Surgeons Commission on Cancer Quality Metric S. Dumitra,* R. Nelson, V. Zheleva, M. Raoof, L. Lai. *City of Hope, Duarte, CA.*

Introduction: One of the American College of Surgeons Commission on Cancer (ACS CoC) quality measures in colon cancer is receipt of chemotherapy (CT) in Stage III disease within 120 days of diagnosis. Minimally invasive surgery (MIS) has been associated with faster recovery times. The aim of this study is to assess whether MIS improves compliance to this metric Methods: Stage III colon cancer patients 80 years old and younger from 2010 to 2012 were identified in the National Cancer Database. Demographic, tumor and treatment characteristics were evaluated including receipt of CT and surgical approach. Uni- and multi-variate logistic regression was used to assess factors associated with CT compliance. Results: Of the 19,963 patients identified, 14,901(74.6%) were compliant while 5,062 (25.3%) were not. Of the patients who were non-compliant, 956 (4.8%) received CT after 120 days. Surgical approach was significantly different between CT compliant and non-compliant groups (MIS 28% vs. 32%, p<0.000). Uni- and multi-variate analyses identified MIS as a significant factor associated with improved compliance to CT with an OR of 1.31 (95%CI 1.22-1.41). Other factors associated with CT compliance were nodal and tumor stage and treatment in an academic program. Non-compliance was associated with age 50-64 (OR 0.76; 95%CI 0.68-0.86), age 65-79 (OR 0.49; 95%CI 0.43-0.56) and increased co-morbidities (OR 0.60; 95%CI 0.53-0.67)). Lack of insurance (OR 0.69; 95%CI 0.58-0.81) or Medicaid (OR 0.54; 95%CI 0.47-0.62) and Medicare (OR 0.69; 95%CI 0.63-0.77) as well as distance to hospital of more than 44 miles were also associated with non-compliance to CT (OR 0.86; 95%CI 0.76-0.97). Conclusion: This is the first study to demonstrate that MIS for Stage III colon cancer improves compliance to receipt of CT within the 120 days. Given the potential survival benefits as a result of adherence to ACS CoC cancer care quality metrics, MIS may benefit patients not only in faster return to recovery but also in improved cancer outcomes.

PT116

The Impact of Primary Colorectal Cancer Location on the Overall Survival in Patients with Colorectal Cancer Liver Metastasis A. Hammad, K. Sasaki, C. Miller, C. Quintini, E. Berber, F. Aucejo.* *Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Background: Right- and left-sided colorectal cancer (CRC) are proposed to differ in molecular genetics and hence, long-term outcomes differ. We sought to investigate the impact of resection margin status on overall survival (OS) after hepatectomy for colorectal liver metastases (CRLM) according to the site of primary CRC. Method: Clinicopathologic characteristics and survival data were examined. Right-sided included lesions of the cecum, right and transverse-colon, while left-sided were lesions of the left-colon and rectum. A margin involvement of ≤1 mm was considered positive. Prognostic significance of positive resection margin according to the primary CRC location

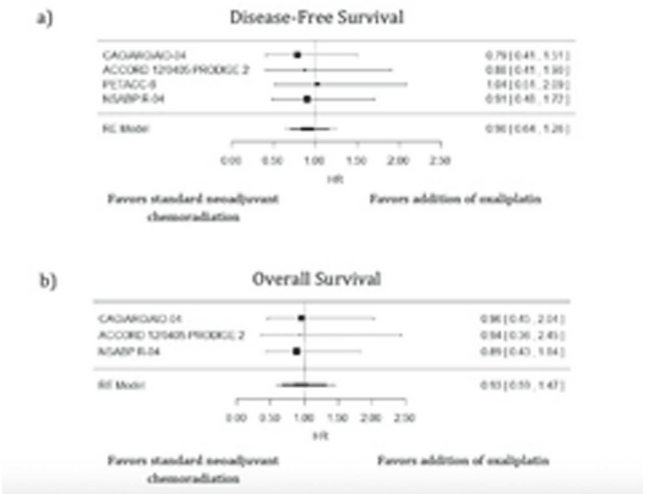
was investigated using multivariate analysis. RESULTS: Three-hundread and nine patients were included and most patients had a left sided primary CRC (69% vs. 31%). Majority of patients (77%) had R0 margins on pathology. Among patients with a right-sided primary CRC, 5-year OS was not correlated with margin status (Negative: 47.2 % vs. Positive: 49.1 %, respectively, p>0.05). Even after adjusting for other clinicopathologic variables, a positive margins was not independent predictor of OS (Hazards Ratio [HR]: 0.98, 95%CI: 0.15–6.42, p=0.946). In contrast, among patients who underwent resection of CRLM from a left-sided primary CRC, 5-year OS varied by margin status (Negative: 62.0% vs. Positive: 57.6%, p<0.05). On multivariable analysis, positive margins remained independently associated with worse OS among patients with a left-sided primary CRC (HR: 4.58, 95%CI: 1.67-12.58, p= 0.003). CONCLUSION: The impact of margins status differs by the site of the primary CRC. Tumor sidedness should be taken into consideration when performing surgical resection for CRLM, and extra emphasis should be placed on achieving R0 resection, especially in patients with left-sided tumors.

PF117

Neoadjuvant Chemoradiation for Locally Advanced Rectal Cancer with Fluoropyrimidine Alone or Intensified with Oxaliplatin: A Systematic Review and Meta-analysis A. Nadler,* E.A. Handorf, E.R. Sigurdson, J.E. Meyer, C.S. Denlinger, J.M. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

INTRODUCTION: Improved outcomes have been demonstrated with the use of neoadjuvant fluoropyrimidine-based chemoradiotherapy and total mesorectal excision for locally advanced rectal cancer. The addition of oxaliplatin in the adjuvant setting has also resulted in improved disease-free survival (DFS). A meta-analysis was performed to evaluate DFS and overall survival (OS) with the addition of oxaliplatin to standard neoadjuvant chemoradiation for locally advanced rectal cancer. METHODS: A systematic literature review was performed. Randomized-controlled trials (RCTs) comparing the addition of oxaliplatin in the neoadjuvant setting (oxaliplatin group) to fluoropyrimidine-based chemoradiation (standard group) were included. The primary outcomes were DFS and OS; secondary outcomes were short-term surgical results, morbidity, and mortality. Results were combined using meta-analysis via linear mixed-effects models. Calculations were performed using R. RESULTS: Of 73 studies identified, 4 reported DFS (n=3829) and 3 reported OS (n=2680). There was no difference in DFS between the standard and oxaliplatin groups amongst RCTs [HR 0.90 (0.64-1.26), p=0.5313]. There was no difference in OS [HR 0.93 (0.59-1.47), p=0.9894]. There was no significant heterogeneity between RCTs for primary outcomes. There was also no difference in pathologic complete response rate [OR 0.93 (0.77-1.14), p=0.4923), resection margin (R0) status [OR 1.01 (0.59-1.72), p=0.9846], circumferential resection margin status [OR 0.84 (0.50-1.41), p=0.5079], sphincter saving surgery rate [OR 0.87 (0.74-1.03), p=0.1103], grade 3-4 toxicity [OR 1.60 (0.88-2.92), p=0.1251], and 60-day mortality [OR 1.27 (0.50-3.25), p=0.6148]. There was significant heterogeneity between RCTs for R0 status, circumferential margin status, and grade 3-4 toxicity. Adjuvant treatment varied across studies. CONCLUSION: There are no short-term or long-term survival benefits with the addition of oxaliplatin to fluoropyrimidine-based chemoradiation in the neoadjuvant setting for locally advanced rectal cancer.

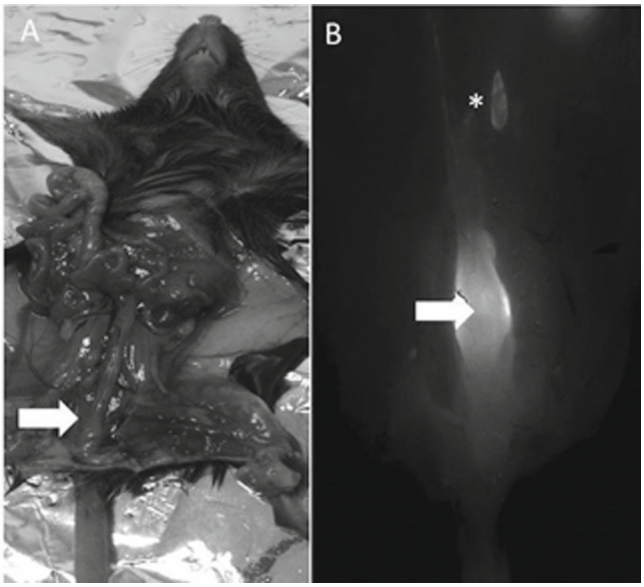
Figure 1. Forest Plots of a) disease-free survival and b) overall survival.



PF118

Intra-operative Localization of Rectal Tumors Using Liposomal Indocyanine Green N. Goder,[1] S. Bar-David,[1] S. Magdassi,[2] G. Lahat,[1] J. Klausner,[1] E. Nizri.[1]* *1. Tel Aviv Medical Center, Tel Aviv, Israel; 2. Hebrew University of Jerusalem, Jerusalem, Israel.*

Background: Tumor localization may pose significant challenge during minimally invasive rectal resection. Near infra-red (NIR) imaging can penetrate biological tissue and afford tumor localization from the external surface of the rectum. NIR technology visualization mode is already integrated in minimally invasive systems used today. Our aim was to develop a NIR-based tool for rectal tumor imaging that can be intra-venously administered. Methods: Our group has recently developed NIR imaging model for intraoperative visualization of ureters and we aimed to expand this technology for visualization of tumors. We prepared Indocyanine-green (ICG) -loaded liposomes by sonication. Liposomes were evaluated for their size and morphology. We then used an endoscopically induced rectal cancer in mice as a model for rectal cancer. After I.V. administration, tumors were evaluated for their fluorescence intensity. Tumor intensity was expressed in relation to the background signal, i.e. tumor to background ratio (TBR). Results: Liposomes in various sizes could be prepared by adjusting sonication time. We selected 100 nm- sized ICG loaded liposomes. The optimal time window for imaging of the rectal tumor was after 12 hours from injection, with TBR=8.1±3.6. These results are much superior to Free ICG TBR=1.9±1.5 (p=0.002). The liposomal ICG based imaging was also able to show draining lymph node of the rectal tumor as shown in the attached figure. Conclusions: Liposomal ICG based NIR imaging enables intra procedural identification of rectal tumor and possibly of lymph nodes. Formulation of ICG in liposome is much superior to free ICG in accumulation inside tumor. Possible explanation is of the enhanced permeability and retention (EPR) effect described for particles and cancer. We postulate that the larger (100nm) liposomes extravagate only from peri-tumoral capillaries at the tumor site.



PF119

Elevated GCSF and GCSF Receptor in CRC Microenvironment is Associated with Worse Survival A. Greenbaum,[2]* M. Xiong,[2] R.D. Berry,[2] L. Luo,[2] F. Schultz,[2] C.F. Martinez,[2] J.A. Hanson,[2] K.T. Morris.[1] *1. Surgery, University of Oklahoma, Oklahoma City, OK; 2. University of New Mexico, Albuquerque, NM.*

Granulocyte colony stimulating factor (GCSF) increases colorectal cancer (CRC) cell proliferation, migration, and stem cell compartments. CRC-associated fibroblasts secrete high levels of GCSF. We hypothesized that higher GCSF/R levels within human CRC tumors would predict worse prognosis. Methods: Annotated CRC samples were retrieved from the Pathology Department of a University Hospital and stained with anti-GCSF and anti-GCSFR antibodies. GCSF/R staining was manually graded by two pathologists blinded to patient outcome, as well as by digital analysis using Halo™ software. Overall stage-specific survival was stratified by expression of GCSF/R and medians (OS) estimated by Kaplan Meier and compared using logrank method. Proportions alive were compared by X^2. Hazard ratios (HR) were determined by Cox regression, and Spearman's was used to test correlations. Results: Stage I/II patients with low intensity staining for tumor GCSF had a HR 3.077 (1.2-7.892, $p<0.05$) for death when compared to those whose tumors did not stain for GCSF. This HR decreased as stain intensity within the tumor increased, suggesting a dose-dependent effect. Stage I/II patients with CRC in the lowest quartile of GCSFR expression had an OS of 232 months as compared to those within the highest quartile (OS 77 months), though this did not reach statistical significance ($p=0.07$). However, 61% of Stage I/II patients in the low GCSFR expression group were alive at last follow up versus 39% in the high expression group ($p=0.05$). Digital analysis for GCSF and GCSFR strongly correlated with manual IHC grading ($R=0.6028$, $p<0.05$ for GCSF, and $R=0.6545$, $p<0.05$ for GCSFR). Normal peri-tumoral tissues had a greater number of cells staining for GCSF (6.67% vs 2.73%, $p<0.05$) but these cells stained with lower intensity than in tumor tissues (OD 0.066 vs 0.080, $p<0.05$). Tumor tissue had both more cells staining for GCSFR (64.4% vs 55.1%, $p<0.05$), and a stronger intensity of stain (OD 0.1250 vs OD 0.1124, $p<0.05$) than the normal appearing peri-tumoral tissue. Conclusion: Expression of GCSF within CRC predicts adverse prognosis. High GCSFR expression is associated with worse outcomes in early stage CRC patients.

Patient Demographics
(N=221, Median follow up 91 months, Range 1-205)

		No.	%	Median OS in months
Age (years)	Mean (Range)	61 (25-90)		
Sex	Female	114	52	
	Male	107	48	
AJCC v. 7 Stage at diagnosis	All Stages	221	100	91
	I	28	13	156
	II	89	40	133
	III	92	42	70
	IV	12	5	24

PF120

Is the Distribution of Peritoneal Disease Predictive of Outcomes in Patients Post Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy? J. Wong,* G.H. Tan, M. Kumar, Q. Gao, M. Teo. *Surgical Oncology, National Cancer Centre, Singapore, Singapore.*

Introduction Sugarbaker's Peritoneal Cancer Index (PCI) is a useful prognostic tool after complete cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal carcinomatosis. In colorectal and ovarian cancer, higher PCI scores have been associated with poor survival outcomes. Both peritoneal implant size and their distribution on the peritoneal surface are used to derive the final PCI. A metastatic implant of 2cm in size will result in a one point contribution to the final score regardless of the abdominal region involved. However, we hypothesize that the involvement of certain regions may portend a worse prognosis compared with others. As such, our study aims to evaluate the relationship between the distribution of peritoneal disease and survival and morbidity outcomes. Methods Data was retrospectively collected from patients who underwent CRS and HIPEC for peritoneal malignancy over a 15 year duration. Patients with colorectal, ovarian, and primary peritoneal malignancies were included. PCI was evaluated intra-operatively and lesion size score was recorded for each of the 13 abdomino-pelvic regions. Involvement of the diaphgram, liver capsule, porta hepatitis, stomach and spleen was recorded. The relationship between distribution of peritoneal disease with survival and morbidity outcomes was evaluated. Results A total of 154 patients underwent complete CRS and HIPEC, median PCI score was 9. A high PCI was significantly associated with recurrence and poor OS. Region 6 was most commonly involved and had the highest frequency of heavy disease burden. Presence of peritoneal implants in regions 4,5,6,7,8,10,11,12 and the porta hepatitis was significantly associated with worse OS and DFS. Metastases in regions 3,9, left diaphgram or antrum resulted in higher rates of post-operative complications. Conclusion The distribution of peritoneal disease as scored by the PCI has an important prognostic role. While involvement of the lower abdominal regions and small bowel was predictive of poor survival, involvement of the upper abdominal regions predicted post-operative morbidity.

PF121

The Effect of a Simultaneous Versus Staged Resection of Metastatic Colorectal Cancer on Time to Adjuvant Chemotherapy E. Le Souder,* A. Elnahas, S. Cleary, A.C. Wei, R. Walker, A. Parsyan, S. Chadi, F.A. Quereshy. *Division of General Surgery, University Health Network, Toronto, ON, Canada.*

BACKGROUND: Select patients presenting with colorectal cancer with synchronous liver metastases (SLM) may undergo a staged or simultaneous resection of the primary tumor and SLM with curative intent. Adjuvant chemotherapy is commonly given to reduce the risk of recurrence. This study aimed to determine if the time to adjuvant chemotherapy was delayed in patients undergoing a simultaneous resection, when compared to a staged approach. METHODS: A retrospective chart review of patients receiving surgical treatment for colorectal cancer with SLM at our institution from January 2005 to July 2016 was preformed. The primary outcome was time to adjuvant chemotherapy, defined as the number of days from complete surgical resection to start of adjuvant chemotherapy. Secondary outcomes included 30-day complication rate, overall survival (OS) and disease free survival (DFS). RESULTS: A total of 155 patients underwent surgery for synchronous metastatic colon cancer for curative intent. There were 127 patients who received a staged resection and 28 who received a simultaneous resection. Patient factors such as age, sex and ASA class as well as tumor factors such as TNM stage, location, and

number and size of metastases were similar between the two groups. Median time to adjuvant chemotherapy was 64 days for the staged group, and 66 days for the simultaneous group and was not significantly different between groups (p=0.98). After adjustment for patient and tumor factors, the time to adjuvant chemotherapy remained comparable (p=0.84). The adjusted 30-day complication rate was higher in the simultaneous group but not statistically significant (OR=2.51, p=0.11). OS and DFS were significantly different between groups, with both favoring the staged approach (p<0.05). CONCLUSIONS: Our study demonstrated that a simultaneous resection of colorectal cancer with SLM does not result in a delay to adjuvant chemotherapy when compared to a staged approach. However, there is a statistically significant reduction in OS and DFS utilizing a simultaneous approach. Further studies are needed to validate these findings and understand factors associated with differences in survival.

PF122

Routine Fecal Diversion is Unnecessary in Patients Undergoing Cytoreductive Surgery L.S. Anewenah,[1]* J. Shia,[2] A. Cercek,[2] P.B. Paty,[2] M.R. Weiser,[2] J.G. Guillem,[2] J. Smith,[2] J. Garcia-Aguilar,[2] G. Nash.[2] *1. Mercy Catholic Medical Center, Drexel Hill, PA; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

Background Cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC) are utilized for selected patients with peritoneal carcinomatosis. Patients may require multiple enteric anastomoses. Nevertheless, use of diverting stoma varies greatly and data are lacking to balance the risk of an enteric leak (EL) and patient preference for avoiding an ostomy. Objective Our aim was to describe the use of diverting stoma and incidence of enteric leak at a center performing a large volume of CRS. Methods This is a retrospective study of patients who underwent CRS (2008-16). EL was defined as anastomotic dehiscence (AD), abdominal abscess (AA), enteric perforation, or enteric fistula resulting in an invasive procedure within 30 days of surgery. Results 250 patients undergoing CRS for appendix (66%) or colorectal cancer were identified. 52% were female. The median age was 56 years (min-max, 20-86). The median peritoneal carcinomatosis index was 13 (IQR 6-23). Optimal CRS was achieved in 81% of patients of whom 88% received IPC. 40 patients had a pelvic anastomosis and 110 had more proximal enteric anastomosis. A diverting loop stoma was created in 18 patients (7%). A permanent end ostomy was created in 10 other patients. Median length of stay was 9 days; 12% were inpatient for >2 weeks. There were no perioperative deaths; 60% of patients had no complications, and 10/18/10/2% of patients had grade I/II/III/IV complications. The incidence of EL was 5.6% including 7 patients with AD or perianastomotic AA, 5 with AA remote to any enteric anastomosis, 1 with a missed enterotomy, and 1 with perforation of an unresectable tumor. EL management included emergent fecal diversion (n=3, rectal anastomotic dehiscence, missed enterotomy, tumor perforation), percutaneous drainage (n=10) and abdominal washout (n=1). There was one AD among patients diverted proximal to that anastomosis (6%); that patient developed peritonitis requiring operative washout. There was one AD among those patients not diverted proximal to an enteric anastomosis (0.8%). Conclusion EL is an uncommon complication among our patients undergoing CRS. Routine fecal diversion is unnecessary in the overwhelming majority of patients.

PF123

Survival Benefit of Obesity in Colorectal Cancer M. Flannery,* A. Stark, C.H. Chan. *The University of Iowa Carver College of Medicine, Iowa City, IA.*

Background: Obesity has been established as a risk factor for cancer development and progression. However, its impact on colorectal cancer (CRC) is debated. While some studies showed worse outcome for early stages of CRC in obese patients, others did not. Recent evidence also suggests obesity may have survival benefit in the metastatic setting. Here we aim to evaluate the impact of obesity on staging at diagnosis and stage-specific survival of CRC. Methods: Retrospective analysis of CRC patients presented to the Holden Comprehensive Cancer Center was conducted between January 2006 and April 2016 under an approved IRB protocol. Clinicopathological and follow up data were prospectively maintained in the institutional cancer registry. Body mass index (BMI) and diabetes status at the time of diagnosis were obtained from the electronic medical records. BMI were grouped as underweight (UW, <18.5 kg/m^2), normal weight (NW, 18.5 – 24.9 kg/m^2), overweight (OW, 25 – 30 kg/m^2) and obese (OB >30 kg/m^2). Stage at diagnosis and stage-specific overall survival (OS) were compared between BMI groups using chi-square and Kaplan-Meier methods, respectively. Results: Records of 1362 patients were obtained including 44 UW, 386 NW, 433 OW, and 499 OB patients. OB patients were more likely to be diabetic than NW patients (29.0% vs 8.3%, P<0.0001) and presented with earlier stages (stage 0-2: 41.8% vs 35.4%, P=0.0068). With a median follow-up of 22.6 months, the overall survival of OB patients was better than NW patients for stage 0-2 CRC (mean OS: 92.2 vs 85.4 months, P=0.016) and stage 4 CRC (median OS: 20.7 vs 15.7 months, P<0.001). There was no difference between BMI groups in terms of age, gender and primary tumor site and type. Conclusions: Obese patients tend to present with earlier disease and have better survival for all stages except stage 3 CRC. Although referral bias cannot be ruled out, obese patients may have earlier detection due to ongoing medical care for their diabetes and related health issues. This earlier detection could translate into better survival for early CRC. Reason for the survival advantage in metastatic CRC is unknown. Perhaps obese patients have more energy reserve that extends their lifespan.

PF124

Minimally Invasive Complete Mesocolic Excision and Central Vascular Ligation for Right Colon Cancer: Defining the Radicality of Central Lymphadenectomy T. Sammour,* S. Malakorn, R. Thampy, H. Kaur, B. Bednarski, C. Messick, G. Chang, Y. You. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction Complete mesocolic excision (CME) with central vascular ligation (CVL) has been advocated for right colon cancer (RC), but the radicality of lymphadenectomy remains controversial. Optimal D2 lymphadenectomy removes all intermediate nodes with high ligation (HL) of feeding vessels, while D3 lymphadenectomy additionally exposes and retrieves nodes along ventral superior mesenteric vessels (SMA/V). We aim to evaluate minimally-invasive CME-CVL, explicitly defining the radicality of central lymphadenectomy. Methods Patients who underwent minimally-invasive curative resection for RC between 2008 and 2016 were identified from a prospective institutional database. CME was standard. The radicality of central lymphadenectomy was defined as high ligation (HL, optimal D2), vs central node dissection (CND, D3) after review of operative reports and/or videos. A blinded radiologist evaluated the pre- and post-operative CT scans for radiographically abnormal nodes. Results Among 200 patients, 169 (84.5%) underwent laparoscopic and 31 (15.5%) robotic resection. Central lymphadenectomy was performed as HL in 58 (29%) and as CND in 142 (71%) patients. Preoperative imaging identified abnormal D2 nodes in 33.0% and D3 nodes in 2.6%, and 73% of those with abnormal D2 and 100% of those with abnormal D3 nodes underwent CLN. Pathologically positive nodes were identified in 41% (37.9% of the HL and 42.3% of the CND, p=0.64). The median number of nodes retrieved was 27 and 32, respectively. No patient had residual abnormal node on post-operative imaging. The 30-day mortality rate was 0%, and morbidity rate was 4% (grade 3, and 11% grades 1-2). After a median of 22 months, one (0.5%) patient recurred locally at the anastomosis. Conclusion Minimally-invasive CME-CVL can be safely performed with excellent nodal yield with both optimal D2 as well as D3 lymphadenectomy. With imperfect clinical nodal staging, the near-zero local recurrence rate observed supports CME with optimal D2 lymphadenectomy as a minimum standard and D3 lymphadenectomy when radiographically abnormal nodes are identified.

PF125

Adequate Lymph Node Evaluation (LNE) in the Elderly is Associated with Improved Survival in Patients with Stage I-III Colon Cancer: A Validation Study Using the National Cancer Data Base (NCDB) J. Reha,* S. Mukkamalla, R. Rathore, P. Somasundar. *Roger Williams Medical Center, Providence, RI.*

Background: Lymph node (LN) involvement is one of the most important prognostic factors in non-metastatic colon cancer, but the variations in lymph node involvement among different age groups are less well known. Adequate LNE requires assessment of 12 or more nodes. We have previously demonstrated that older patients are less likely to have node positive disease, when adequately staged. The current study was undertaken to validate our findings using the NCDB. Methods: The NCDB was queried for patients diagnosed with stages I-III colon adenocarcinoma from 2004 to 2008 who underwent surgical resections. Survival information was available through 2013. Pearson Chi-square test was used to analyze descriptive data. Survival analysis was performed using Kaplan-Meier survival curves and Cox proportional hazards regression modeling. Results: A cohort of 97,831 patients was identified for

analysis. Among patients belonging to 18-64, 65-74 and ≥75 years age groups, the frequency of adequate LNE was 73.6%, 69% and 67.4% respectively, while pathologically confirmed LN involvement was 42%, 34.9% and 27.2% respectively ($p<0.0001$). Adequate LNE was associated with an improved 5-year overall survival outcomes regardless of age, gender, race, comorbidity index, insurance status, income level, year of diagnosis, pathologic tumor status, stage, grade, type of colectomy, adjuvant chemotherapy and academic level of treating institution. Rates of adequate LNE increased from 2004 to 2008, with a corresponding increase in survival outcomes noted ($p<0.0001$). Conclusions: Assessment of LN involvement requires a minimum of 12 nodes by current guidelines, is very crucial for appropriate staging of colon cancer, and carries a high prognostic value. This study validates our previous findings of lower rates of LN involvement in elderly and reiterates the importance of adequate LNE, which is proven to be associated with improved survival in colon cancer. Also identified were increasing rates of adequate LNE over the years of evaluation with corresponding increases in survival outcomes.

PF126

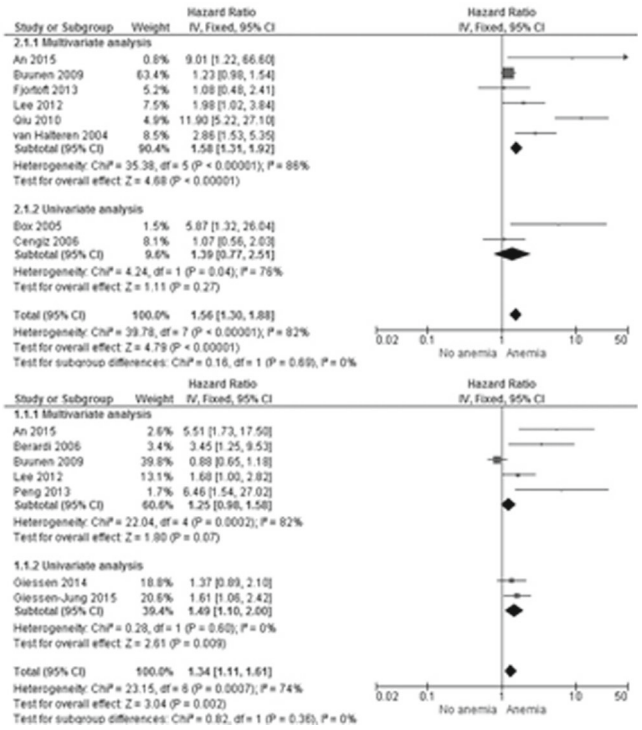
Characterization of the Role of C-terminal Binding Protein (CtBP2) in Colon Cancer Progression R. Seth,[1]* A. Chawla,[2] E. Sumner,[3] B. Szomju,[2] S. Grossman.[2] *1. Division of Surgical Oncology, Virginia Commonwealth University, Massey Cancer Center, Richmond, VA; 2. Department of Internal Medicine, Virginia Commonwealth University, Massey Cancer Center, Richmond, VA; 3. Department of Microbiology and Immunology, Virginia Commonwealth University, Massey Cancer Center, Richmond, VA.*

Background: Prognosis for advanced colorectal cancer remains poor due to disease relapse in which cancer stem cells (CSC) play a key role. Overexpression of NADH dependent transcriptional regulator CtBP2 is often seen in colon cancer. Previous work characterized CtBP2's promotion of TCF4 signaling as critical to colon cancer CSC growth and self renewal. Tumor suppressor APC is a negative regulator of CtBP. We thus utilized in-vitro CSC-enriched spheroid cultures to determine if CtBP2 is active in colon cancer CSC's and examined CtBP dependence of Apc^{min} mouse polyposis using a novel CtBP inhibitor. Methods: Human colon cancer cell lines HCT116 and HT29 were grown in spheroid or monolayers with or without CtBP2 inhibitor 4CHIPP. Expression of CtBP2, its associating protein b-catenin, and CtBP's transcriptional targets (TIAM1, TCF4 and cmyc, a CSC marker) was assessed using western blot and qPCR. CSC growth and self renewal was assessed by primary and secondary spheroid assays with or without 4CHIPP. For in vivo studies, Apc^{min} mice were treated with a 1st generation CtBP inhibitor, MTOB. After sacrifice, intestinal polyps were counted and analyzed using western blot for CtBP2 and b-catenin. Results: In both cell lines, increased mRNA and protein expression of CtBP2, b-catenin, TIAM1, cmyc and TCF4 was seen in spheroid cultures compared to monolayers. Treatment with 4CHIPP resulted in abrogation of CtBP2 protein in spheroids and decrease in downstream CtBP targets. A 50% reduction in spheres was seen with 4CHIPP in primary and secondary CSC assays compared to untreated controls. In Apc^{min} mouse model, MTOB resulted in 50% reduction in polyp number and reduction in CtBP2 and b-catenin protein. Conclusion: We characterized the role of CtBP2 in an in-vitro CSC model and in-vivo model of intestinal polyposis. We show a potential link between CtBP2 and CSC phenotype in in-vitro system, mechanistic details of which are under active investigation. Our inhibitor study in vivo reveals a critical role for CtBP in Apc^{min} polyposis. Better understanding of these mechanisms will pave the way for developing anti-CSC agents with emphasis on novel anti-CtBP2 therapies for cancer treatment.

PF127

Long-term Prognostic Value of Preoperative Anemia in Patients with Colorectal Cancer: A Systematic Review and Meta-analysis M. Wilson,[1]* M. van Haaren,[2] J. Harlaar,[3] H. Park,[4] J. Bonjer,[3] B. Groot Koerkamp,[1] J. Jeekel,[1] J. Zwaginga,[5] M. Schipperus.[6] *1. Surgery, Erasmus Medical Center, Rotterdam, ROTTERDAM, Netherlands; 2. OLVG, Amsterdam, Netherlands; 3. VU Medical Center, Amsterdam, Netherlands; 4. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea (the Democratic People's Republic of); 5. LUMC, Leiden, Netherlands; 6. Hagaziekenhuis, Den Haag, Netherlands.*

Objective: To evaluate the long-term prognostic factor of preoperative anemia is colorectal cancer patients Introduction: Anemia is frequently observed in colorectal cancer patients, with a case incidence of 30 to 67 percent. Besides an indicator of tumor-induced blood loss and inflammation, anemia in cancer is also suggested to be a cause of inferior outcome, possibly via worsening of tumor hypoxia. As surgery is likely to enhance anemia, the long-term prognostic value of preoperative anemia seems most interesting. Methods: Comprehensive searches were carried out in all relevant databases, including MEDLINE, Embase and Web-of-Science. To include studies addressing overall survival, follow-up had to be at least 24 months or till death. For pooling of survival results, a mixed-linear (fixed-effects) model was fit to the reported hazard ratios (HRs) to calculate a pooled estimate and confidence interval. Results: We included 12 studies comprising 3588 patients to estimate the association between preoperative anemia and overall survival (OS) and disease-free survival (DFS). In a fixed-effects meta-analysis of eight studies, including both colon and rectal cancer, preoperative anemia was significantly associated with poor OS (HR 1.56; 95% CI 1.30 to 1.88; $p< 0.001$). A meta-analysis of seven studies also showed that preoperative anemia was significantly associated with poor DFS (HR 1.34; 95% CI 1.11 to 1.61; $p= 0.002$). Restricted to studies exclusively on colon cancer or rectal cancer, HRs for OS were 1.25 (95% CI 1.00 to 1.55; $p= 0.05$) and 2.59 (95% CI 1.68 to 4.01; $p<0.001$), respectively, while HRs for DFS were 1.21 (95% CI 0.96 to 1.52; $p= 0.11$) and 1.61 (95% CI 1.18 to 2.21; $p= 0.003$). Conclusion: The present meta-analysis reveals the independent prognostic value of preoperative anemia for long-term OS and DFS for rectal cancer, but not for colon cancer patients. These findings are supported by subgroup analyses of studies adjusting for important prognostic factors, such as age and tumor stage. These results justify a raised awareness about the impact of preoperative anemia on long-term survival.



Forest plot of 8 evaluable studies assessing OS in colorectal cancer according to methods of analysis by a fixed-effects model (above) and forest plot of 7 evaluable studies assessing DFS in colorectal cancer according to methods of analysis by a fixed-effects model (under). HR = hazard ratio, CI = confidence interval, IV = inverse variance (statistical method RevMan)

PF128

LY6E (Lymphocyte Antigen 6 Complex Locus) is Associated with Invasion and Poor Prognosis in Colorectal Cancer

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BACKGROUND: Mortality of colorectal cancer is strongly associated with the metastatic spread of the disease. Lymphocyte antigen 6 complex locus (LY6E) is a glycosylphosphatidylinositol (GPI)-linked cell-surface protein that is induced by Interferon (IFN). LY6E mRNA was found to be overexpressed in colorectal cancer (CRC) suggesting a role in carcinogenesis. However, function of LY6E remains largely unknown. The aim of this study was to define the role and clinical relevance of LY6E in colorectal cancer. METHODS AND MATERIALS: A total of 101 tissue samples were obtained from surgically resected specimens from patients with CRC in Soonchunhyang University Cheonan Hospital between January 2006 and December 2009. The expression of LY6E were examined by immunohistochemistry. The expression of LY6E and clinical factors including survival were analyzed. We also performed the functional study of LY6E using colon cancer cell lines. RESULTS: The seventy-three of 101 (72.3%) tissues from patients with CRC had LY6E expression. We found LY6E expression is associated with advanced stage (P = 0.004) and lymph node status (P = 0.027) in patients with CRC. Most notably, patients with LY6E overexpression showed a significantly worse prognosis after surgery (P = 0.034). And functional analysis revealed LY6E-depleted cancer cells exhibited markedly reduced migration and invasion ability in vitro (P <0.05). CONCLUSIONS: Altogether, these data indicate that LY6E is a marker for poor prognosis in colorectal cancer and may be a promising target for cancer treatment.

PF129

Histone Demethylase NO66 is Crucially Involved in Colorectal Cancer Progression

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Background: Molecular targeted anticancer drugs should be highly specific to malignant cells and have fewer side effects. Targeting epigenetic regulators is a promising therapeutic strategy against cancer. However, because of the ubiquitous expression patterns of targets, selective inhibition of cancer-associated genes remains a major challenge. To address this issue, we focused on the oncogene-regulated histone demethylase, nucleolar protein 66 (NO66 [C14orf169/MAPJD]), which is known to work coordinately with the well-characterized oncogene, c-MYC. Materials and Methods: To investigate expression patterns and clinical significance of NO66 in colorectal cancer (CRC), we performed immunohistochemical staining in 114 CRC cases. To elucidate how NO66 is involved in cancer progression, we investigated phenotypic changes of colorectal cancer cells by manipulation of NO66 expression. Results: NO66 was preferentially expressed in cancer tissues, while the expression was weak in normal tissues. Furthermore, clinicopathological analysis revealed that high expression levels of NO66 were associated with cancer metastatic potential, including lymphatic duct invasion (p = 0.047), venous invasion (p = 0.033), and lymph node metastasis (p = 0.015). Multivariate analysis indicated that NO66 was an independent prognostic factor for overall survival (odds ratio [OR], 5.7341; 95% confidence interval [CI], 1.111–105.01; p = 0.0346). In vitro assays revealed that NO66 expression is closely associated with malignant potential including proliferation, migration and anti-apoptotic activity. Conclusions: High expression levels of NO66 was related to poor prognosis and high relapse rate in CRC. Furthermore, multivariate analysis indicated that NO66 was an independent prognostic factor for overall survival. The cancer-selective expression patterns and its involvement in metastatic phenotypes suggest that NO66 is not only a crucial biomarker but also a promising therapeutic target in colorectal cancer.

PF130

Metabolic Phenotyping Provides Unique Insight into the Biology of Plastic IL17^{+}Foxp3^{+} and ex-Th17 Foxp3^{+} Regulatory T-Cells

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Regulatory T (T_{reg}) cells are associated with the immunosuppression observed in cancer and the expansion of T_{reg} cells within the tumor is a known barrier to successful cancer immunotherapy. We have demonstrated in previous experiments that Th17 cells are a novel source of tumor-induced forkhead box P3 (Foxp3+) cells. During tumor growth, Th17 cells progressively transdifferentiate into IL17A^{+}Foxp3^{+} and ex-Th17 IL17A^{neg}Foxp3^{+} T cells. Furthermore, we have described the immunosuppressive effects of these Th17-T_{reg} subsets. In order to support their specific functional needs, functionally distinct T cell subsets require specific energetic and biosynthetic pathways. Here we aim to better characterize the biology of the Th17-T_{reg} subsets by evaluating their metabolic phenotype. Additionally, we compared the metabolic profile of IL17$^{+/-}$Foxp3^{+} cells with their immunosuppressive function. We have used novel Th17^{eYFP}-Foxp3^{mRFP} fate reporter mice to study Th17 cell plasticity and Th17-into-T_{reg} cell transdifferentiation. T helper cells from these mice were sorted into Th17-T_{reg} subsets: eYFP^{+}IL17A^{+}Foxp3^{neg} (true Th17 cells), eYFP^{+}IL17A^{+}Foxp3^{+} (plastic subset), eYFP^{+}IL17A^{neg}Foxp3^{neg}, eYFP^{+}IL17A^{neg}Foxp3^{+} (exTh17 T_{reg} cells), eYFP^{neg}IL17A^{neg}Foxp3^{neg} and eYFP^{neg}IL17A^{neg}Foxp3^{+} (inducible (i)T^{reg} cells), and then analyzed to determine their metabolic profile. We found that exTh17 Foxp3^{+} T_{reg} cells have a low glycolysis rate, similar to the iT_{reg} cells. In contrast, plastic IL17^{+}Foxp3^{+} cells have a high rate of glycolysis that is comparable to the IL17^{+}Foxp3^{neg} cells (i.e. true Th17 cells). Combined with our previous observations that both Foxp3^{+}IL17^{+} and exTh17 Foxp3^{+} T_{reg} cells are immunosuppressive, the data demonstrate that the metabolic programs are independent of the suppressive functions of the Th17-T_{reg} subsets. While Foxp3 imprints the immunosuppressive

function in T cells, it does not control their metabolic phenotype. Th17 into Foxp3$^+$ T cell transdifferentiation presents an alternative route of T_{reg} cell development in tumors and controlling metabolism of the Th17-T_{reg} subsets may serve as a valuable targeting strategy in tumor immunotherapy.

PF131

Rectal Cancer Downstaging After Neoadjuvant Chemoradiation in Hispanics and Non-Hispanic Whites A. Greenbaum,* R. Rodriguez, J. Lee, B. Fahy, A. Rajput. *Surgery, University of New Mexico, Albuquerque, NM.*

Introduction: We previously found that Hispanic patients in our state present with more advanced stages of rectal adenocarcinoma than non-Hispanic Whites (NHW). However, recent large population-based studies have shown no ethnic differences in rectal cancer overall survival. In this study, we hypothesized there are no ethnic differences in response to neoadjuvant chemoradiation. Methods: We queried our university's NCI-designated Comprehensive Cancer Center tumor database for Hispanic and Non-hispanic White (NHW) patients diagnosed with rectal adenocarcinoma from 2009 through July 2016 who underwent neoadjuvant chemoradiation and subsequent tumor resection. Variables included clinical and pathologic AJCC 7th edition TNM staging, surgical approach, type and duration of treatment. Student's T-tests were used to compare means of nominal values. Chi-square and Fisher's exact tests were used to compute p-values, with ≤ 0.05 considered significant. Results: We found 73 patients meeting inclusion criteria, including 43 Hispanics and 30 NHW. Hispanic patients were younger at diagnosis (mean age 54 vs. 60 years respectively; p=0.02). Duration of radiation (5.7 vs. 5.5 weeks; p=0.19), and chemotherapy (5.7 vs. 5.5 weeks; p=0.68) were similar in NHW and Hispanics. The majority of patients in both groups received 5040 cGy, and either single agent capecitabine or combination protocol of oxaliplatin, capecitabine and celebrex. No differences in treatment toxicities, pre-operative staging method, chemotherapy regimen, and R0 resections were observed. NHW underwent APR more often than Hispanics (41 vs. 17%; p=0.03). Neoadjuvant-induced regression on final pathology had nearly equal distributions (p=0.99) with no differences in complete response (20% NHW vs. 21% Hispanic; p=0.84). Significant differences in response by T-stage were found between the two groups as Hispanics were more likely to have a change in T-stage (Table 1). Conclusions: Hispanics with rectal cancer in New Mexico present at a more advanced stage of disease. In regards to downstaging after neoadjuvant chemoradiation, Hispanics have an increase in T-stage migration and sphincter-preserving surgery as compared to NHW.

Response after neoadjuvant chemoradiation by TNM staging

Response, n (%)	Hispanic (n=43)	non-Hispanic White (n=30)	p-value
T-STAGE			
Upstaged	11 (27)	15 (52)	0.05
No change	11 (27)	15 (52)	
Downstaged			
Missing	3	1	
N-STAGE			
Upstaged	5 (12)	5 (17)	0.82
No change	14 (34)	10 (35)	
Downstaged	22 (54)	14 (48)	
Missing	2	1	
OVERALL TNM STAGE			
Upstaged	3 (7)	2 (7)	0.62
No change	14 (33)	13 (43)	
Downstage	26 (60)	15 (50)	
Missing	0	0	

PF132

Early Challenges to Engaging Refugee Populations in Community Based Cancer Prevention Measures S. Misra,[1]* D. Cox,[1] M. Saucedo,[1] M. Marsh,[1] N. Aydin,[1] A. Mishra.[2] *1. Surgery, TTUHSC, Amarillo, TX; 2. Northwest Texas Hospital, Amarillo, TX.*

Background: In dealing with cancer prevention there are barriers in screening, however dealing with refugees is an added challenge. Our county is a refugee re-settlement area with 35 different languages and ethnicities. Refugees here only receive assistance from re-settlement organizations for a short time, causing distrust with the mainstream community. This study, as part of a grant funding to improve local colorectal cancer (CRC) screening rates, focuses on identifying opportunities to engage these isolated communities. Methods: Initially relationships were established with local refugee service organizations, which provided insight of basic cultural differences and taboos but were not helpful on how to best reach out to them. Refugee leaders were identified by working with local churches. CRC education videos were developed in key languages. Focus groups were developed and participation incentivized with food and gift cards. Focus groups began with lunch, and ample time to build trust and break down barriers. Participants viewed a video in their native language educating them on CRC and the screening process. Subsequently, they participated in open discussion using an interpreter. Participants gave feedback on the video clarity, the best way to reach their community, as well as their likelihood to get screened for CRC. Results: Swahilis and Laotians provided our team with information to improve the program for their communities, and highly valued the screenings. Somali leaders were harder to engage as culturally Somali men do not engage in business or casual conversation with unrelated women. Somalis also said they are afraid of the word cancer and screenings, because in their culture cancer means death. All three groups were more comfortable when they met in a casual atmosphere with researchers in casual dress. Financial incentives helped establish trust and showed program commitment to provide screening. Conclusion: Identifying community leaders of various refugee groups is crucial to opening communication and engaging these populations. Community champions and faith based leaders help researchers understand and respect cultural values and improve screening.

PF133

Perioperative and Long-term Results of Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy and Synchronous Liver Metastases Resection A. Zendel,[1]* J. Dux,[1] A. Ben-Yaacov,[1] M. Goldenshluger,[1] A. Ariche,[2] A. Nissan.[1] *1. Department of General and Oncologic Surgery C, Chaim Sheba Medical Center, Ramat Gan, Israel; 2. Department of Hepatobiliary Surgery, Chaim Sheba Medical Center, Ramat Gan, Israel.*

Background: Over the last decade a synchronous resection of liver metastases and cytoreductive surgery with hyperthermic intraperitonea Background: Over the last decade a synchronous resection of liver metastases and cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) have emerged. It is still more widely accepted in cases of small peripheral hepatic lesions. We report short- and long-term outcome of patients undergoing CRS/HIPEC combined with liver resections. Methods: A prospectively collected database of colorectal cancer patients undergoing CRS/HIPEC was reviewed. Patients with liver resection (Group 1) were compared with patients without liver resection (Group 2) in terms of perioperative results and survival. Results: Types of hepatectomy in group 1 (n=40) included segmentectomies (n=5), non-anatomical resection (n=24), glissonectomy with peripheral lesions resection only (n=7) and ablation only (n=4). In 5 patients ablation was combined with resection and 1 patient underwent portal vein embolization. In 15 patients, 2 or more intra-parenchymal metastases were resected. Compared with group 2 (n=104) group 1 had higher peritoneal cancer index (PCI), increased intraoperative blood loss and packed cells transfusion and longer operation time (all p<0.05). There was no difference in intensive care unit stay and hospital stay duration. The perioperative morbidity presented as highest Clavien-Dindo complication score and mortality rate were similar between two groups (p=0.08 and p=0.69, respectively). We found a tendency to better overall and disease-free survival in group without liver resection, but the difference was not statistically significant. Conclusion: A complete cytoreduction combined with liver metastases resection is feasible and associated with reasonable morbidity and mortality. Moreover, despite higher PCI our study cohort patients had overall and disease-free survival comparable to CRS patients without liver resection.

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Postoperative, Rather than Preoperative CEA Predicts Outcome in Colon Cancer T. Konishi,* Y. Shimada, M. Morris, J. Smith, G. Nash, L. Temple, J.G. Guillem, P.B. Paty, J. Garcia-Aguilar, M.R. Weiser. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Backgrounds: Preoperative (preop) CEA is a prognostic marker in colorectal cancer and elevation is associated with tumor recurrence. However, normalization of an elevated preop CEA can occur following resection. We hypothesize that postoperative (postop), rather than preop, CEA is more predictive of outcome following resection of non-metastatic colorectal cancer. Methods: A single-institution prospective database was queried for consecutive

patients who underwent curative resection for Stage I-III colon adenocarcinoma from 1/2007-12/2014. Patients were staged with abdominal imaging, usually including CT chest/abdomen/pelvis with oral and IV contrast. Postop CEA was measured within 12 weeks postop but before initiation of adjuvant chemotherapy. CEA >5.0 ng/mL was defined as elevated. Patients were grouped into those with normal preop CEA (Normal-preop), elevated preop but normalized postop CEA (Normalized-postop) and persistently-elevated postop CEA (Elevated-postop). Recurrence free survival (RFS) was compared. Results: The study cohort consisted of 914 patients, including 715 Normal-preop, 142 Normalized-postop and 57 Elevated-postop groups. Normalized-postop group showed similar RFS with Normal-preop group (87.9% vs. 89.8% at 3yr), while Elevated-postop group had significantly worse RFS (74.5% at 3yr, p=0.004). When analyzed by stage, difference of RFS was particularly evident in Stage III (Normal-preop 79.3%, Normalized-postop 84.7%, Elevated-postop 55.2%, p=0.001). Multivariate analyses revealed that Elevated-postop CEA (HR 2.0, 95% CI 1.1-3.5), but not Normalized-postop CEA (HR 0.79, 95% CI 0.46-1.3), was independently associated with worse RFS along with higher TNM stage, older age and lymphovascular invasion. Repeat analysis using cut-off value of 10 ng/mL produced the similar results. Conclusions: Patients with elevated preop CEA which normalizes after resection have similar outcome as those with normal preop CEA. Postop CEA is more prognostic than preop CEA. Further investigations are warranted to confirm that postop CEA can replace routine use of preop CEA in Stage I-III colon cancer in the setting of modern abdominal imaging.

PF135

Clinical Risk Factors and Biomarkers for Cancer Associated Venous Thromboembolism: A Predictive Model in Patients with Peritoneal Metastasis Treated with Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy C. Ihemelandu.*
Surgical Oncology, MedStar Washington Hospital Center, Washington, DC.

Introduction: - Our aim was to develop a predictive model for venous thromboembolism (VTE) following cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (POIC) in patients with peritoneal metastasis, in an effort to individualize initiation of VTE prophylaxis in this cohort of high risk patients. Methods: - A retrospective analysis of a prospectively maintained database for all patients treated for peritoneal metastasis from 2013-2015. Results: - There were 61(42.4%) males vs. 83(57.6%) females. The mean age at presentation was 54.1 years. Predictive variables identified in a univariate analysis included: Gender, BMI, intra-operative INR, Platelets, Tumor site, Tumor histology, Peritoneal Carcinomatosis Index (PCI), age at diagnosis, Completeness of cytoreduction score, Use of POIC. A risk model was derived and validated in an independent cohort of patients. Predictive variables identified in a multivariate analysis included: platelet count, INR, PCI, and BMI. A predictive index was derived and four risk groups categorized. The overall rate of VTE was 17.4%, there was no significant difference between VTE and non-VTE group patients regarding age, CA 125. VTE events were more likely to occur at presentation (36.4%) and recurrence (33.3%), followed by the POIC period (18.2%). Conclusion: - Our predictive model demonstrates a significant difference in overall risk for VTE stratified by our derived predictive scores. Outside validation of this model in other cohort of patients is needed.

PF136

Impact of Adjuvant Chemotherapy on Recurrence Risk in Stage II Colon Cancer T. Adesoye,* C. Hu. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: Clinical guidelines recommend adjuvant chemotherapy in high-risk stage II colon cancer but the impact on recurrence risk and cancer related survival is unclear. Among Medicare patients, adjuvant chemotherapy was not associated with improved survival. We examine the effect of adjuvant chemotherapy on recurrence risk and overall survival in a diverse population. Methods: 6,095 patients who underwent surgery for stage II-III colon cancer (2006-2007) were randomly selected from the National Cancer Data Base for additional abstraction of tumor information, 5 year recurrence and survival. Death or second cancer within 6 months were excluded. Patients were classified as high or low risk using standard pathologic factors. Multivariate Cox regression with propensity score weighting was performed to compare recurrence risk and overall survival. Results: Of 3,423 patients with stage II colon cancer, 26.9% (n=883) received chemotherapy compared to 76.2% (n=1,839) of stage III patients. Among stage II patients, 47.8% (n=1,636) had at least one high risk feature and 30.8% (n=481) of these received chemotherapy. 5-year recurrence rate in the stage II group was 13% (n=392), greater in high risk compared to non-high risk patients (13.3% vs 9.3% p<0.0001) and 24.4% (n=874) in stage III patients. Chemotherapy did not improve recurrence risk in stage II patients regardless of risk status (High risk: hazard ratio [HR], 1.37; 95% CI, 0.96-1.97; Non-high risk: HR, 1.39; 95% CI, 0.91-2.11). Chemotherapy was associated with improvement in recurrence risk among stage III patients (HR, 0.79; 95% CI, 0.63-0.96). However, chemotherapy was associated with improved overall survival among both high (HR 0.69; 95% CI 0.51 - 0.92) and non-high risk stage II patients (HR 0.76; 95% CI 0.55-1.04), and also in stage III patients (HR 0.47; 95% CI 0.41-0.54). Conclusion: Adjuvant chemotherapy was not associated with a lower rate of recurrence among stage II colon cancer patients. The observed survival benefit associated with chemotherapy is likely attributable to non-oncologic factors such as patient selection. Decision-making regarding chemotherapy use in this cohort should be carefully approached.

PF137

Colorectal Cancer Screening in Rural Populations: Challenges Addressed by Group Education and Call Reminders K. Dowd,[1] A. Mishra,[2] D. Yang,[1] M. Marsh,[1] D. Cox,[1] N. Aydin,[1] S. Misra.[1]*
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Background: The Texas Panhandle has a high incidence of colorectal cancer (CRC), with a dismal screening rate of 41% compared to national average of 65%. Barriers to increasing screening are lack of patient awareness, cost, language barriers, and lack of access. National recommendations are to provide healthcare education via 1:1 for best outcomes; however, with an area of 25,887 square miles and a population density of 17 people per square mile, the challenge of providing effective education and screening for CRC requires a unique approach. Methods: Education in our area was conducted via group or individual learning to increase patient understanding and screening rates of CRC utilizing fecal immunochemical tests (FIT) at no cost for participants. Call reminders were used to increase return rates of FIT. Education was conducted by Community Health Workers (CHW) using flip charts, translation services and FIT demonstrations. Results: CRC educational outreach sessions have covered 1,129 people, with 622 completing FIT screening. 55.9% of participants were female and 44.1% male. 94.3% underwent group instruction as opposed to individual education. Analysis showed no statistically significant difference between these two methods of education for overall FIT kit return rates (55.58% for group vs 68.97% for individual, p-value 0.18). Average time to return FIT was quicker for group education with 11 days, compared to 14 days for individual education. Call reminder frequencies were investigated and determined to increase return rates. 50.9% of FIT kits returned were done without any call reminders, but this return rate doubled by adding a three-call reminder system. Participants in a group setting were more active and engaged in the conversations when compared to participants in 1:1 education. Conclusion: Unique strategies are needed when facing disparities in rural communities to break down the barriers to health care. Group education sessions offer more interaction, a unique comfortable setting, and cut costs without jeopardizing patient satisfaction or FIT return rates. Complex information can be delivered in meaningful ways by utilizing group education.

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Comparative Analysis of Survival in Colon Cancer Undergoing SLNM Versus Conventional Surgery Based on Number of Positive Lymph Nodes S. Saha,[1]* S. Mukkamala,[1] S. Ramanathan,[1] M. Hicks,[2] P. Knight,[1] D.M. Mazzaferro,[3] T. Siva,[1] V. Bajaj,[1] L. Hutcherson,[1] A. Chang,[1] D. Livert,[1] R. Oza.[1] *1. Surgery, Easton Hospital, Easton, PA; 2. Michigan State University, East Lansing, MI; 3. Drexel University School of Medicine, Philadelphia, PA.*

Introduction: Unlike in breast cancer or melanoma, resection during sentinel lymph node mapping (SLNM) in colon cancer (CCa) includes regional lymphadenectomy including SLNs and non SLNs. However, SLNM often identifies micrometastases due to ultrastaging which can be missed by conventional (Conv) surgery and pathologic examination. It is unknown whether SLNM in CCa impacts survival or recurrence. Hence, a retrospective analysis was undertaken to study overall (OS) and disease -specific (DSS) survival

between patients (pts) with CCa undergoing SLNM vs Conv surgery based on the number of nodes with metastasis. Methods: SLNM was done by peritumoral subserosal injection with blue dye followed by segmental resection including regional lymphadenectomy. All SLNs were ultrastaged with IHC and other nodes were examined by conv. methods with H&E. Results: There are 309 pts in SLNM (GpA) and 499 pts in Conv surgery (GpB); with average no. of lymph nodes (LNs) and +ve LNs 17.3/1.6 vs 14.4/2.49 respectively. For GpA, success rate was 99.6% and the average no of SLN was 3. Of the pts included in the analysis of OS and DSS between GpA and GpB, 1+ve LN were found in 38% vs 27%, 2+ve LNs in 10% vs 16%, and >2 LNs in 53% vs 57%, respectively. Comparing 5 years OS between GpA vs GpB, for 1+ve LN was 62.8% vs 52.38%, for 2 +ve LNs 72.7% vs 48.65% and for > 2 +ve LNs 35% vs 33.33%, respectively. Similarly, DSS for 1 +ve LN was 54.4% vs 47.6%, 2+ve LNs 40% vs 40.54% and >2+ve LNs, 30.4% vs 25.76%, respectively(Table1.). Conclusion: Compared to Conv surgery, SLNM identified higher no. of LNs per pt with high success rate. Five-year OS and DSS also are better in SLNM Gp compared to Conv surgery. Hence, SLNM in CCa may have prognostic value. A larger multicenter trial needs to be done to validate such data.

Comparison of 5-year OS and DSS between SLNM and Conventional

	SLNM (n=309) Group A	Conventional (n=499) Group B
Average # of LNs examined	17.3	14.48
Average # of +ve LNs	1.6	2.49
Average # of SLNs	3	n/a
Average # of +ve SLNs	0.6	n/a
SLNM Success Rate	99.60%	n/a
OS		
1+ve node	62.8% (n=43)	52.38% (n=63)
2+ve nodes	72.7% (n=11)	48.65% (n=37)
>2 +ve nodes	35% (n=60)	33.33%(n=132)
DSS		
1+ve node	54.4% (n=46)	47.6% (n=63)
2+ve nodes	40% (n=15)	40.54% (n=37)
>2+ve nodes	30.4% (n=69)	25.76% (n=132)

Predictors of recurrence-free and overall survival by Kaplan-Meier estimates.

	5-year RFS	*p*-value	5-year OS	*p*-value
Preop Stage				
II	68%	0.6	86%	0.1
III	59%		68%	
IV	33%		33%	
CRT Chemotherapeutic Agent				
5-FU	65%	0.3	75%	0.5
Capecitabine	58%		77%	
Post-CRT PET SUV_{max}				
< 4.3	76%	0.01	86%	0.01
≥ 4.3	52%		66%	
Percent SUV_{max} decrease				
> 66%	75%	0.01	82%	0.05
≤ 66%	54%		66%	
Post-SUV_{max} < 4.3 & RI SUV_{max} > 0.66				
Yes	78%	0.02	86%	0.03
No	55%		66%	
Pathological complete response				
Yes	81%	0.04	85%	0.2
No	55%		71%	

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Predictive Value of PET/CT for Pathological Complete Response and Survival in Patients with Locally Advanced Rectal Cancer
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Background: A major challenge in identifying candidates for nonoperative management of locally advanced rectal cancer is predicting pathological complete response (pCR) following chemoradiation therapy (CRT). We evaluated the ability of pre- and post-CRT PET imaging to predict pCR and long-term prognosis. Methods: We retrospectively identified patients at our institution from 2002–2015 with locally advanced rectal cancer who underwent CRT, pre- and post-CRT PET imaging, and surgical resection. Logistic regression and Kaplan-Meier estimates were used to analyze the association of PET variables with tumor pCR and survival outcomes. Receiver operator characteristic curves were generated to define optimal cutoff points for predictive PET variables. Results: 140 patients matched the inclusion criteria. The pCR rate was 28%, and median follow-up time was 48 months. On multivariable analysis, pCR was associated with lower median post-CRT SUV_{max} (3.2 vs 5.2, p=0.009) and higher median SUV percent decrease (72 vs 58%, p=0.009). ROC curves were generated for SUV percent decrease (AUC=0.70) and post-CRT SUV (AUC=0.69) to estimate cutoff points for maximum specificity and sensitivity to predict pCR. Post-CRT SUV <4.3 and SUV percent decrease of >66% were equally predictive of pCR with a sensitivity of 65%, specificity of 72%, PPV of 44%, and NPV of 86%. Median 5-year OS and RFS were significantly improved for patients with post-CRT SUV <4.3 (OS, 86 vs 66%, p=0.01; RFS, 75 vs 52%, p=0.01) or SUV percent decrease of >66% (OS, 82 vs 66%, p=0.05; RFS, 75 vs 54%, p=0.01). Patients with stage III disease and a post-CRT SUV <4.3 were in effect downstaged, with a median 5-year OS equivalent to that of patients with stage II disease (Table 1; 86 vs 86%). Conclusions: PET/CT may be a useful modality in predicting pCR and overall survival in patients undergoing CRT for rectal cancer. Inclusion of pre-CRT PET does not appear to add prognostic value for pCR compared with post-CRT PET alone. Patients with a post-CRT SUV of >4.3 should not be considered for nonoperative management, as an estimated 86% of these patients will not have a pCR.

PF140

Elevated Brain Natriuretic Peptide (BNP) is an Early Marker for Patients at Risk for Complications After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS and HIPEC)
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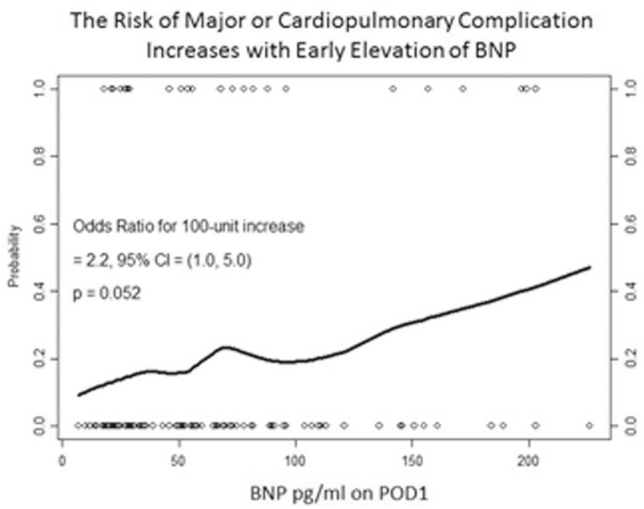
Introduction: Elevated BNP correlates with adverse outcomes after cardiac surgery and reflects fluid balance following trauma and pancreatectomy. We assessed serial BNP values as markers of perioperative fluid status and as a risk factor for major and/or cardiopulmonary (CP) complications following CRS and HIPEC. Methods: Perioperative fluid balance, daily BNP levels, and morbidity data were retrospectively collected for all patients undergoing CRS+HIPEC between 6/2014 and 2/2016. Results: CRS+HIPEC was performed in 129 patients for appendiceal adenocarcinoma (n=99), mesothelioma (n=16), and colon cancer (n=14). The median age was 54 years (range 24-75) and <10% had pre-existing CP comorbidities. Mitomycin C was used in 94 (73%), cisplatin in 24 (19%), and oxaliplatin in 11 (9%). The median PCI was 14 (range 4-39) and 89% underwent CC0/1 resection (n=115). Intraoperative transfusion was required in 39 (30%), median blood loss (EBL) was 497 ml (range 50-2700). Complications occurred in 77 (60%) and were major (Clavien III-V) in 16 (12%), CP in 17 (13%); 24 (18%) had either major or CP complications. Thirty-day mortality occurred in 2 (1.5%). The median BNP was 52 (range 7-226) on POD1 and 149 (range 18-889) on POD2. Patients with an average BNP>250 in the first 48 hours postoperatively were more likely to experience major or CP complications than those with lower BNP (42% vs 16%, p=0.048). Elevated BNP on POD1 correlated with increased risk of major or CP complications (Figure). This effect was most pronounced in the 25 patients receiving cisplatin: for each 100 unit increase in BNP the OR for major or CP complication was 7.4 (1.4 -39.9), versus 1.2 (0.4-3.7) for the remaining patients, p=0.083. Multivariate analysis identified increased EBL (OR 2.4, p=0.010) and a trend toward increased BNP on POD1 as risk factors for major or CP complications (OR 2.0, p=0.10). Conclusion: Postoperative BNP is an objective measure that facilitates early identification of patients at risk for major and/or cardiopulmonary complications after CRS and HIPEC.



PF141

The Comprehensive Complication Index: A Novel Method of Quantifying the Economic Burden of Complications After Hyperthermic Intraperitoneal Chemotherapy S. Dumitra,* M. O'Leary, M. Raoof, O.S. Eng, M. Wakabayashi, T.D. Dellinger, E. Han, S. Lee, B. Lee. *City of Hope, Duarte, CA.*

INTRODUCTION: Cytoreductive surgeries with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) are complex and morbid procedures. The Comprehensive Complication Index (CCI) is a 0-100 score, calculated using all complications and their treatment. The aim of this study is to assess the impact of complications as measured by the CCI on admission and readmission costs. METHODS: A review of the 2009-2015 institutional database was undertaken. Patient demographics, pathology, peritoneal carcinomatosis index (PCI), complications, length of stay (LOS), admission and readmissions costs were reviewed. Linear regression was used to assess whether CCI predicts cost of admission and readmission after HIPEC. RESULTS: Of the 157 patients reviewed, 115(73.2%) underwent HIPEC. The majority were female (n=77,66.9%) with a mean age of 53.7years. Mitomycin C was the most commonly used agent in 84 patients (73%). The mean PCI was 13.2, with three 30-day mortalities (1.9%). The mean CCI was 21.4 with a median LOS of 11 days (IQR 8-15). The 30-day and 90-day readmission rates were 20.9% and 27.3%, respectively. The CCI correlated with admission cost (r2=0.74) more strongly than the Clavien-Dindo-Classification (r2=0.69). After correcting for age and PCI, admission cost was increased by 2195.59 US Dollars (95%CI 1671.38-2719.81, p=0.000) with each 1 point increase in CCI. CCI was also a strong predictor of readmission cost (coef 718.96; 95%CI 27.62-1410.2, p=0.043). CONCLUSION: This study is the first to quantify the monetary impact of HIPEC complications and to show that CCI correlates better with admission and readmission cost than the Clavien-Dindo-Classification. With each increase in complications as measured by one CCI point, there is an associated increase in direct cost of 2195.59 USDollars. In the future, the CCI can be used to compare the HIPEC burden on the health care system across groups.

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Prognostic Factor of Lower Rectal Cancer with Lateral Pelvic Lymph Node Metastasis Treated with Lateral Lymph Node Dissection S. Yamauchi,* S. Okazaki, A. Kikuchi, M. Ishiguro, T. Ishikawa, H. Uetake, M. Yasuno, K. Sugihara. *Digestive and General Surgery, Tokyo Medical and Dental University, Graduate School, Tokyo, Japan.*

Background: Approximately 20% of lower rectal cancers with the tumor invaded through the muscularis propria into perirectal tissues or more have positive lateral pelvic lymph node metastasis and their prognosis are poor. Therefore, mesorectal excision with lateral lymph node dissection (LLND) is the standard surgical procedure in Japan. We analyzed the association between clinicopathological factors in patients who have lower rectal cancer (RC) with positive lateral lymph node and prognosis, and discussed about the significance of LLND. Methods: A total of 1363 stage II or III RC patients who underwent curative surgical resection with LLND on during the period from 1997 to 2006 were retrospectively investigated. Among them, we focused on 211 patients who had tumor with lateral pelvic lymph node metastasis which diagnosed pathologically and analyzed them. The impact of several risk factors on survival was analyzed using Cox's proportional hazard model Results: Median relapse free survival (RFS) and overall survival (OS) of all patients were 22.6 and 65.0 months, respectively. Multi-variate analysis revealed that poorly differentiated tumor / undifferentiated tumor, the number of node positive (more than 5), and present of lymph node metastasis at the root of the feeding artery were independent risk factors for RFS (Hazard ratio [HR] 0.58, 0.54, 0.37, respectively). The same factors that were significance for RFS, and age (over 59) were independent risk factors for OS (Hazard ratio [HR] 0.56, 0.39, 0.38, 0.65, respectively). Although 62.1% patients had recurrence after curative surgery, 5-year survival rate of patients who underwent resection of recurrence sites curatively was 47%. Conclusion: Lower rectal cancer with lateral lymph node metastasis has a poor clinical outcome as it's known. Even though there is a limitation, it is a possibility that patients who have RC with positive lateral lymph node and without poor risk factors for survival receive benefit from LLND.

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Relationship Between Colorectal Cancer Tumor Staging and Solitary Metastasis: Can We Predict the Site of Metastases? C. Seo,* G.H. Tan, M. Teo. *Division of Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: The most common site of colorectal cancer (CRC) metastasis is the liver, followed by lung and peritoneum. Patients at risk of developing metastasis are given adjuvant systemic chemotherapy. However, we believe that those at risk of developing peritoneal disease may respond better to targeted locoregional therapies such as adjuvant HIPEC. We aim to investigate the relationship between the pathological tumour stage with site of metastasis, postulating that tumour (T) and nodal (N) staging can predict for site of metastasis, allowing for a personalized approach to the management of colorectal cancer. Methods: Data was collected from CRC patients with solitary metastases to liver, lung, and peritoneum, who received treatment at a high volume tertiary hospital, between April 2002 and April 2015. American Joint Committee on Cancer (AJCC) pathological T, N, and metastases (M) to the liver, lung or peritoneum were recorded. The T and N staging were analysed and relative risk of developing each metastasis was calculated using the Pearson chi-square test and multivariate logistic regression. Results: A total of 650 CRC patients with solitary metastasis were included with T staging divided into T1 0.8%, T2 1.8%, T3 56.9% and T4 40.5%, and N staging to N0 24%, N1 28.3% and N2 47.7%. Overall, 64.3% of patients had liver metastasis, 15.7% lung and 20% peritoneal metastasis. By comparing the incidence of each metastasis, we found that peritoneal metastasis occurred in patients with higher T staging ($p<0.001$). The data showed that for all T4 tumours, irrespective of the nodal status, 38.4% developed peritoneal metastasis. 11.8% of T4 tumours had lung metastasis. As for liver metastasis, the main factor was N status, where 63.3% of patients with higher N developed liver metastasis. No significant difference was found in the relative risk of developing liver and lung metastasis when compared to each other. Conclusion: We can predict the site of metastasis, especially peritoneal metastasis, based on the AJCC CRC T staging. This allows us to predict the risk of developing peritoneal metastasis on follow up and intervening early to improve overall survival.

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Colorectal Peritoneal Carcinomatosis: A True Depiction of Clinical Outcomes with Planned Systemic Chemotherapy Warrants Consideration of CRS and HIPEC N. Thiruchelvam,[1]* C. Chia,[2] G.H. Tan,[2] M. Teo.[2] *1. General Surgery, Singapore General Hospital, Singapore, Singapore; 2. National Cancer Centre Singapore, Singapore, Singapore.*

The management of peritoneal carinomatosis (PC) in colorectal (CLR) cancer remains a challenge. Whilst there are consensus guidelines that advocate cytoreductive surgery (CRS) and hyperthermic intra-peritoneal chemotherapy (HIPEC) in select patients without extra-abdominal disease, a significant proportion undergo the alternative treatment arm of systemic chemotherapy in view of the postulated high morbidity of CRS/HIPEC. Unfortunately, PC often results in complications of the peritoneal disease load that disrupt

chemo-therapeutic plans, such as tense ascites, hydronephrosis and intestinal obstruction(I/O). This study aims to provide a true depiction of the clinical outcomes of patients with PC who were planned for systemic chemotherapy. A retrospective review of a prospectively maintained database of patients at the National Cancer Centre Singapore who were diagnosed with metastatic CLR cancer limited to PC between Jan 2006 and Dec 2014 was conducted. CRS/HIPEC patients were excluded. OS was calculated from point of diagnosis of PC till death. Secondary outcomes of delays in planned chemotherapy cycles, need for surgical interventions and total duration of hospitalisation for PC complications were evaluated. We analysed 152 patients with metastatic CLR cancer limited to PC who were planned for systemic chemotherapy. 92%(140) of them were ECOG 0-1 status. 75%(114) received systemic chemotherapy, of whom 71% of patients (80) had treatment disruptions. 60% (48) of these delays were secondary to complications of PC, most commonly I/O. 15% (17) required emergency surgery for I/O, 23% (26) required abdominal cope loop, ureteric stent insertion or proximal urinary diversion. Median total duration of unforseen hospitalisation post-initiation of chemotherapy was 15 days (0-85). The median follow-up was 1.7 years with median OS of 10.5 months (1-90). Patients with CLR PC suffer significant morbidity from complications of peritoneal disease which disrupts chemotherapy regimens. With morbidity of less than 20% from CRS/HIPEC in high volume centers, consideration of this modality of treatment is warranted in selected patients.

PT146

Nationwide Analysis of Adrenocortical Carcinoma Reveals Higher Perioperative Morbidity in Functional Tumors P.P. Parikh,* G.A. Rubio, J.C. Farra, J.I. Lew. *Surgery, University of Miami, Miami, FL.*

Introduction: Adrenocortical carcinoma (ACC) is a rare tumor that may lead to excess hormone production, clinically manifesting as Cushing's Syndrome, Conn's Syndrome or virilization. Perioperative outcomes after adrenalectomy for functional ACC remain unclear. This study examines nationwide in-hospital outcomes after adrenalectomy for ACC. Methods: A retrospective cross-sectional analysis using the Nationwide Inpatient Sample database (2006-2011) to identify patients who underwent unilateral adrenalectomy for functional or nonfunctional ACC was performed. Patient demographic, comorbidities and postoperative outcomes were evaluated by univariate and risk-adjusted multivariate logistic regression. Univariate analyses included two-tailed Chi-square and t-tests. Results: Of 4,095 patients who underwent adrenalectomy, 93% (n=3790) had nonfunctional and 7% (n=305) had functional ACC. Mean age was 46 and 32 years, respectively ($p<0.01$). Among patients with functional ACC, 86% (n=262) had hypercortisolism (Cushing's syndrome) and 14% (n=44) primary hyperaldosteronism (Conn's Syndrome). Hyperandrogenism was identified in 5% (n=14) of all functional ACC patients. Functional ACC patients had two-fold higher rate of all preoperative comorbidities including hypertension, diabetes, obesity, congestive heart failure and coagulopathy compared to nonfunctional ACC ($p<0.01$). Functional ACC patients had more postoperative complications including wound issues, pulmonary embolism, acute kidney injury and adrenocortical insufficiency compared to nonfunctional ACC patients ($p<0.01$). Mean hospital stay was 9 and 7 days, and mean total hospital cost was $110,000 versus $67,000, respectively ($P<0.01$). On risk-adjusted multivariate analyses, functional ACC was an independent risk factor for in-hospital death (5.3, 95% CI 1.7-15.9). Conclusion: Among functional ACC, patients with Cushing's represent the majority with significant preoperative comorbidities, postoperative complications, and longer and more expensive hospitalizations. Such patients at high risk should undergo appropriate preoperative medical optimization and counseling in preparation for adrenalectomy.

Analysis of perioperative outcomes in nonfunctional and functional ACC

	Overall (n=4095)	Nonfunctional (93%, n=3790)	Functional (7%, n=305)	P Value
Demographics				
Mean age (SD)	33 (±28)	32 (±28)	46 (±20)	<0.01
Women	50%	48%	65%	<0.01
Preoperative co-morbidities				
Hypertension	39%	36%	78%	<0.01
Diabetes mellitus type 2	12%	11%	30%	<0.01
Obesity	8%	6%	28%	<0.01
Congestive heart failure	3%	2%	10%	<0.01
Coagulopathy	5%	4%	9%	<0.01
Liver disease	3%	3%	5%	0.027
Chronic lung disease	9%	9%	11%	0.243
Renal failure	3%	3%	5%	0.143
Laparoscopy	7%	7%	0%	<0.01
Elective (versus emergent)	78%	78%	75%	0.163
Postoperative events				
Overall complication	31%	30%	45%	<0.01
Wound complication	1%	1%	5%	<0.01
Acute kidney injury	4%	3%	13%	<0.01
Pulmonary embolism	1%	1%	3%	<0.01
Adrenocortical insufficiency	4%	4%	13%	<0.01
In-hospital death	1%	1%	2%	0.015

All values approximated to the nearest tenth of a number; Overall complications include cardiopulmonary complications, kidney injury and pulmonary embolism; Wound complications include wound infection, dehiscence and necrosis

PT147

Determinants of Survival in Patients with Pancreatic Neuroendocrine Tumors K. Keck,[1]* P. Breheny,[2] A. Choi,[1] J.E. Maxwell,[1] J.S. Dillon,[3] C.H. Chan,[1] H. Hoshi,[1] A. Bellizzi,[4] T. O'Dorisio,[3] J.R. Howe.[1] *1. Department of Surgery, University of Iowa Carver College of Medicine, Iowa City, IA; 2. Department of Biostatistics, University of Iowa Carver College of Medicine, Iowa City, IA; 3. Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, IA; 4. Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA.*

Background: Pancreatic neuroendocrine tumors (PNETs) have one of the worst prognoses among NET subtypes. The increasing incidence of PNETs and recent advances in treatment make further stratification of patients important for determining their optimal treatment and follow-up. We set out to determine factors associated with survival in patients with PNETs resected at a single institution. Methods: We retrospectively reviewed our surgical NET database for patients with PNETs. The effects of clinicopathologic variables on survival were evaluated in a univariate analysis (UVA) using the Kaplan-Meier method and in a multivariate analysis (MVA) using Cox proportional hazards modeling. Results: A total of 111 patients were identified with a mean follow-up of 53 mos.; 31/66 variables were significantly associated with overall survival (OS) on UVA. OS was not affected by age, sex, operation type or pancreatic location. Eight variables with low rates of missing data were selected for MVA; 103 patients had data for all 8 variables. Higher Ki-67 values, primary size, and M stage significantly decreased OS on MVA, as did elevated preoperative pancreastatin (PST), which was analyzed in a smaller group of 79 patients with available data. Functional tumors were associated with improved OS by MVA (Table 1). The independent predictor of survival with the highest hazard ratio (HR) on MVA was M stage (6.4), followed by Ki-67 (3.7). PST level and primary size each had a HR of 1.6. The continuous variables (Ki-67, tumor size, and PST) were further analyzed using different thresholds. No specific Ki-67 cutoff (2, 4 or 6%) reached significance. PST >197 (1.5x normal) along with tumor size cutoffs of 2, 4 and 6 cm significantly affected OS in UVA. Median OS of patients with tumors >6 cm was 5.6 vs. 11.4 yrs. in those <6 cm; this size cutoff was an independent predictor of OS on MVA. Conclusion: Ki-67, primary size, M stage, PST, and functional status are independent prognostic factors for survival in patients with PNETs. Patients with these risk factors are at higher risk of recurrence and death, and their routine evaluation is important for helping to select patients who will benefit from additional therapies.

Table 1: Results of univariate (UVA) and multivariate analysis (MVA).

Variable (n)	UVA		MVA		
	HR	P-value	HR	95% CI	P-value
M Stage (103)	2.26	<0.01	6.4	1.8 - 22.7	<0.01
Ki-67 of Primary (103)	3.22	<0.01	3.7	1.6 - 8.5	<0.01
Pancreastatin (63)	1.59	<0.01	1.6	1.1 - 2.2	0.01
Size of Primary (103)	1.76	<0.01	1.6	1.1 - 2.5	0.02
Functional Tumor (103)	0.43	0.01	0.4	0.1 - 1.0	0.05
Age at Surgery (103)	1.18	0.18	1.3	0.9 - 2.0	0.22
Liver Surgery (103)	3.52	< 0.01	0.5	0.2 - 1.7	0.28
Familial Syndrome (103)	0.20	<0.01	1.8	0.2 - 14.4	0.59
Multifocality (103)	0.28	0.01	0.7	0.1 - 3.6	0.65

HR=hazard ratio; CI=confidence interval

PT148

Thyroid Gland Stem Cells; A Potential Treatment for Thyroid Cancer Patients Suffering from Hypothyroidism? A.H. Groen,[1]* N. Hosper,[2] M. Maimets,[2] A. Jellema,[2] M. Baanstra,[2] H. Faber,[2] T. Links,[3] J.T.M. Plukker,[1] R. Coppes.[2] *1. Department of Surgical Oncology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; 2. Department of Radiation Oncology and Cell Biology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; 3. Department of Endocrinology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands.*

Patients with well differentiated thyroid cancer are usually treated with total thyroidectomy followed by radioactive iodine therapy. These patients need life-long daily administration of thyroid hormones. Of the adult patients 10-15% suffers from persisting complaints related to thyroid hormone replacement therapy. Thyroid stem cell therapy would restore life-long tissue functioning and avoid side-effects of hormone replacement therapy. The aim of this study is to isolate stem cells from thyroid tissue and to study their potential to generate normal functioning thyroid tissue in vivo. Cells were isolated from murine and human thyroid gland tissue, which in serum-free conditions formed thyrospheres. Primary spheres expressed thyroid specific genes confirming that the cells were derived from the thyroid gland. Some of these cells were able to form secondary spheres after passaging, which have been continued for more than 15 passages, confirming their self-renewal capacity and expansion potential. Furthermore, these cells are capable of forming organoids, expressing major thyroid gland lineages as indicated by expression of e.g. thyroglobulin. Eight to sixteen weeks after (xeno-) transplantation of dissociated mouse or human organoids underneath the kidney capsule in radioactive I^{131} treated athyroid (immune-deficient) mice, thyroid follicles were present under the kidney capsule and grew in size in time. These follicles contained thyroid specific cell types, visualized by thyroglobulin and thyroid transcription factor-1, indicating that adult stem cells isolated from both murine and human thyroid tissue can generate thyroid tissue in athyroid mice. In conclusion, both murine and human adult thyroid stem cells can be isolated, expanded in vitro and form fully functional thyroid follicles in athyroid mice. Culture of human thyroid tissue is very promising and shows the therapeutic potential of stem cell therapy to thyroid hormone replacement therapy after total thyroidectomy in a selected group of thyroid cancer patients.

PT149

Management and Outcomes in Patients with Metastatic Adrenocortical Carcinoma E. Postma,[2]* Y. Lu,[2] M. Moore,[2] M. Vriens,[1] T. Fahey 3rd,[2] R. Zarnegar.[2] *1. UMC Utrecht, Utrecht, Netherlands; 2. New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY.*

Introduction: Due to the rarity of adrenocortical malignancies and the consequent paucity of papers with a high level of evidence, an optimized treatment regimen, especially for patients presenting with metastatic disease, has been difficult to define. We aim to evaluate the association between treatment strategy and overall survival (OS) in patients with metastasized adrenocortical carcinoma in a large contemporary cohort of patients. Methods: Adults with adrenocortical carcinoma registered in the National Cancer Database who were diagnosed between 2010-2014 and had metastatic disease at presentation were included. Cox proportional hazards models were applied to measure the association between the type of treatment and OS while adjusting for patient demographic and clinical factors, including comorbidities, site and number of metastases. Results: Among the 422 patients who presented with metastatic disease, 63% of the patients had a single metastatic site, 30% had metastases at 2 sites and 7% at 3 sites. Surgery only was performed in 11%, while 42% underwent treatment with radiotherapy (RT) or chemotherapy (CT) only. Surgery was combined with RT or CT in 29%, while 18% received no treatment. The overall median OS was 5.3 months. After multivariable adjustment surgery of the primary tumor (with or without RT and CT) was independently associated with improved survival (p<0.001, HR 1.92). Site and number of metastases did not influence survival. Conclusion: In this large contemporary cohort of patients with adrenocortical carcinoma we observed poor overall survival. Surgical management of the primary tumor, improves overall survival in the setting of metastatis disease.

Variables	Univariate Analysis		Multivariate Analysis	
	Hazard Ratio	*P-value*	*Hazard Ratio*	*P-value*
Age >55y	1.560	**.001**	1.410	**.027**
Sex, female	.819	.129		
Surgery				
Resection of primary site	.520	**<.0001**	.535	**<.0001**
Resection of distant site	.469	**.004**	.656	.141
Lymph node resection	.918	.089	.906	.606
Facility Type				
Community cancer program	1.515	.238		
Academic/Research Program	1.026	.942		
Integrated network cancer program	Reference			
Metastasis				
>1	1.165	.271		
Brain	2.981	**.005**	2.066	.219
Lung	1.255	.094	1.368	**.046**
Liver	1.205	.169		
Bone	.907	.571		
Tumor Size >25 cm	1.151	.438		
Charlson-Deyo Score				
0	Reference			
1	.738	.209		
2	1.057	.840		
Chemotherapy	.608	**.001**	.478	**<.0001**
Radiotherapy	.879	0.279		

Table 1 Multivariate Cox proportional hazards survival analysis.

PT150

Timing of Thyroidectomy Does Not Affect Overall Survival in Papillary Thyroid Carcinoma P. Suman,* N. Calcatera, C. Wang, T.A. Moo-Young, R.A. Prinz, D.J. Winchester. *NorthShore University HealthSystem, Evanston, IL.*

Introduction: Appropriate timing of thyroidectomy after diagnosis of papillary thyroid carcinoma (PTC) is not well-defined. We analyzed the impact of timing of thyroidectomy on overall survival (OS) in PTC. Methods: The National Cancer Data Base was queried from 2004 to 2012 for biopsy-proven PTC > 1 cm cN0M0 undergoing lobectomy/near/subtotal or total thyroidectomy without adjuvant RAI. Timing of surgery was categorized as > 1 month, 1-2 months, 2-3 months and 3-6 months categories. Survival analysis was performed after adjusting for patient and tumor-related variables. Results: There were 5,432 patients with PTC > 1 cm. 93% of patients underwent near/sub/total thyroidectomy. 2,160 (39.8%) had surgery within 1 month of diagnosis while 2,145 (39.5%), 687 (12.6%) and 480 (8.1%) patients had thyroidectomy between 1-2 months, 2-3 months and 3-6 months respectively. Mean tumor size did not vary significantly (P= .110) among time categories (< 1 month- 2.3 ± 1.9 cm, 1-2 months- 2.2 ± 1.9 cm, 2-3 months- 2.2 ± 1.7 cm, 3-6 months- 2.2 ± 1.9 cm). 5 year OS rates for surgery at < 1 month, 1-2 months, 2-3 months and 3-6 months were 96%, 95.8%, 94.5% and 95.5% respectively. Kaplan–Meier analysis did not show a statistically significant difference in OS for different time categories (P= .591). After adjusting for patient, socioeconomic, tumor and treatment related variables, timing of surgery failed to impact OS in Cox multivariable survival analysis. In comparison to < 1 month, thyroidectomy between 1-2 months (HR 1.04, 95% CI .68-1.60, P= .837), 2-3 months (HR 1.02, 95% CI .57-1.80, P= .952) and 3-6 months after diagnosis (HR .42, 95% CI .15-1.18, P= .098) did not affect OS. Conclusion: The timing of thyroidectomy after diagnosis of PTC > 1 cm does not affect OS. These results can be utilized in making informed decisions about thyroidectomy, mitigate patient anxiety, and improve judicious resource utilization.

PT151

Novel Point-of-Care Imaging for Medullary Thyroid Carcinoma K. Rossfeld,* S. Justiniano, H. Ding, L. Gong, S. Kothandaraman, C. Wright, M. Saji, M. Ringel, M. Tweedle, J.E. Phay. *Surgery, The Ohio State University Wexner Medical Center, Columbus, OH.*

Introduction: The treatment for medullary thyroid carcinoma (MTC) is primarily surgical as most cases are resistant to chemotherapy and radiation. Enhanced intraoperative visualization may improve surgical outcomes by ensuring complete resection of the tumor and nodal deposits. We have developed a novel molecule (Compound 17) labeled with infrared dye to allow intraoperative visualization. We also developed an orthotopic mouse model for MTC to best simulate surgical utility. Methods: Dosing and kinetics of Compound 17 were tested in an in vitro system using two MTC cell lines (MZ-CRC-1 & TT). A flank xenograft mouse model was used in preliminary studies to evaluate in vivo binding. To better simulate neck surgery and avoid the background fluorescence of the kidneys and bowel, an orthotopic model of MTC was developed by micro-injecting the respective cell lines into the thyroid bed. After 9 weeks of tumor growth, the labeled compound (Compound 17) or labeled scrambled control (Compound 83a) was delivered via tail vein injection. To evaluate kinetics in vivo, incubation periods of 8, 24, 32, and 48 hours were evaluated. Animals were euthanized and the tumors were evaluated in situ and ex vivo for fluorescence using Fluorbeam. Results: In vitro binding for Compound 17 was observed using concentrations from 1 to 10 μM in both MTC cell lines examined. Characterization of the MTC orthotopic xenograft model confirmed the location and histological characteristics expected of MTC development and progression. These orthotopic xenografts showed increased fluorescent signal from Compound 17, much higher than that observed for the scrambled control (Figure 1, TT cell orthotopic tumors at 32 hours). Conclusions: Compound 17 demonstrates increased binding and fluorescence over the scrambled control both in vitro and in vivo including in the orthotopic MTC model. These data suggest that Compound 17 has the potential to become a surgical adjunct for treating medullary thyroid cancer.

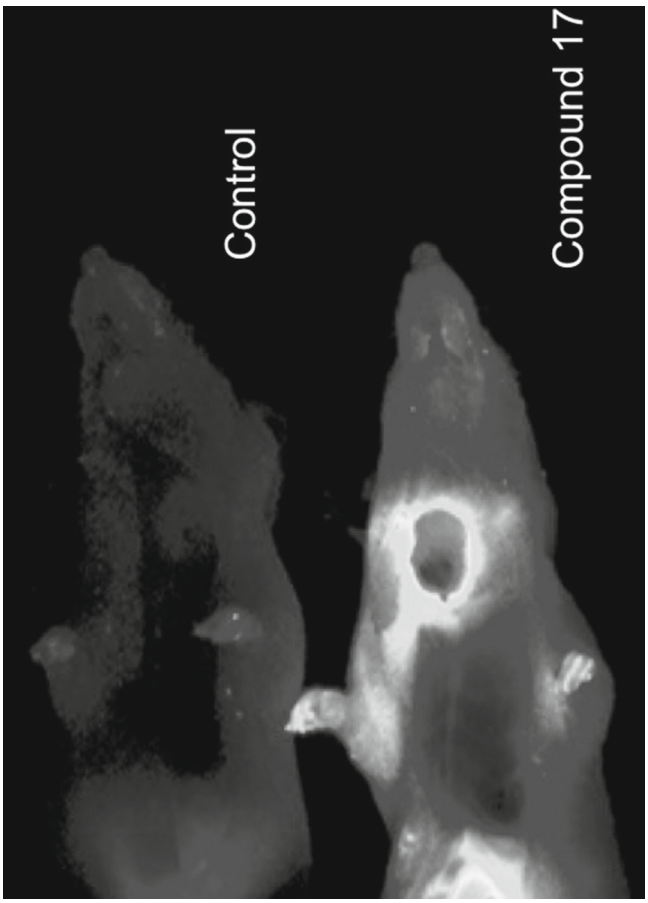


Figure 1. TT cell orthotopic xenografts, injected with the labeled control vs. Compound 17, imaged after 32 hours post injection.

PF152

Routine Surveillance Ultrasound in Screening for Recurrence After Neck Dissection in Patients with Thyroid Cancer O.S. Eng,[1] S.B. Grant,[3]* H. Ashforth,[2] J. Weissler,[2] T. Davidov,[2] S.Z. Trooskin.[2] *1. Surgery, City of Hope National Medical Center, Duarte, CA; 2. Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ; 3. The University of Chicago Medical Center, Chicago, IL.*

Background Treatment of lateral compartment metastases in patients with papillary thyroid carcinoma includes ipsilateral modified radical neck dissection (MRND). This group is at risk for recurrent/residual disease. We sought to evaluate the role of routine ultrasound surveillance in patients after thyroidectomy and MRND at our institution. Methods Patients from 2007-2015 with papillary thyroid carcinoma were identified from a retrospective database at a tertiary care center with a history of total thyroidectomy, lateral compartment lymph node metastases, and ipsilateral MRND. Patients were divided into two groups: those who experienced disease recurrence and those who did not. Patient and tumor data were compared between the groups. All patients received a surveillance neck ultrasound yearly at a minimum. Results A total of 87 patients were identified. Median age was 43 years (range 15-84. The median lymph node yield from MRND was 26 (range 5-87). Median overall primary tumor size was 1.7cm (range 0.3-8.0). Recurrent disease was found in 23 (26%) patients, via routine surveillance ultrasound in 22 (96%). Disease detected via ultrasound was palpable in only 2 (9.1%) patients. Ipsilateral and contralateral recurrences were found in 14 (61%) and 10 (43%) of patients respectively. Patients who experienced recurrence were more likely to have a history of radiation exposure (21.7 vs. 4.7%, p=0.02), larger median primary tumor size (2.2 vs. 1.5cm, p=0.03), and presence of vascular invasion (47.9 vs. 21.9%, p=0.02) in the primary tumor. On multivariate analysis, only a history of radiation exposure was significantly associated with both ipsilateral and contralateral recurrence. Conclusion The majority of patients with recurrence after MRND for papillary thyroid cancer with lateral lymph node metastases have non-palpable disease. A history of radiation exposure is associated with the development of ipsilateral and contralateral recurrence. Routine surveillance ultrasound is an important screening tool for detecting recurrence after MRND for papillary thyroid cancer.

PF153

Malignancy Rate of Thyroid Nodules and Role of Gene Expression Classifier Testing at an Academic Institution E. Murphy,* M. Affi, B. Javorsky, T. Yen, K. Doffek, G. Fareau, B. Hunt, P. Tolat, T. Carroll, T. Giorgadze, A. Carr, D. Evans, T.S. Wang. *Medical College of Wisconsin, Milwaukee, WI.*

Background: Up to 30% of thyroid nodules evaluated by fine needle aspiration (FNA) have indeterminate cytology. The mRNA-based gene-expression classifier (GEC) test has a high negative predictive value, but use is contingent on individual institutional rates of clinically significant malignancy (CSM) for indeterminate thyroid nodules. The aim of this study was to define the institutional malignancy rate of thyroid nodules and clarify the role of GEC testing for FNA indeterminate cytology. Methods: This is a retrospective review of patients (pts) from 10/12-5/16 who underwent thyroidectomy or had repeat FNA for GEC testing and did not undergo surgery. Cytology results were based on Bethesda criteria. Bethesda III/IV were considered indeterminate. We defined a CSM based on histologic evaluation of the thyroidectomy specimen. Results: Of 564 pts, 510 underwent thyroidectomy (32 had GEC testing) and 54 had GEC testing but no surgery. On final pathology, 177/510 (35%) pts had a CSM, including 32/175 (18%) with indeterminate FNA cytology. Overall, 86 had repeat FNA sent for GEC testing and 41 (47%) did not undergo GEC testing as cytologic review disagreed with the initial indeterminate diagnosis—38 (44%) were benign, 2 (2%) suspicious and 1 (1%) nondiagnostic. The two pts with suspicious cytology had surgical confirmation of a CSM. Of 45 (53%) samples that had GEC testing, 17 (38%) were GEC-benign and did not have surgery and 28 (62%) were GEC-suspicious. Of these 28 GEC-suspicious samples, 27 had surgery and 22% (6/27) had a CSM. Therefore, of the 86 patients who underwent repeat FNA for GEC testing, 32 (37%) had surgery with a CSM rate of 25% (8/32)—8 (9%) of the 86 pts sent for GEC. In comparison, 143 pts with indeterminate nodules underwent surgery without GEC testing and 24 (17%) had a CSM (p=0.2). Conclusions: At our institution, repeat FNA as part of GEC testing reclassified about 2/3 of nodules as benign and the rate of CSM was about 1/2 of previously published rates for GEC-suspicious nodules. Therefore it is unclear if GEC testing for patients with indeterminate thyroid nodules provides added value over repeat FNA alone.

Clinically significant institutional malignancy rates

	Definition	Surgical cohort (n=510)
Bethesda I	Nondiagnostic or unsatisfactory	0% (0/9)
Bethesda II	Benign	5% (9/182)
Bethesda III	Atypia of undetermined significance or follicular lesion of undetermined significance	14% (13/95)
Bethesda IV	Follicular neoplasm or suspicious for follicular neoplasm	24% (19/80)
Bethesda V	Suspicious for malignancy	85% (40/47)
Bethesda VI	Malignant	99% (96/97)

PF154

Can Suspicious Surgeon-Performed Ultrasound Features Predict BRAFV600E Status in Papillary Thyroid Carcinoma? H. Khadra,* K. Mohsin, F. Murad, D. Monlezun, E. Kandil. *Surgery, Tulane University School of Medicine, New Orleans, LA.*

Background: Papillary thyroid carcinoma (PTC) can be predicted from certain suspicious ultrasound (US) features of thyroid nodules. The aim of this study is to examine if these suspicious features can predict the more aggressive PTC associated with B-type Raf kinase (BRAFV600E) mutations. Methods: This is a retrospective review of prospectively collected data on patients with PTC and known BRAFV600E status. The patients underwent preoperative ultrasound by the same surgeon who performed all the operations. We divided patients into BRAFV600E positive and negative groups. All ultrasonographic data were collected including nodule size, echogenicity, solid or cystic nature, presence of calcifications, irregular margins, and internal vascularity. Results: Of 145 patients with PTC, BRAFV600E mutation was detected in 48 (33.1%) patients. There was no significant difference in nodule size (2.06 cm ±1.37 vs. 2.15 cm ±1.55, p= 0.75) between BRAFV600E positive and negative groups. BRAFV600E positivity was associated with higher rates of hypoechogenicity (57.4% vs. 36.5, p= 0.019), calcifications (48.9% vs. 19.3%, p< 0.001), and irregular margins (21.3% vs. 6.4%, p= 0.009). There was no significant difference in non-cystic nature or internal vascularity between BRAFV600E positive and negative groups. The absence of calcifications combined with irregular margins is associated with a negative predictive value of 96.0%. In the absence of all suspicious features, negative predictive value was 83.3%. When suspicious lymph nodes detected by preoperative US were compared, there was no significant difference between BRAFV600E positive and negative groups (28.2 vs. 21.4%, p= 0.41). Conclusion: The presence of multiple suspicious US findings of thyroid nodules can predict the BRAFV600E mutation status of papillary thyroid cancer nodules. Presence of hypoechogenicity, intra-nodular calcifications and irregular nodular margins were the most predictive features of BRAFV600E positivity. Future multi-institutional studies are warranted to help surgeons with risk stratification and surgery planning for patients with papillary thyroid cancer.

PF155

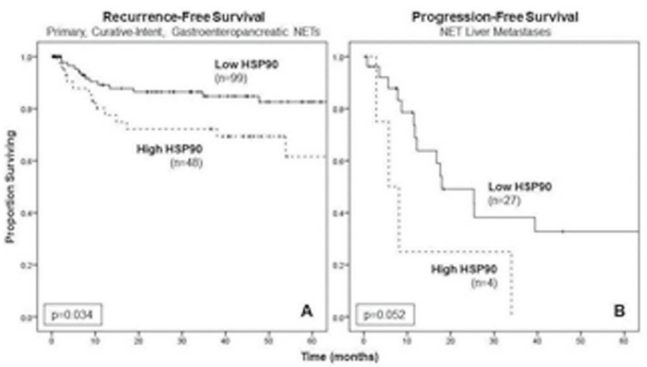
Predictors of Malignancy in Pheochromocytoma and Paraganglioma Patients M. Dhir,* W. Li, M. Hogg, D. Bartlett, S.E. Carty, K.L. McCoy, S.M. Challinor, L. Yip. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Malignancy in patients with pheochromocytoma (Pheo) and paraganglioma (PGL) can be diagnosed decades after initial adrenalectomy, and longterm surveillance is needed. Although histopathologic factors may predict malignancy, these lack sensitivity and are limited by inter-observer variability. The primary aim of this study is to investigate the genetic and clinical factors which may be associated with malignancy in Pheo/PGL patients. Methods: Single institution retrospective review of all patients who had surgery for Pheo/PGL (1/95-1/15) was performed. Malignancy was defined as histology-confirmed distant metastasis, lymph nodal involvement, or local recurrence. Results: 157 Pheo/PGL patients with a mean follow-up of 87 months (range 1–580) were included. Median age at initial diagnosis was 48 y (range 9-78). Malignancy was diagnosed in 46 patients (29%) and was synchronous in 18 (39%) patients. Metachronous malignant Pheo/PGL was diagnosed in 28 (61%) at median time of 68 months. Patients with malignant Pheo/PGL were younger (median 41 v 50 y, p 0.003), had larger primary tumors (median 6 v 4 cm, p <0.001), had PGL (61 v 5%, p <0.001) and had an existing family history of a genetic predisposition syndrome (23 v 10%, p = 0.04). Genetic testing was performed in 60 Pheo/PGL patients and 38 (63%) were positive for VHL (22%), SDHB (18%), NF1 (10%), RET (8%), and SDHD (5%). Although positive genetic testing results were equally likely in malignant compared to benign Pheo/PGL (74 v 54%, p 0.2), all 11 patients with germline SDHB mutations had malignant disease. In multivariable analysis including only clinical variables, increasing age (OR 1.04), larger tumor size (OR 1.3) and PGL (OR 57.1) were associated with malignancy (p <0.05). Pheo patients with negative genetic testing who developed metachronous metastases all had primary tumors ≥4 cm in size (sens 100%, spec 54%). Conclusions: All SDHB positive Pheo/PGL patients had malignant disease. Patients who are young, have larger tumors, and/or have PGL also need to undergo continued follow-up. Patients with negative genetic testing and Pheos <4 cm have a minimal risk of developing malignancy and may not require prolonged surveillance.

PF156

HSP90 Expression and Early Recurrence in Gastroenteropancreatic Neuroendocrine Tumors: Potential for Novel Therapeutic Targets C.G. Ethun,[1]* L.M. Postlewait,[1] A.G. Lopez-Aguiar,[1] K. Zhelnin,[2] A. Krasinskas,[2] B. El-Rayes,[3] M. Russell,[1] D. Kooby,[1] C.A. Staley,[1] K. Cardona,[1] S.K. Maithel.[1] *1. Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Pathology, Winship Cancer Institute, Emory University, Atlanta, GA; 3. Department of Hematology Oncology, Winship Cancer Institute, Emory University, Atlanta, GA.*

Background: Heat shock protein (HSP) 90 promotes tumor growth and is overexpressed in many malignancies. HSP90 expression profile and its potential as a therapeutic target in primary and metastatic neuroendocrine tumors (NETs) are not known. Methods: HSP90 cytoplasmic expression and Ki-67 index were re-reviewed and scored by a pathologist blinded to all other clinicopathologic variables using tissue microarray (TMA) blocks created in triplicate for patients who underwent resection of primary and metastatic gastroenteropancreatic (GEP) neuroendocrine tumors at a single institution from 2000-2013. Primary outcome was recurrence-free survival (RFS). Results: Of 278 tumors reviewed, 194 (68%) were primary GEP NETs, and 31 (11%) were NET liver metastases. Of the primary GEP NETs, mean age was 56yrs, 42% were male; 103 (53%) were pancreas and 44 (23%) were small bowel. HSP90 expression was high in 66 (34%) and low in 128 (66%). Compared to low expression, high HSP90 was associated with lymphovascular invasion (70vs42%; p=0.049) and advanced T-stage (T3/T4) tumors (48vs27%; p=0.01). Among patients who underwent curative-intent resections for primary, non-metastatic NETs (n=147), high HSP90 was associated with decreased RFS compared to low (HR 2.5, 95%CI 1.04-4.9; p=0.04; Fig 1A), which persisted on multivariable analysis (HR 5.2, 95%CI 1.7-16.0; p=0.004), after accounting for positive margin, LN involvement, increased tumor size, site of primary tumor, and Ki-67 index. When assessing NET liver metastases, high HSP90 expression was seen in 4 (13%) patients and low in 27 (87%). Similar to primary GEP NETs, patients with liver metastases that exhibited high HSP90 expression had decreased progression-free survival compared to those with low HSP90 (p=0.052; Fig 1B). Conclusion: Heat shock protein 90 exhibits differential expression in resected GEP NETs and liver metastases. High cytoplasmic expression is associated with early recurrence of disease, even after accounting for other adverse pathologic factors, including Ki-67 index. HSP90 inhibition is a potential target for novel therapeutic strategies for neuroendocrine tumors.



Recurrence-Free Survival	1-yr	3-yr	5-yr
Low HSP90	89%	86%	83%
High HSP90	80%	72%	62%

Progression-Free Survival	1-yr	3-yr	5-yr
Low HSP90	69%	49%	33%
High HSP90	25%	25%	0%

PF157

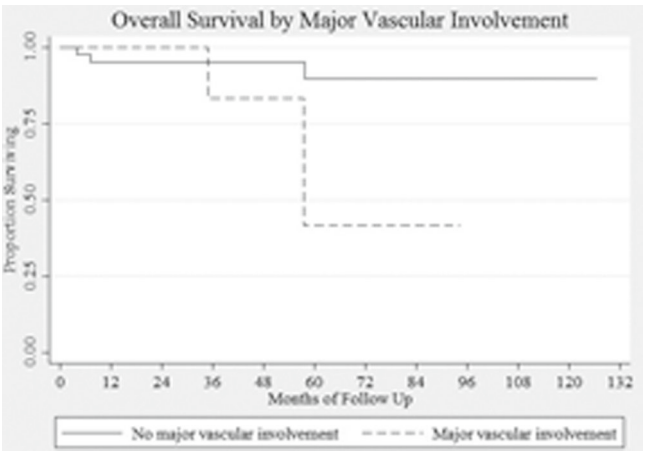
Clinical and Biologic Impact of Body Mass Index on Adrenocortical Carcinoma A. Weisbrod,[1]* K. Rossfeld,[1] L. Yu,[1] T. Tran,[2] L.M. Postlewait,[3] S.K. Maithel,[3] J.D. Prescott,[4] T.S. Wang,[5] J. Glenn,[5] R. Fields,[6] L.X. Jin,[6] S.M. Weber,[7] A. Salem,[7] J.K. Sicklick,[8] S. Gad,[8] A. Yopp,[9] J.C. Mansour,[9] Q. Duh,[10] N. Seiser,[10] C.C. Solorzano,[11] C.M. Kiernan,[11] K. Votanopoulos,[12] E.A. Levine,[12] I. Hatzaras,[13] R. Shenoy,[13] T. Pawlik.[1] *1. The Ohio State University Wexner Medical Center, Columbus, OH; 2. Stanford University School of Medicine, Stanford, CA; 3. Emory University, Atlanta, GA; 4. The Johns Hopkins University School of Medicine, Baltimore, MD; 5. Medical College of Wisconsin, Milwaukee, WI; 6. Washington University School of Medicine, St. Louis, MO; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. University of California San Diego, San Diego, CA; 9. University of Texas Southwestern Medical Center, Dallas, TX; 10. University of California San Francisco, San Francisco, CA; 11. Vanderbilt University, Nashville, TN; 12. Wake Forest Baptist Medical Center, Winston Salem, NC; 13. New York University School of Medicine, New York, NY.*

Purpose: Obesity is an established risk factor for many types of cancer. While obesity has been linked to worse long-term outcomes among patients with breast and colorectal cancer, the relationship of body mass index (BMI) and adrenocortical carcinoma (ACC) remains ill-defined. Since ACC can express adipokine and estrogen receptors, the impact of BMI on outcomes in this patient population is important. We sought to define the association of BMI on ACC clinical and biologic factors, as well as long-term survival. Methods: Data was obtained on 187 patients who underwent surgery for ACC at 13 institutions for whom BMI data were available. Patients were stratified according to the WHO classification of BMI: BMI<25, 25-29.9, 30-34.9, 35-39.9 and ≥40. Demographics, tumor biology, management strategies and clinical outcomes were assessed relative to BMI category. Categorical data were analyzed by Fisher's exact test, while continuous variables were analyzed by ANOVA model; disease-free and overall survival were analyzed by Kaplan-Meier survival curves. Results: Mean BMI was 29.5, with a range of 19 to 69. Patient age was comparable among all BMI groups (p=0.9917). Patient sex (p=0.0079) and race (p=0.0373) varied by BMI category. Mean tumor size was 12.1 cm and mean tumor weight was 875 grams, which was similar in all BMI groups. AJCC stage (Stage I: n=12; Stage II: n=62; Stage III: n=47; and Stage IV: n=48) and ENSAT stage (Stage I: n=12; Stage II: n=62; Stage III: n=72; and Stage IV: n=23) did not vary by BMI. BMI tended to be associated with mean mitotic rate (BMI<25: 12.4; 25-29.9: 14.2; 30-34.9: 21.0; 35-39.9: 33.8 and ≥40: 8.7; p=0.0773) and percent lymphatic invasion (BMI<25: 37%; 25-29.9: 68%; 30-34.9: 60%; 35-39.9: 67% and ≥40: 44%; p=0.0818). In addition, R0 resection rate differed by BMI group (BMI<25: 68%; 25-29.9: 76%; 30-34.9: 50%; 35-39.9: 27% and ≥40: 71%; p=0.0029). BMI was not associated with disease-free interval or overall survival. Conclusion: Increased BMI was associated with ACC tumor characteristics but did not affect disease-free or overall survival in our cohort. Further studies are needed to evaluate whether the endocrine effect of lipocytes influences ACC pathology.

PF158

Management of Extraadrenal Abdominal Paraganglioma with Vascular Involvement A. Sinnamon,* S. Zaheer, S. BenMaimon, M. Neuwirth, D.L. Cohen, K.L. Nathanson, G. Karakousis, E.Y. Woo, B.M. Jackson, R. Roses, D.L. Fraker. *General Surgery, Hospital of the Univ of Pennsylvania, Philadelphia, PA.*

Background Malignant extraadrenal abdominal paragangliomas (PGLs) are endocrine tumors that may involve major vascular structures. Little is known regarding surgical and oncologic outcomes in patients undergoing en bloc resection. Methods Retrospective review was performed to identify patients with PGL managed at our institution. Tumors with vascular involvement were resected in coordination with the vascular surgery service. Catecholamine-secreting tumors were medically blocked. Patients were referred to medical genetics and genetic testing was performed as appropriate. Survival analysis was performed using Cox proportional hazard and Kaplan-Meier modeling to evaluate overall survival (OS) and recurrence. Results From 1998 to 2016, 63 patients with PGL were managed and 58 underwent resection with curative intent. Median age was 49y. Fifty-five (87%) were proven to be biochemically active; 2 were proven non-functional. Nine patients presented with major involvement or encasement of aorta or IVC. Tumors with vascular involvement were larger (median 8.1 vs 4.5cm, p=0.005) with higher PASS score (median 9 vs 4, p=0.003). En bloc resections were performed in conjunction with major vascular procedures including aorta replacement (n=5), IVC replacement (n=4), common iliac vein replacement (n=1), and primary vascular defect repair (n=2). Disease progression occurred in 6 at median 10.5mo and 3 were progression-free at last follow up (range 16-50mo). Five year OS was 51% in the vascular group compared to 90% among tumors without vascular invasion (p=0.127, figure). There were 3 venous and no aortic graft thrombosis complications. Eight of 9 patients had a mutation in the SDHB gene. The overall rate of associated genetic mutation was 67% (32 of 48) in SDHB (23), SDHD (5), SDHA (2), VHL (1), and NF1 (1). Four patients in the overall cohort with significant family histories were identified and referred for surgery solely based on genetic screening. Conclusions PGLs with vascular involvement can be safely resected with preoperative planning. Recurrence is common but progression free survival may be achieved. Referral to medical genetics is indicated as the rate of associated genetic mutation is high.



PF159

A Comparison of Minimally Invasive and Open Adrenalectomy for Adrenocortical Cancer N. Calcatera,* C. Wang, D. Winchester, R.A. Prinz. *Surgery, Northshore University Healthsystem, Chicago, IL.*

Introduction: The role of a minimally invasive surgical approach for adrenocortical carcinoma is unclear. This study aims to compare the characteristics and overall survival of patients undergoing successful minimally invasive adrenalectomy to those having an open operation using a large national database. Methods: Adrenocortical carcinoma patients with surgical approach data [from 2010-2013] were identified in the National Cancer Database. A retrospective review of patient demographics, tumor and treatment characteristics was conducted. Multinominal logistic regression was performed to identify independent predictors of overall survival. Results: We identified 531 patients. Of these, 337/531(63.5%) were female and 450/531(84.7%) Caucasian. 133 patients (25%) had a laparoscopic or robotic approach while the remaining 398 had an open operation. The minimally invasive patients had a smaller average tumor size (8.4 versus 13cm), more tumors confined to the adrenal (64.9 versus 48.9%) and a shorter hospital length of stay (4.2 versus 7.7 days). Positive pathologic margin status (p=0.80) and presence of lympho-vascular invasion(p=0.28) did not differ between groups. The open patients were more likely to receive chemotherapy (p=0.0003), radiation (p=0.0138), present with more locally advanced disease (p=0.003) as well as distant metastases (p=0.0156). On multinomial logistic regression analysis only positive margin status, lympho-vascular invasion and distant metastases predicted worse overall survival. There was no difference in overall survival with a minimally invasive or open adrenalectomy (p=0.4131). Conclusion: Minimally invasive adrenalectomy for adrenocortical carcinoma may be appropriate when disease is confined to the adrenal gland and complete resection is possible. Incomplete resection, lympho-vascular invasion and extra-adrenal disease are associated with worse overall survival.

PT160

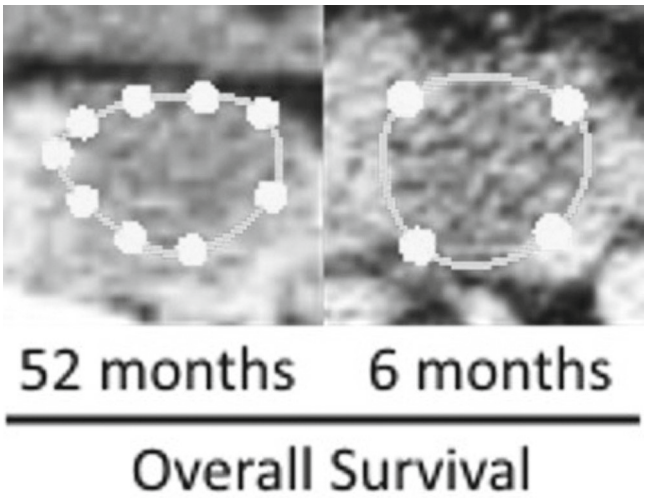
Identification of Tumorigenic Cells and Therapeutic Targets in Pancreatic Neuroendocrine Tumors G.W. Krampitz,[2]* B.M. George,[1] S.B. Willingham,[1] J.P. Volkmer,[1] K.A. Weiskopf,[1] N.S. Jahchan,[1] A.M. Newman,[1] D. Sahoo,[2] A. Zemek,[1] R.L. Yanovsky,[3] J.K. Nguyen,[1] P.J. Schnorr,[1] P.K. Mazur,[1] J. Sage,[1] T.A. Longacre,[1] J.A. Norton,[1] I.L. Weissman.[1] *1. Surgery, Stanford School of Medicine, Stanford, CA; 2. University of California San Diego, San Diego, CA; 3. Tufts University School of Medicine, Boston, MA.*

Introduction: Pancreatic neuroendocrine tumors (PanNETs) are a type of pancreatic cancer with limited therapeutic options. Consequently, most patients with advanced disease die from tumor progression. Current evidence indicates that a subset of cancer cells are responsible for tumor development, metastasis, and recurrence, and targeting these tumor initiating cells is necessary to eradicate tumors. However, tumor initiating cells and the biological processes that promote pathogenesis remain largely uncharacterized in PanNETs. Methods: We used 39 human tissue specimens, developed a novel cell line, generated xenograft models in NOD-SCID Gamma (NSG) mice, and employed a RIP-Cre Rb/p53/p130 genetic mouse model to identify tumor initiating, select therapeutic targets, and validate potential immunotherapies. Results: Here we profile primary and metastatic tumors from an index patient and demonstrate that MET activation is important for tumor growth in PanNET xenograft models. We identify a highly tumorigenic cell population within several independent surgically acquired PanNETs characterized by increased CD90 expression and ALDHA1 activity and provide in-vitro and in-vivo evidence for their stem-like properties. We performed proteomic profiling of 332 antigens in 2 cell lines and 4 primary tumors and showed that CD47, a "don't eat me" signal co-opted by cancers to evade innate immune surveillance, is ubiquitously expressed. Moreover, CD47 co-expresses with MET and is enriched in the $CD90^{hi}$ cells. Furthermore, blocking CD47-SIRPα interaction promotes engulfment of tumor cells by macrophages in vitro and inhibits xenograft tumor growth, prevents metastases, and prolongs survival in vivo. Conclusion: These findings provide a foundation for developing therapeutic strategies that eliminate tumor initiating cells in PanNETs and show how deep examination of individual cases can lead to potential therapies.

PT161

Through the Looking-Mass: Preoperative Survival Prediction in Pancreatic Ductal Adenocarcinoma (PDAC) by Quantitative CT Analysis M.A. Attiyeh,* J. Chakraborty, L. Langdon-Embry, V. Balachandran, M.I. D'Angelica, R. DeMatteo, M. Gönen, T. Kingham, S.A. Lawrence, S. Mainarich, W. Jarnagin, P.J. Allen, R.K. Do, A.L. Simpson. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Pancreatic cancer is a highly lethal cancer with no established a priori markers of survival. Existing nomograms rely mainly on post-resection data (pre and postoperative CA 19-9, margin status, differentiation, etc.) and are of limited utility. This study investigated the use of computationally derived quantitative CT features to preoperatively assess survival in PDAC. Methods: A prospectively maintained database identified consecutive patients with resected PDAC between 2009 and 2012. Chemotherapy-naïve patients with adequate CT angiography were included in this study. Variation in CT enhancement patterns was extracted from the tumor region using quantitative techniques previously described. A five-year survival model was constructed with 70% of the data (training set) using Cox regression based on preoperative serum CA19-9 levels and image features. The remaining 30% of the data (test set) were reserved for validation. Results: A total of 161 patients were included in the analysis. Median age was 67 years [interquartile range (IQR) 59–74]. Gender was distributed equally [male: 82 (51%), female: 79 (49%)]. Nearly all CT scans were ≤6 months before surgery (95%). Median overall survival was 24 months (IQR 13–42). Training and test sets contained 113 and 48 patients, respectively. Cross-validation on the training set using a model with CA19-9 alone resulted in a C-index of 0.514 [integrated brier score (IBS) 0.170], only slightly better than chance. Adding quantitative imaging features improved the C-index to 0.623 (IBS 0.154). Evaluation on the independent test set yielded a C-index of 0.531 (IBS 0.213) with CA19-9 only which improved to 0.638 (IBS 0.207) with the addition of imaging features. Conclusion: We present a preliminary preoperative survival prediction model for resected PDAC patients using quantitative CT analysis and CA19-9 levels. Further analyses with other imaging features, clinical variables, and models are ongoing and may lead to stronger predictive power. In the future, this novel non-invasive tool may prove useful for preoperative selection of patients who would most benefit from surgical resection.



Comparison of CT imaging of PDAC (yellow outline) between short-term and long-term survivors. Left: 52 months overall survival. Right: 6 months overall survival.

PT163

Cytology Specimens Can Identify Potential Molecularly-Guided Therapy Options for Patients with Pancreatic Adenocarcinoma R. Saunders,[1]* D. Chesla,[2] S. Alberta,[2] B.R. Lane,[3] G.P. Wright,[4] M. Chung.[4] *1. Grand Rapids Medical Education Partners, Grand Rapids, MI; 2. Spectrum Health Hospitals, Grand Rapids, MI; 3. Division of Urology, Spectrum Health Medical Group, Grand Rapids, MI; 4. Division of Surgical Oncology, Spectrum Health Medical Group, Grand Rapids, MI.*

Introduction: Diagnoses of pancreatic tumors are frequently made from small tissue samples acquired via fine needle aspirations from endoscopic ultrasound (EUS) or biliary brushings from endoscopic retrograde cholangiopancreatography (ERCP). Identification of tumor-specific molecular markers via next-generation sequencing (NGS) techniques could aid clinicians in determining appropriate targeted neoadjuvant therapies for pancreatic adenocarcinoma. We investigated whether the tissue acquired via EUS and ERCP would provide adequate tissue for diagnosis and NGS. Methods: We previously identified pathogenic alterations in 10 genes via the Cancer Hotspot Panel in 28 patients' surgically resected pancreatic adenocarcinomas. Of those 28 patients, 16 had available tissue from a diagnostic EUS (13) or ERCP (3). Cells from diagnostic cytology slides were reviewed and utilized for downstream extraction without amplification kits. A custom Pancreatic Panel of 10 genes was created based off the pathogenic alterations identified in the surgically resected tumors. Extracted cells were analyzed with NGS utilizing the custom Pancreatic Panel. Results: There were 32 pathogenic alterations detected (range: 1-4 per patient) in the surgically resected tumor tissue of the 16 patients. Of those 32 pathogenic alterations, 24 (75%) were detected in the cytology material. ERCP pre-operative specimens made up 19% of the samples. Please refer to Figure 1. Among the 16 patient samples, actionable mutations were present in 12 (75%). Concordances of all detected pathogenic variations were noted in 10 cases (63%). Concordance rates of KRAS (63%), TP53 (89%), CDKN2A (67%), SMAD4 (100%), and GNAS (100%) mutations were detected. Conclusions: Identification of mutational profiles could help to guide personalized systemic therapy in the neoadjuvant and adjuvant setting. NGS of material obtained during EUS or ERCP detected actionable mutations in 12 of 16 samples (75%). Further investigation into refining collection, extraction, and amplification techniques is warranted.

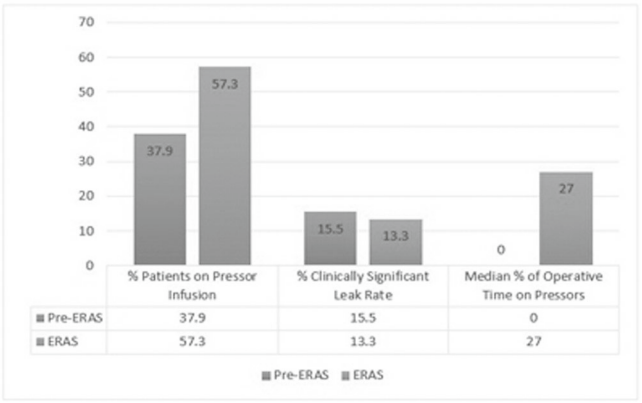
Figure 1: Stratification of Study Cohort and Results

PT164

Enhanced Recover After Surgery (ERAS) for Pancreatectomy: Increased Intraoperative Vasopressor Use Does Not Increase Pancreatic Fistula Rates S. Laks,* L.M. Kolarczyk, P.D. Strassle, R.S. Isaak, L. Hance, H. Kim. *Department of Surgery, University of North Carolina, Cary, NC.*

Background: ERAS pathways have been increasingly implemented in a variety of surgical pathways, including pancreatic surgery. Goal directed fluid therapy (GDFT) is a core component of ERAS pathways, and selectively limits volume administration with increased intraoperative vasopressor use. The effects of vasopressors on surgical outcomes, and pancreatic fistula rates are inadequately defined in the literature. We propose that vasopressor use in an ERAS GDFT algorithm does not increase pancreatic fistula rates. Methods: We reviewed all adult patients undergoing pancreatic resections at a high-volume academic institution from January 2013 to February 2016, before and after implementation of a pancreatectomy ERAS pathway in July 2014. The ERAS pathway was a prospective, funded quality initiative. Retrospective chart review was performed for demographics, comorbidities, intraoperative vasopressor use, and pancreatic fistulas as defined by the International Study Group of Pancreatic Surgery (ISGPS). Results: One hundred thirty-three patients were included in the study: 75 (56.4%) in the ERAS cohort. No significant differences were noted in demographics, comorbidities or preoperative risk factors between the groups. There was a significant increase in vasopressor usage among the ERAS cohort (57.3% vs. 37.9%), p=0.04. Patients in the ERAS cohort also spent an increased median proportion of the total OR time on a vasopressor (ERAS median 27.0% vs. pre-ERAS median 0.0%), p=0.02. No significant differences between ERAS and pre-ERAS cohorts were seen in ISGPS grade B and C fistulas, 10/75 patients (13.3%) as compared to 9/58 patients (15.5%), p=0.98.(Figure 1) Vasopressor use was examined independently of the ERAS pathway, and also failed to show any significant change in pancreatic fistula rates, p=0.72. Conclusions: Increased use of vasopressor infusions as part of an ERAS pathway for pancreatic surgery does not lead to an increase in the rate of clinically significant pancreatic fistulas. Our quality initiative suggests that the intraoperative principles of GDFT do not adversely affect perioperative surgical outcomes.

Figure 1.



PT165

A Novel CCL2 Inhibitor Reduces Tumor Associated Macrophage Infiltration in a Murine Model of Pancreatic Cancer J. Lazarus,* M. Lanfranca, A.A. Girgis, H. Nathan, M.P. Di Magliano, W. Zou, T.L. Frankel. *University of Michigan, Ann Arbor, MI.*

Introduction: A hallmark of pancreas adenocarcinoma (PDAC) is its immunosuppressive microenvironment. A key component of this is tumor-associated macrophages (TAM) which are recruited by the tumor derived chemokine CCL2. We evaluated the efficacy of a novel CCL2 inhibitor, mNOX-E36 (NOXXON Pharma AG, Berlin, Germany) on TAM infiltration in PDAC. Methods: Syngeneic mice were subcutaneously inoculated with PDAC tumor cells and treated with CCL2 neutralizing mNOX-E36 or a non-binding control (revmNOX-E36) either before or after tumor establishment. Mice were sacrificed at three weeks and tumor size and weight measured. After processing to single cell suspension, TAM and T-cell infiltration were assessed by flow cytometry. Results: A cell line (PD2560) was established from a spontaneous murine pancreas cancer and robust CCL2 production confirmed by western blot and qRTPCR compared to negative controls (muscle and the colon cancer line MC38). Mice inoculated with PD2560 and treated with mNOX-E36 showed no toxicity compared to controls and there was a trend towards decreased tumor size and weight at 3 weeks. Delivery of mNOX-E36 resulted in a statistically significant decrease in infiltrating CD45+CD11b+F4/80+ immune cells consistent with TAMs (Figure 1). There was a trend towards increased numbers of infiltrating CD8+ lymphocytes, but this was not statistically significant. Conclusion: The tumor microenvironment of PDAC promotes immunosuppression which contributes to tumor growth and resistance to modern immunotherapeutics. Efforts to reduce suppressive elements including TAMs by targeting the receptor CCR2 on monocytes has been met with some success but neutralization of its ligand, CCL2, has not been previously investigated. We demonstrated that mNOX-E36, a novel CCL2 neutralizing L-RNA aptamer (Spiegelmer^{TM}), was able to reduce TAM infiltration in a murine model of PDAC. Trends towards decreased tumor size and T-cell infiltration suggest this may provide a novel adjunct therapy to decrease the immunosuppressive cellular infiltrate and heighten tumor destruction.

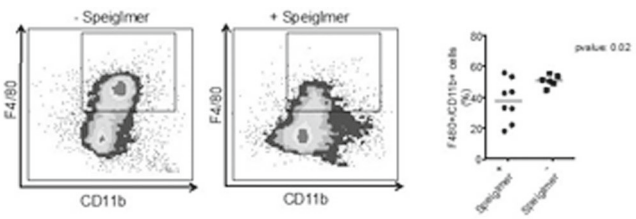
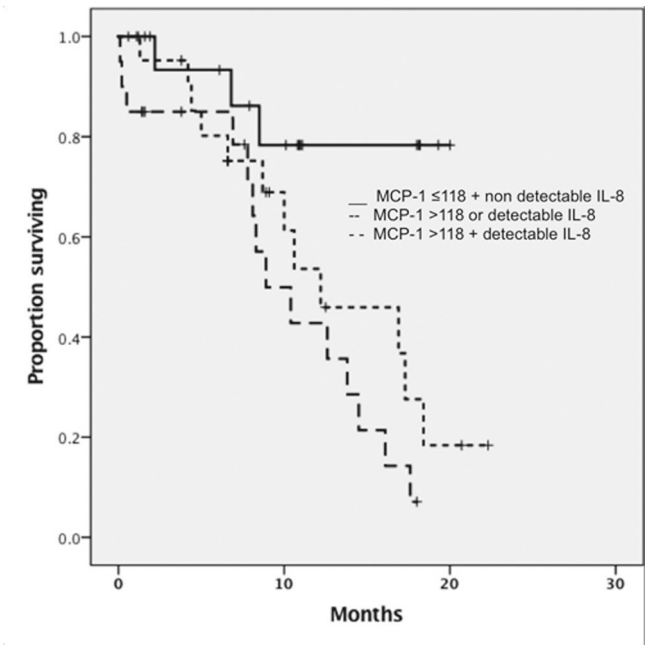


Figure 1: CCL2 neutralization results in decreased TAM infiltration in an in-vivo model of PDAC

PT166

Perioperative Cytokines Levels Portend Early Death After Pancreatectomy for Ductal Adenocarcinoma H. Lewis,[1]* E.E. Talbert,[1] E. Haverick,[1] P. Rajasekera,[1] M. Dillhoff,[1] P. Hart,[1] M. Bloomston,[2] D.C. Guttridge,[1] T. Pawlik,[1] C. Schmidt.[1] *1. Ohio State Wexner Medical Center, James Comprehensive Cancer Hospital, Columbus, OH; 2. 21st Century Oncology, Ft Meyers, FL.*

Despite recent advances, pancreatic adenocarcinoma (PDAC) remains a significant cause of cancer mortality. Cytokines are soluble signaling molecules that may play an important role in malignant pathogenesis, as well as be useful as prognostic markers. We hypothesize perioperative cytokine levels are associated with outcomes in patients undergoing pancreatectomy. 119 patients were enrolled in a prospective study involving collection of serum, tumor, muscle and adipose tissue at the time of pancreatectomy for malignant or benign pancreatic disease. Serum samples were stored at -80C. Serum levels of 25 different cytokines were determined using a multiplex panel and analyzed relative to perioperative and survival outcomes. Of 119 patients enrolled, 86 (72%) had a diagnosis of PDAC and 61 (51%) underwent partial pancreatectomy. Median age was 67 years and 36 patients (54%) were female. The majority underwent pancreaticoduodenectomy (n=40, 65%), followed by distal pancreatectomy and splenectomy (n=21, 34%). Vascular resection was required in 7 (11%) patients; 51 (84%) had lymph node metastasis and an R0 resection was achieved in 52 (85%) patients. Preoperative chemotherapy +/- chemoradiation was given to 21 (34%) patients with borderline/locally advanced disease. No cytokine level was associated with complications, including pancreatic leak or 30-day readmission. In contrast, a serum level of monocyte chemoattractant protein-1 (MCP-1) pg/mL ≤118 was associated with better median overall survival (OS) compared with MCP-1 >118 (median survival 10.4 months versus not reached, p=0.002). There was a trend toward improved survival among patients with non-detectable interleukin-8 (IL-8) pg/mL (median not reached) versus detectable IL-8 (10.6 months, p=0.079). Patients with both MCP-1>118 and detectable IL-8 had a median survival of only 8.9 months (p=0.008) (Figure). Perioperative MCP-1 and IL-8 cytokine levels are associated with survival outcomes following pancreatectomy for PDAC and may be associated with more aggressive tumor biology. Collection of serum and tissue for patients with PDAC should be encouraged to help identify biomarkers and potential novel targets for therapy.



PT167

Local Recurrence After Laparoscopic Radiofrequency Ablation of Malignant Liver Tumors: Results of a Contemporary Series H. Takahashi,* M. Akyuz, E. Berber. *General Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Introduction: There are scant data in the literature about local recurrence (LR) after radiofrequency ablation (RFA) of malignant liver tumors in patients who have been followed long-term in a prospective manner. LR after RFA is classically reported to be seen within the first year after treatment. The aim of this study is to determine the incidence of LR in patients who have been followed at least a year after laparoscopic RFA (LRFA) from a contemporary series. Methods: Three hundred sixteen patients with 901 malignant liver tumors underwent LRFA between 2005 and 2014 by a single surgeon. Patient demographics, tumor character, and perioperative outcome were reviewed on IRB-approved prospectively collected RFA database. Univariate Kaplan-Meier and Cox proportional hazard model were used for statistical analysis. Results: Nine hundred one malignant liver lesions on 316 patients were treated with LRFA. The LR per lesion was 18.4% and per patient 35.8% in the whole cohorts. Median follow-up was 25 months [12-46] with 75.9 % of the patients having completed at least a year of follow up. The LR per lesion in patients followed for less than 12 months was 13.8%, at least for 12 months 20.3%, and at least 18 months 19.7% (p=0.0224). One-fourth (38/161) of the LRs were seen after the 1st year of follow up. Morbidity was 8.9% and mortality 0.3%. Tumor type, size, ablation margin and surgeon experience were found to affect LR on univariate analysis, of which tumor type (Hazard ratio (HR): CRC 6.4), size (HR: 2.6) and ablation margin (HR: 1.6) were independent predictors of LR. Conclusions: This contemporary study shows that patients need to be followed closely also beyond the 1st year after LRFA to be able to promptly identify local treatment failures. Beyond tumor characteristics, our results indicate that the ablation margin is the only parameter that the surgeon can manipulate to minimize treatment failures and hence should be at least 0.5 cm around the tumor.

Cox proportional hazard model for local recurrence

	Hazard Ratio	95% Confidence Interval	P Value
Tumor Type (vs. Neuroendocrine tumor)	CRC 6.43 HCC 5.22 Others 3.76	3.19 – 15.4 2.14 – 13.9 1.67 – 9.57	< 0.001
Tumor Size (>3cm vs. <3cm)	2.64	1.81 – 3.80	< 0.001
Ablation Margin (>0.5cm vs. <0.5cm)	1.6	1.03- 2.41	0.029
Surgeon Experience (Period I vs. II)	0.76	0.52 – 1.10	0.148

CRC Colorectal Cancer; HCC hepatocellular carcinoma

PT168

3-D Pancreatic Microtumors as a Screening Model for Chemotherapeutic Agents M. Goodwin,* S. Urs, Z. Sila, D.M. Simeone. *Surgery, University of Michigan, South Rockwood, MI.*

Introduction: The current standard for screening of potential chemotherapeutic agents is on 2D monolayer cell culture. We propose that 3D pancreatic microtumors composed of pancreatic tumor cells, fibroblasts and tumor associated macrophages (TAM) provide a platform for screening of chemotherapeutic agents that more accurately represents a patient's tumor microenvironment. Methods: Pancreatic microtumors were generated by combining primary pancreatic cancer cells, human fibroblasts and TAMs with collagen in a non-adherent U-botton 96-well plate. For generation of TAMs, peripheral blood mononuclear cells were isolated from human blood and enriched for CD14+ cells. TAMs were then generated by growing them in culture and characterizing them by flow cytometry. Microtumor viability following treatment with chemotherapeutic agents was assessed for viability using a 3D luminescence assay. Results: 3D pancreatic microtumors remain viable in culture overtime and develop a similar histology to that of pancreatic adenocarcinoma with development of duct-like structures. Using our primary pancreatic cancer cells we demonstrate that 3D cultures demonstrate increased resistance to gemcitabine compared to 2D monolayer culture (6-fold increase, $p< 0.05$) and that addition of TAMs and fibroblasts to the 3D cultures to create microtumors that are more resistant to gemcitabine then both 2D and 3D tumor cells alone (2-fold increase, $p<0.05$). Conclusion: 3D pancreatic microtumors provide a novel platform for screening of chemotherapeutic agents that is more reflective of the heterogeneous pancreatic tumor microenvironment. This model may allow a more cost effective screening platform for chemotherapeutic agents,

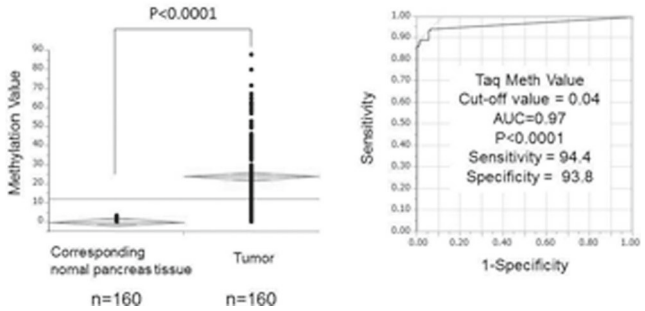
and potentially immunomodulators prior to in vivo animal models. Microtumors demonstrate increased resistance to gemcitabine and further testing will be done to determine if this principal holds true for other agents.

PT170

Potential Utility of Cysteine Dioxygenase 1 Gene Promoter Methylation as a Marker of Tumor Diagnosis in Pancreatic Adenocarcinoma N. Nishizawa,* K. Yamashita, S. Ishii, T. Tanaka, K. Yokoi, R. Nishiyama, H. Katoh, T. Kaizu, Y. Kumamoto, M. Watanabe. *Surgery, Kitasato University School of Medicine, Sagamihara, Japan.*

Background Using pharmacological unmasking microarray, we identified promoter DNA methylation of cysteine dioxygenase 1 (CDO1) gene specifically in human cancer. The aim of this study was to investigate methylation level of CDO1 and its clinical relevance in pancreatic adenocarcinoma (PDAC). Methods CDO1 promoter methylation was assessed in 8 human PDAC cell lines and a total of 160 patients with PDAC underwent pancreatectomy between 1986 and 2013. We extracted DNA from the formalin-fixed, paraffin embedded primary PDAC tissues and the corresponding normal pancreas tissues (CN). The CDO1 DNA methylation was quantified by TaqMan methylation specific PCR (Q-MSP). Results (1) CDO1 expression was silenced in all PDAC cell lines tested, and its expression could be restored by treatments with demethylating agents. (2) The mean methylation value (MV) was 23.9, ranging from 0 to 87.5 in primary PDAC tumor tissues, and the mean MV was 0.08, ranging from 0 to 3.4 in CN. PDAC tissues had CDO1 gene hypermethylation as compared to the CN, and its uniqueness was robust to discriminate tumor from normal tissues (AUC=0.97, p<0.0001) (Figure 1). (3) A Kaplan–Meier curve for the 160 patients was analyzed by the log rank plot method to determine the most optimal cut-off value. Then we identified the cut-off value of CDO1 MV to discriminate prognosis as 19.0 (p=0.024, Relative risk=2.3) (4) Correlation of clinicopathologic factors including prognostic factors such as TNM was assessed according to CDO1 methylation status in PDAC. The CDO1 gene hypermethylation group was significantly associated with UICC stage (p=0.007), T factor (p=0.0018), N factor (p=0.006), intrapancreatic nerve invasion factor (p=0.036), retropancreatic tissue invasion factor (p=0.003), portal venous system invasion factor (p=0.01), extrapancreatic nerve plexus invasion factor (p=0.016) and arterial system invasion factor (p=0.016). Conclusions These results suggested that promoter DNA methylation of CDO1 gene is extremely specific for PDAC, and accumulates with PDAC tumor progression. It could be a potential diagnostic marker of PDAC in liquid biopsy.

Figure 1



PT171

When to Wait: the Impact of Time from Completion of Neoadjuvant Radiation to Pancreaticoduodenectomy K.A. Mirkin,* C. Hollenbeak, J. Wong. *Department of Surgery, Penn State, Hershey, PA.*

Background: Neoadjuvant radiation therapy (neoRT) is an often used treatment strategy in pancreatic cancer. Typically, surgery is recommended within 6-8 weeks following completion of radiation to avoid a potentially more challenging operation and thus worse outcomes. This study evaluates the impact of time from completion of neoRT to pancreaticoduodenectomy in resectable pancreatic adenocarcinoma on perioperative outcomes and survival. Methods: The U.S. National Cancer Data Base (2003-2011) was reviewed for patients with clinical stage I-III pancreatic adenocarcinoma, who underwent neoRT and pancreaticoduodenectomy. Patients were stratified by time from completion of neoRT to surgery: £4, 4-8, 8-12, and 12-20 weeks. The primary endpoint was survival; secondary endpoints were hospital length of stay (LOS), readmission, and 30- and 90-day mortality. Univariate and multivariate analyses were performed. Results: 474 patients with clinical stages I-III resected pancreatic adenocarcinoma were included. Of these, 0.8% (N=4) of patients had surgery within 4 weeks of neoRT completion, 5.9% (N=28) 4-8, 39.5% (N=187) 8-12, and 46.6% (N=221) 12-20 weeks. Patients who underwent surgery in 12-20 weeks tended to receive greater regional neoRT dosage (4578.8 cGy, p<0.001), greater number of neoRT treatments (25.9, p<0.001), and had fewer positive regional lymph nodes (0.9, p=0.0031). Time from completion of neoRT to surgery did not significantly impact survival in any pathologic stage of disease (I: p=0.1483, II: p=0.7342, III: p=0.1345, IV: p=0.0775). On multivariate analysis, increased time between completion of neoRT and surgery was independently associated with reduced mortality (12-20 weeks: HR=0.47, p=0.010). Time from completion of neoRT to surgery was not associated with a significant impact on LOS, readmissions, 30- or 90-day mortality on univariate or multivariate analyses (p>0.05). Conclusion: Time from completion of neoRT to pancreaticoduodenectomy did not significantly impact perioperative outcomes. However, increased time from neoRT to surgery is an independent predictor of improved long-term survival.

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Greater Lymph Node Retrieval and Lymph Node Ratio Does Not Impact Survival in Non-functional Pancreatic Neuroendocrine Tumors K.A. Mirkin,* C. Hollenbeak, J. Wong. *Department of Surgery, Penn State, Hershey, PA.*

Background: Non-functional pancreatic neuroendocrine tumors (PNETs) are uncommon. While surgical resection offers potential for cure, there is no clear consensus on extent of lymphadenectomy. This study evaluated if number of examined lymph nodes (eLN), a proxy for lymphadenectomy, and lymph node ratio (LNR) impact survival. Methods: The U.S. National Cancer Data Base (1998-2012) was reviewed for patients with nonfunctional PNETs. Patients were stratified by eLN: 0-6, 7-12, 13-15, and >15, and LNR (LNR= #positive nodes/ #eLN):0, 0-0.2, 0.2-0.4, 0.4-0.8, and >0.8. Survival analyses were performed. Results: 1,479 patients with clinical stages I-III non-functional resected PNETs were included. Of these, 35.6% (N=527) of patients had 0-6 eLN, 25.7% (N=380) had 7-12, 11.9% (N=176) had 13-15, and 26.8% (N=396) had >15 eLN. The majority of patients underwent distal pancreatectomy (N=813, 55.0%), while the remainder underwent pancreaticoduodenectomy (N=467, 31.6%), total pancreatectomy (N=170, 11.4%), and local excision (N=29, 2.0%). Median eLN by surgery type included: pancreaticoduodenectomy (14), distal pancreatectomy (8), total pancreatectomy or unlisted procedure (11), local excision (1). Greater eLN, based on the mentioned eLN groupings, did not significantly impact survival in node negative or node positive disease (P=0.4474, P=0.2958, respectively). After controlling for patient, disease, and treatment characteristics, eLN still did not significantly impact survival (eLN 7-12: HR 1.06, p=0.833, eLN 13-15: HR=0.74, p=0.429, and eLN >15: HR=1.22, p=0.483). 66.3% (N=980) of patients had a LNR of 0, 14.7% (N=218) ≤0.2, 9.5% (N=140) 0.2-0.4, 6.7% (N=99) 0.4-0.8, and 2.8% (N=42) had a LNR >0.8. LNR did not significantly impact survival (T1: p=0.8756, T2: p=0.1542, T3: p=0.0863, T4: p=0.1774). On multivariate analysis, LNR of 0.4-0.8 was negatively associated with survival, although a higher LNR was not (LNR 0-0.2: HR 1.32, p=0.327, LNR 0.2-0.4: HR 1.10, p=0.771, LNR 0.4-0.8: 2.27, p=0.012, LNR >0.8: HR: 0.87, p=0.81). Conclusion: Greater lymph node retrieval and lymph node ratio does not appear to carry prognostic significance in PNETs.

PT173

Significant Upstaging of Patients with Stage I Pancreatic Cancer from Clinical to Pathologic Staging H. Stuart,* C. Ripat, B. Azab, D. Yakoub, D. Franceschi, A.S. Livingstone, V. Dudeja, N. Merchant. *Surgical Oncology, University of Miami, Miami Beach, FL.*

Introduction: Clinical staging of patients with pancreatic cancer is essential to determine if neo-adjuvant treatment, surgery or palliative treatment is required. Patients with early stage disease often receive upfront surgery, where

as patients with more advanced disease often receive neo-adjuvant therapy. Therefore the accuracy of clinical staging significantly influences management decisions. This study investigates the correlation between clinical and pathologic staging for patients with stage I pancreatic cancer. Methods: A retrospective review of patients with pancreatic cancer in National Cancer Data Base from 1998-2006 was preformed. The clinical stage of patients with presumed stage I disease was compared to the postoperative pathologic stage. Cox proportional hazard ratio model and regression analysis were used to determine factors associated with mortality and upstaging, respectively. Results: 1697 patients with clinical stage I pancreatic cancer were divided into two groups. Group 1 was comprised of patients who were stage I postoperatively and Group 2 was comprised of patients that were upstaged to either stage II, III or IV postoperatively. There were 704 (41%) in group 1 and 993 (59%) in group 2. Within group 2, 595 (60%) were stage II, 321 (32%) were stage III and 77 (8%) were stage IV. Patients that were upstaged after surgery had an increased risk of mortality (HR 1.414, p<0.001), whereas patients that received adjuvant chemotherapy had a decreased risk of mortality (HR 0.799, p<0.001). Compared to Grade 1 tumors, Grade 2 and 3 tumors on biopsy were most likely to be upstaged on final pathology (p<0.001). Conclusion: Patients with stage I pancreatic cancer are often candidates for upfront surgery, however this study demonstrates that a large number are upstaged on postoperative staging. Recognizing this may lead clinicians to administer neo-adjuvant treatment in a greater number of patients with early stage disease in order to optimize survival.

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Cost Comparison of Laparoscopic Radiofrequency Ablation Versus Resection of Small Solitary Colorectal Liver Metastasis H. Takahashi,* M. Akyuz, Y. Zaid, D. Vogt, C. Quintini, F. Aucejo, J. Fung, E. Berber. *General Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Introduction: Our previous studies suggested that in selected patients with small (<3 cm) solitary colorectal liver metastasis (CRLM), disease-free and overall survival may be similar after liver resection (LR) or laparoscopic radiofrequency ablation (LRFA). The aim of this report is to study the financial impact of both treatments to medical institutions. Method: Between 2006 and 2015, 63 patients underwent open or laparoscopic LR, and 22 patients underwent LRFA of solitary CRLM less than or equal to 3cm. Using a prospectively-maintained IRB-approved database, clinical, oncologic and financial parameters were compared. Results: Patients in LRFA group had more co-morbidities, including cardiopulmonary, compared to LR group. Hospital stay, total operation time (OT), and estimated blood loss (EBL) were significantly less in RFA group. No significant difference was noted in postoperative complications, readmission rate, and local recurrence rate between two groups. Median follow up was 26.5months for RFA, and 36months for LR (p=0.92). The mean cancer-specific survival was 51.3months for RFA and 63months for LR (p=0.64). The median disease-free survival (DFS) was 18months for RFA, and 21months for LR (p=0.60). The mean operation cost and the mean hospital cost were approximately 107% and 83% higher in LR group (p=0.001 and p<0.001, respectively). However, the reimburse rate from the third payer was not significantly different on both groups (44.3% for RFA vs. 42.8% for LR, p= 0.77). Conclusion: Our results suggested that operative and hospital costs of laparoscopic RFA for small solitary CRLM might be lower than those of liver resection with similar reimbursement rates and oncological outcomes.

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A Murine Model of Micrometastatic Pancreas Cancer A. Patel,* N.M. Figueroa, B.A. Belt, A. Muthy, K.A. Connolly, B. Han, S. Gerber, D.C. Linehan. *Surgery, University of Rochester Medical Center, Rochester, NY.*

Introduction: Pancreas cancer (PC) maintains a high mortality rate due to early metastatic spread to the liver. It has been shown that PC induces changes in the liver microenvironment (LME), which include an infiltration of myeloid-derived cells prior to development of detectable metastasis. We have developed a murine model of metastatic PC designed to monitor the progression of a single micrometastatic (mM) cell, and are able to characterize the changes in the LME in the presence of single mM cells. Methods: The murine PC cell line KCKO was transfected with a plasmid to express both Green Fluorescent Protein (GFP) and β-Galactosidase (β-Gal). C57BL/6 mice underwent orthotopic pancreas tumor implantation with luciferase-labeled KCKO cells and PC burden was monitored with bioluminescent imaging. Seven days later, the mice underwent a second stage surgery involving primary tumor resection, splenic injection of KCKO/GFP/ β-Gal, followed by hemi-splenectomy. At varying time points thereafter (24, 48, & 72 hours) the mice were sacrificed and individual liver lobes were processed. Results: β-Gal expressing mM single tumor cells can be seen in liver tissue sections by X-gal staining. Immunohistochemistry staining with anti-GFP and anti-β-Gal antibodies also confirmed the presence of the mM cells. Analysis of the liver tumor microenvironment (TME) at 24, 48, & 72 hours after splenic injection revealed an increase in myeloid cells, including inflammatory monocytes, macrophages, and granulocytes by flow cytometry, immunofluorescence, and immunohistochemistry. There was an up regulation of tumor-promoting and immunosuppressive genes associated with the development of metastasis by RT-PCR. Using $CCR2^{-/-}$ mice, there was a noted decrease of the myeloid cell infiltrate and mM in the liver TME, reinforcing the importance of the mobilizing signal of the CCR2-CCL2 chemokine axis. Conclusion: We developed a mouse model to recapitulate early micrometastatic PC occurrence in the liver after primary tumor resection. We can use this model to assess the progression of single cell liver mM and associated changes in the liver TME. Using this model, we have identified that the CCR2-CCL2 chemokine axes promotes metastatic progression.

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Analysis of the Effect of Adjuvant Therapy on Overall Survival for Resected Gallbladder Adenocarcinoma Using the National Cancer Data Base D. Brauer,* K. Lim, M. Doyle, W. Hawkins, W. Chapman, R. Fields. *Surgery, Washington University School of Medicine, Saint Louis, MO.*

Background: The effect of adjuvant chemotherapy on survival after resection for gallbladder adenocarcinoma (GBC) is based on limited evidence. Current guidelines of the National Comprehensive Cancer Network reflect this limited knowledge. Since prospective trials are not generally practical for GBC, we sought to evaluate current best evidence to evaluate the role of adjuvant chemotherapy in multiple clinical scenarios by analyzing data from the U.S. National Cancer Database (NCDB). Methods: Patients who underwent resection for GBC diagnosed between 2004 and 2012 were identified in the NCDB. The effect of adjuvant therapy on overall survival (OS) was assessed using Kaplan-Meier analysis and Cox proportional hazards regression modeling. Results: 10,402 patients met inclusion criteria. Median follow-up was 14 months (Interquartile Range (IQR) 5 – 32 months) and median survival was 16 months (95% Confidence Interval (CI) 15 – 17 months). One- and five-year OS were 57% and 23%, respectively. 3,509 patients (34%) received any modality of adjuvant therapy, with an increasing frequency in more recent years. On univariate analysis, receipt of adjuvant therapy improved one-year OS (63% vs 55%, p<0.01), but median OS was minimally changed (17 vs 15 months, NS). After multivariate Cox regression modeling for variables including age, gender, race, comorbidity, and margin status, any adjuvant therapy was associated with improved one-year OS in T3 disease and T4N1 disease (Table 1). Only chemoradiation therapy was associated with improved one-year OS for T2 disease. Adjuvant chemotherapy was associated with worse one-year OS in T1N0 disease. Conclusion: Using data from the US NCDB, adjuvant therapy for resected gallbladder adenocarcinoma is associated with improved one-year overall survival with the exception of T1N0 disease. Combination chemoradiation therapy is associated with greater benefit in the majority of pathologic stages. In the absence of prospective studies in this rare disease, retrospective data can provide insights into successful treatment strategies and guidelines for GBC.

			Adjuvant Radiation Therapy Alone				Adjuvant Chemotherapy Alone				Adjuvant Chemoradiation Therapy			
		n	p-value	Hazard Ratio	95% Confidence Interval		p-value	Hazard Ratio	95% Confidence Interval		p-value	Hazard Ratio	95% Confidence Interval	
T1	N+	93	0.465	1.76	0.39	8.00	**0.031**	**0.13**	**0.02**	**0.83**	0.400	0.63	0.21	1.86
	N-	875	0.767	0.81	0.20	3.33	**<.001**	**3.10**	**1.66**	**5.80**	0.197	1.68	0.76	3.71
T2	N+	922	0.323	0.80	0.52	1.24	0.088	0.76	0.55	1.04	**<.001**	**0.34**	**0.24**	**0.49**
	N-	2219	0.050	0.64	0.40	1.00	0.289	1.16	0.88	1.53	**<.001**	**0.53**	**0.38**	**0.73**
T3	N+	1238	**<.001**	**0.48**	**0.32**	**0.72**	**<.001**	**0.56**	**0.46**	**0.67**	**<.001**	**0.22**	**0.17**	**0.29**
	N-	1209	**<.001**	**0.38**	**0.25**	**0.59**	**0.005**	**0.73**	**0.58**	**0.91**	**<.001**	**0.29**	**0.21**	**0.40**
T4	N+	248	**0.025**	**0.25**	**0.08**	**0.84**	**<.001**	**0.34**	**0.22**	**0.51**	**<.001**	**0.17**	**0.10**	**0.31**
	N-	111	0.282	0.41	0.08	2.09	0.085	0.52	0.25	1.09	0.082	0.50	0.22	1.09

Multivariate significance levels and hazard ratios for the effect of adjuvant therapy on one-year overall survival. Bold text indicate statistical significant (p<0.05). * excludes patients with missing data for any variables in the model

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Development of a Novel Model for Intrahepatic Cholangiocarcinoma R.K. Marcus,[1]* W. Foo,[3] D. Evans,[2] A. Maitra,[1] S. Gupta.[1] *1. Sheikh Ahmed Bin Zayed Al Nahyan Center for Pancreatic Cancer Research, The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Department of Surgery, Froedtert and the Medical College of Wisconsin, Milwaukee, WI; 3. Department of Pathology & Laboratory Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Intrahepatic cholangiocarcinoma (ICC) is a poorly understood primary liver cancer arising from cholangiocytes. Surgery currently offers the only potential for cure, but most patients present with unresectable disease. Genomic studies have revealed a subset of ICCs characterized by loss-of-function mutations in the gene encoding BRCA associated protein 1 (BAP1), a chromatin regulatory factor. While elucidating the molecular pathogenesis of ICC may identify potential targeted therapies and improve early detection, inquiry into this disease has been hampered by a lack of genetically faithful animal models. We sought to develop a genetically engineered mouse model (GEMM) of ICC that incorporates an inactivating mutation in BAP1. Methods: A GEMM incorporating deletion of BAP1 and Kras activation (LSL-Kras; $BAP1^{F/F}$) was developed. Hepatoblast-specific mutations were induced using an Albumin-Cre promoter. Results: Mutant Kras cooperates with loss of BAP1 resulting in lethal hepatic transformation and dose-dependent survival. Loss of BAP1 or Kras activation alone results in disease latency and survival > 45 weeks. Heterozygous loss of BAP1 combined with mutant Kras shortens disease latency, with mice surviving approximately 40 weeks. A significant reduction in survival to 23 weeks ($p \leq 0.01$) is seen with homozygous loss of BAP1 and Kras activation. On histopathologic evaluation these mice demonstrate biliary precursor lesions, ICC, and hepatocellular carcinoma (HCC). Mice with all other genotypes exhibit HCC only. Given the bipotential nature of hepatoblasts, biliary tree-specific mutations may enhance the ICC phenotype of LSL-Kras; $BAP1^{F/F}$ mice. Adenoviral Cre enzyme (Ad-Cre) permits such combinatorial specificity, and a novel surgery enabling retrograde biliary tree administration of Ad-Cre was developed. Proof-of-principle was established using GFP-tagged adeno-associated virus to confirm expression of Cre recombinase within the biliary tree. Conclusions: Loss of BAP1 and Kras activation results in the development of ICC and HCC in a mouse model. Ad-Cre enables biliary tree-specific mutations. Evaluation of the effects of such mutations in LSL-Kras; $BAP1^{F/F}$ mice is ongoing.

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T-Cell Receptor Deep Sequencing Reveals Novel Insights into the Immune Response to Human Pancreatic Cancer Y.D. Seo,[1]* F. Jalikis,[1] X. Jiang,[1] H. Robins,[2] V.G. Pillarisetty.[1] *1. General Surgery, University of Washington, Seattle, WA; 2. Fred Hutchinson Cancer Research Center, Seattle, WA.*

Introduction Pancreatic ductal adenocarcinoma (PDA) is an aggressive cancer with high mortality. It is characterized by a dense inflammatory response including many T cells, but it remains unclear whether these T cells signify a true anti-tumor response. Methods Archival resected PDA tumors from 53 patients were analyzed by histopathology to determine which blocks contain lymph nodes (LN), as LN would likely bias the results. T cell receptor (TCR) deep sequencing was performed on tissue from the same blocks to determine the extent of clonal expansion. Productive clonality was calculated using relative clonal frequencies (1-Pielou's evenness). Two-tailed t-test was used to compare TCR data among different subgroups. TCR data were compared with whole genome expression data from a subset of tumors using a Spearman's rank correlation. Immunohistochemistry (IHC) was performed on 39 of the samples to quantify expression of FOXP3, CD3, CD4, CD8 and CD11b. Results The mean TCR fraction in PDA was 0.33, and the mean clonality was 0.13 (typical peripheral blood mononuclear cell clonality is 0.08). TCR fraction was positively correlated with clonality (R^2=0.23, p=0.007). TCR fraction was higher in patients with positive nodal status (0.32 vs. 0.23, p=0.02), but lower in patients who received neoadjuvant chemotherapy (0.22 vs. 0.33, p=0.02). With respect to survival, there was no difference between high or low TCR fraction or clonality. TCR fraction was positively correlated with the IHC expression of CD3 (R^2=0.19, p=0.03), CD8 (R^2=0.17, p=0.04), and FOXP3 (R^2=0.23, p=0.01), while clonality was positively correlated with FOXP3 (R^2=0.22, p=0.02). Whole genome expression analysis revealed correlations with multiple genes involved in adaptive immunity and tumorigenesis: TCR fraction positively correlated with CTLA4, CXCR5, CD1E; clonality positively correlated with VEGFB; maximum clonal frequency negatively correlated with PDCD1 (PD-1) and CSF1. Conclusions There is evidence of clonal expansion of T cells in the PDA microenvironment. Correlations of TCR data with gene expression and IHC may represent a novel model to identify targets to enhance adaptive immunity to PDA.

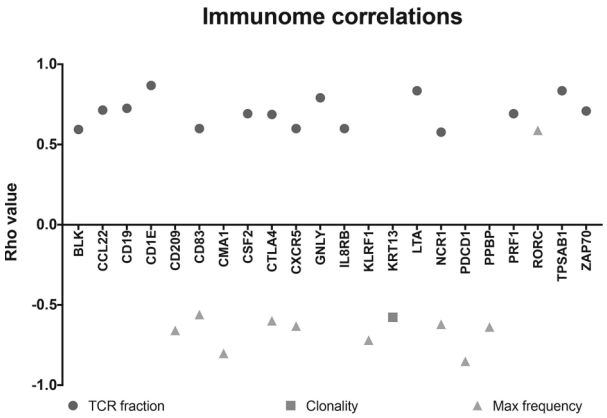

Figure 1: Gene expression data related to adaptive immunity, as identified by the tumor immunome by Bindea et. al (*Immunity* Oct. 2013, doi 10.1016/j.immuni.2013.10.003) were compared with TCR data to identify positive and negative correlations using a Spearman's rank correlation

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Progression in the Pancreatic Remnant Following Resection of Intraductal Papillary Mucinous Neoplasms (IPMN) of the Pancreas: A Need for Long-term Surveillance M. Al Efishat,[1]* M.A. Attiyeh,[2] A. Eaton,[2] M. Gönen,[2] O. Basturk,[2] M.I. D'Angelica,[2] R. DeMatteo,[2] T. Kingham,[2] V. Balachandran,[2] W. Jarnagin,[2] P.J. Allen.[2] *1. Johns Hopkins University School of Medicine, Baltimore, MD; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

BACKGROUND: IPMN is generally considered to be a "whole-gland" process, yet segmental resection remains the most frequently performed procedure for this disease. This results in a pancreatic remnant that is presumably at an increased risk for recurrence or malignant progression. In this study, we sought to determine the rates, patterns and predictors of IPMN progression following partial pancreatectomy for non-invasive or micro-invasive IPMN. METHODS: A prospectively maintained pancreas database was queried to identify all patients who underwent resection of non-invasive or micro-invasive IPMN (≤10 mm of invasive component) between 1989 and 2015. "Progression" in the remnant was defined as: development of invasive cancer in the remnant, a new cystic lesion >1cm, ≥ 50% increase in the diameter of residual IPMN lesions, or development of metastatic cancer. Univariate and multivariable Cox models were created to determine predictors of progression. Time to progression was censored at the time of last followup or death without recurrence. RESULTS: A total of 319 patients underwent resection for non-invasive and micro-invasive IPMN during the study period. The median age was 68 years (range 33- 89), 53% had branch-duct (BD) IPMN, and 6% had micro-invasive IPMN. After a median follow-up of 42 months, 71 patients had experienced progression (27 %) at 5 years. Within the group of 71 patients, there were 11 patients who developed invasive cancer. The rate of cancer development at 5 years was 4.2%. One-year survival and five-year survival rates for the entire cohort were 97% and 86%, respectively. In a multivariable model, initial grade of dysplasia, margin status, duct type and the presence of radiographically identifiable residual disease were not independently associated with progression. CONCLUSIONS: In this study of non-invasive and micro-invasive IPMN, the pancreatic remnant progression rate was 27% at 5 years, and the rate of development of invasive disease was 4%. These patients represent a high-risk group for the development of pancreatic cancer and lifelong surveillance of this patient population is critical.

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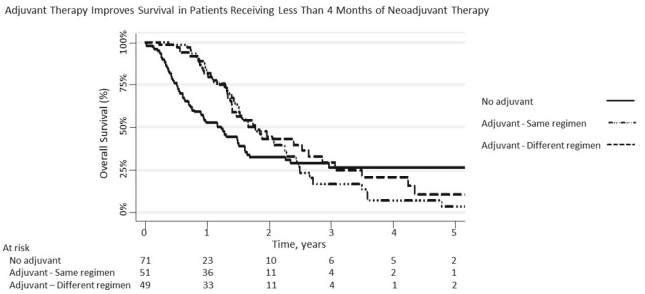
Neoadjuvant and Adjuvant Chemotherapy in Pancreatic Ductal Adenocarcinoma: Does Drug Selection, Duration, or Sequence Affect Outcomes? A. Javed,* R. Burkhart, S. Ronnekleiv-Kelly, A. Hasanain, L.M. Rosati, J. He, M. Makary, D.A. Laheru, R.H. Hruban, L. Zheng, J.M. Herman, J. Cameron, C. Wolfgang, M. Weiss. *Surgery, Johns Hopkins Hospital, Baltimore, MD.*

Introduction: Surgery, the only potentially curative therapy for pancreatic ductal adenocarcinoma (PDAC), is only possible in 20% of patients at presentation. Modern neoadjuvant chemotherapeutics can increase the cohort eligible for surgery. There are two common chemotherapeutic backbones for PDAC, 5-fluorouracil (5FU) and gemcitabine (GEM). Guidelines for therapy in the neoadjuvant and adjuvant setting are limited. Methods: A single-institution, prospectively-collected database review of borderline resectable (BR) or initially locally-advanced PDAC (LAPC) who underwent resection after neoadjuvant therapy. Patients were stratified by type and duration of neoadjuvant therapy. Adjuvant therapy was catalogued and survival was analyzed. Results: Over 10 years, 293 patients underwent resection after neoadjuvant therapy for an initial diagnosis of BR or LAPC. 5FU and GEM-based therapy was most common (46.4% and 39.6%, respectively). A complete resection (R0) was achieved in 72.1%, R1 in 21.8%, and R2 in 6.1%. After surgery, half received no adjuvant chemotherapy. Of the remainder, half received the same chemotherapeutic backbone as before surgery. Median overall survival (OS) for the entire cohort was 18.1 months. The neoadjuvant chemotherapeutic backbone (5FU or GEM) did not impact OS. Patients receiving the same regimen postoperatively had an OS similar to those who switched drugs (19.9 months same-agent, 21.4 months for therapeutic switch, p=0.09). For those receiving less than four months of neoadjuvant therapy, receipt of adjuvant therapy was associated with an improved median OS (no adjuvant vs. same-regimen vs. different-regimen: 9.1 vs. 23.7 vs. 21.4 months, p=0.036). In those patients receiving four or more months of neoadjuvant therapy, no association was found between OS and adjuvant therapy. Conclusion: There is considerable variability in neoadjuvant and adjuvant therapy use in PDAC. A therapeutic switch in the adjuvant period does not appear to improve overall survival. In patients receiving fewer than four months of neoadjuvant therapy, the administration of adjuvant treatment is associated with improved overall survival.



Overall survival for patients who received less than 4 months of neoadjuvant chemotherapy stratified by adjuvant therapy choice. Solid bar indicates no adjuvant therapy given, dash-dot indicates adjuvant delivered with the same chemotherapeutic backbone, and dash indicates adjuvant delivered with a change in chemotherapeutic backbone.

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Arid1a Deletion Results in Intraductal Papillary Mucinous Neoplasm Formation S.C. Wang,[1] I. Nassour,[1]* X. Sun,[2] J. Chuang,[2] L.H. Nguyen,[2] S. Zhang,[2] L. Peng,[3] H. Zhu.[2] *1. Department of Surgery, The University of Texas Southwestern Medical Center, Dallas, TX; 2. Children's Research Institute, The University of Texas Medical Center, Dallas, TX; 3. Department of Pathology, The University of Texas Southwestern Medical Center, Dallas, TX.*

Background: ARID1A, a member of the SWI/SNF chromatin-remodeling complex, is mutated in up to 30% of pancreatic ductal adenocarcinoma (PDAC). Here, we studied the effect of Arid1a loss in pancreatic tumorigenesis in the setting of a constitutively activated Kras allele ($Kras^{G12D}$), which is the basis of a well-established mouse model of pancreas cancer. Methods: Arid1a was deleted during embryogenesis in acinar, duct, and islet cells in Ptf1a-Cre; $Arid1a^{f/f}$ (CA) and $Kras^{G12D}$; Ptf1a-Cre; $Arid1a^{f/f}$ (KCA) mice. Arid1a was inducibly deleted in adult mice specifically in duct or acinar cells with $Kras^{G12D}$; Sox9-Cre^{ER}; $Arid1a^{f/f}$ ($KS^{ER}A$), and $Kras^{G12D}$; Ptf1a-Cre^{ER}; $Arid1a^{f/f}$ ($KP^{ER}A$) mice, respectively. Tamoxifen was given at 4 weeks of age. Results: Genotyping of CA mice toes and pancreata showed Arid1a loss only in the latter confirming pancreas-specific recombination. Western blot confirmed decreased protein expression and immunohistochemistry (IHC) demonstrated Arid1a loss in most of the acini and half of the ducts. ~35% of CA mice developed benign appearing cysts by 4 months. KCA mice had macroscopic cysts by 3 weeks. The cyst fluid was thick and amylase rich. These cysts resembled intraductal papillary mucinous neoplasm (IPMN) as they had papillary features and stained for Alcian blue, confirming the presence of mucin. Muc protein staining pattern was consistent with pancreaticobiliary type IPMN. The stroma was negative for estrogen and progesterone receptors. $KS^{ER}A$ mice developed large mucin producing ductal lesions by 12 weeks while only pancreatic intraepithelial neoplasias were seen in $KP^{ER}A$ mice. Conclusions: Arid1a loss in the pancreas leads to pancreaticobiliary IPMN that appear to arise from the duct cells. Future directions include aging studies to determine if these cysts transform to frank PDAC, determining the status of ARID1A in human IPMN, and elucidating the mechanisms for cyst formation. Finally, this model may be useful as a platform to test therapeutic interventions to treat IPMN.

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Expression of MicroRNA-221 and miR-18a in Patients with Hepatocellular Carcinoma and Its Clinical Significance M. Baek,[1]* S. Lee,[2] D. Park,[3] J. Um,[4] T. Ahn,[1] H. Jung.[1] *1. Surgery, Soonchunhyang University Hospital, Cheonan, Korea (the Republic of); 2. Chungbuk National University Hospital, Cheongju, Korea (the Republic of); 3. Dankook University Hospital, Cheonan, Korea (the Republic of); 4. Korea University Ansan Hospital, Ansan, Korea (the Republic of).*

Introduction:Recently, microRNA (miRNA) have been evaluated to provide a new diagnostic and therapeutic modality hepatocellular carcinoma (HCC) and other tumors. They are small non-coding RNA molecules that function as transcriptional and post transcriptional regulators of gene expression by silencing target genes. The aim of this study was to evaluate the clinical significance of microRNA-18a, 221 (miR-18a, 221) expression in hepatocellular carcinoma (HCC) formalin-fixed paraffin-embedded (FFPE) tissues. Materials and methods:MiR-18a and miR-221 expressions were assessed by reverse transcription and real-time PCR (RT-PCR) in 50 pairs of FFPE HCC and the adjacent noncancerous liver tissues. And we evaluated the expression level in HCC tissues as compared with their adjacent noncancerous counterparts. And the relationship between miR-18a, 221 level and clinicopathological data and survival rates were analyzed. Results:At first, miR-221 expression and miR-18a was up-regulated in HCC tissues as compared with their adjacent noncancerous liver tissues ($p < 0.001$). Then the miR-221 expression was found to be correlated with larger tumor size ($p = 0.048$). MiR-18a expression was correlated with modified UICC stage ($P = 0.05$). After that, survival analysis found that the overall survival ($p = 0.02$) of HCC patients with high miR-221 expression was significantly poorer compared to those patients with low expression. Multivariate analyses demonstrated that miR-221 may be a poor prognostic factor of HCC patients. However, miR-18a was not correlated with survival. Conclusions:High expression of miR-221 in FFPE tissues could provide significance for prognosis of HCC patients. Although, miR-18a expression was significantly up- regulated in HCC tissues, they are not correlated with prognosis. More larger study and functional study will be needed.

PT183

Neoadjuvant FOLFIRINOX Improves Progression Free Survival Compared to Gemcitabine/Abraxane in Pancreatic Adenocarcinoma B.C. Chapman,* A. Gleisner, D. Rigg, W. Messersmith, A. Paniccia, C. Meguid, M.D. McCarter, C. Gajdos, R. Schulick, B. Edil. *Surgery, University of Colorado School of Medicine, Denver, CO.*

Introduction: Neoadjuvant chemotherapy is increasingly used in borderline resectable pancreas cancer to facilitate surgical resection. Our objective is to compare progression free survival (PFS) and overall survival (OS) in patients receiving neoadjuvant FOLFIRINOX with those receiving

gemcitabine/abraxane (gem/abx). Methods: We analyzed data at our institution in patients receiving neoadjuvant FOLFIRINOX or gem/abx for pancreatic adenocarcinoma (2012-2016). The Kaplan-Meier method for PFS and OS were compared between the two groups and differences were tested with a log-rank test. Results: We identified 70 (75%) patients receiving a median of 4 cycles of neoadjuvant FOLFIRINOX and 24 (25%) patients receiving a median of 2 cycles of gem/abx. The FOLIFRINOX group was younger (median 63 years) than the gem/abx group (median 72 years) ($p<0.05$). Neoadjuvant radiation was given to 41 (59%) patients receiving FOLFIRINOX and 19 (79%) receiving gem/abx ($p=0.07$). Patients were more likely to experience disease progression on gem/abx (n=10, 42%) compared to FOLFIRINOX (n=12, 17%) ($p<0.05$). Six (10%) patients receiving FOLFIRINOX and 4 (31%) receiving gem/abx were unresectable at surgery (0.06). Only 38% (n=9) of patients in the gem/abx group were surgically resected compared to 74% (n=52) in the FOLFIRINOX group ($p<0.05$). Adjuvant chemotherapy was given to 37 (71%) patients receiving FOLFIRINOX and 6 (67%) receiving gem/abx ($p=0.357$). Median follow up time was 15.8 months. Overall median PFS was 17 months in the FOLFIRNOX group and 9 months in the gem/abx group ($p<0.05$); median OS was similar (FOLFIRINOX 27 vs. gem/abx 19 months; $p=0.49$). In resected patients, median PFS was 19 months in the FOLFIRINOX group and 14 months in gem/abx; $p=0.61$); median OS was 35 months in the FOLFIRINOX group and was not reached in the gem/abx group. Conclusions: Patients receiving neoadjuvant FOLFIRINOX are more likely to make it to surgery and have longer PFS compared to patients receiving neoadjuvant gem/abx. Improved understanding of the role for selection bias and longer follow up are needed to better define the impact of neoadjuvant FOLFIRINOX on overall survival.

PT184

Determinants of Systemic Recurrence After "Liver first" Approach for Synchronous Colorectal Cancer Liver Metastases D. Henault,* F. Vandenbroucke-Menu, B. Nguyen, G. Soucy, C. Richard, M. Plasse, A. Roy, M. Dagenais, R. Létourneau, R. Lapointe, S. Turcotte. *Surgery, University of Montreal, Longueuil, QC, Canada.*

Introduction: Approximately 25% of patients with a new diagnosis of colorectal cancer present with synchronous liver metastases. Surgery combined with chemotherapy is the standard of care, yet uncertainty remains regarding the optimal treatment sequence and patient selection for best outcomes. Our institutional policy has been a "Liver First" approach, whereby liver metastases are resected prior to the asymptomatic primary tumor in chemo-responsive/stable patients. This study evaluates the clinical and pathological factors associated with overall (OS) and disease-free (DFS) survival in these patients. Methods: Retrospective analysis of prospectively collected data in patients with resectable synchronous colorectal cancer liver metastases (CRLMs), who underwent liver prior to primary tumor resection and peri-operative chemotherapy in one institution (2011-2015). Association between clinico-pathological factors and OS and DFS were evaluated by the Kaplan-Meier method and log-rank test. Results: Fifty-one patients were followed for a median time of 20 months. Thirty-six (70.6%) were male, mean age 62 years, 24 (47.1%) rectal cancer, 34 (66.7%) bilobar CRLMs, median number of 2 CRLMs, of 2.5cm median size, and median pre-op CEA 7.9 ng/mL. Pre-hepatectomy chemotherapy was given for 5 cycles on average (82% Folfox). The median OS and DFS were 41.3 months (death rate 25.5%) and 11.4 months (recurrence rate 54.9%), respectively. All recurrences were found in the liver and/or lungs, except for carcinomatosis in 3 patients. The factors significantly associated with shorter DFS and OS were unfavorable pathologic response to chemotherapy (Blazer score) and positive liver resection margins. The Fong clinical risk score had no significant impact on OS or DFS. Conclusion: Patients with synchronous CRLMs undergoing a "Liver first" approach are at high risk of systemic recurrence, especially those with suboptimal control of their metastases. Biomarkers of resistance to first line chemotherapy and of early systemic recurrence are needed to identify patients in whom surgery is unlikely to confer survival benefit.

PT185

Two-Stage Hepatectomy for Colorectal Liver Metastases: A Multi-Institutional Retrospective Review N.G. Berger,[1]* K.J. Bradford,[2] S. Gholami,[5] G.A. Margonis,[3] C.G. Ethun,[4] J. Silva,[1] S. Tsai,[1] K. Christians,[1] H. Mogal,[1] C. Clarke,[1] S.K. Maithel,[4] T. Pawlik,[6] M.I. D'Angelica,[5] T.A. Aloia,[2] T. Gamblin.[1] *1. Surgery, Medical College of Wisconsin, Milwaukee, WI; 2. MD Anderson Cancer Center, Houston, TX; 3. Johns Hopkins, Baltimore, MD; 4. Emory University School of Medicine, Atlanta, GA; 5. Memorial Sloane Kettering Cancer Center, New York, NY; 6. Ohio State University, Columbus, OH.*

Introduction A significant number of patients with colorectal liver metastases (CRLM) present with unresectable bilobar disease. Two-stage hepatectomy with portal vein embolization (PVE) have been described as a treatment for CRLM allowing for volume regeneration of a functional liver remnant. No large-scale multi-institutional studies exist. The aim of this project was to describe outcomes following two-stage hepatectomy, including overall survival (OS), recurrence-free survival (RFS), and complications. Methods Patients completing two-stage hepatectomy for CRLM at five US institutions were identified and retrospectively analyzed (2000-2015). Overall survival and recurrence-free survival following second-stage surgery, short-term mortality, Clavien-Dindo complications, and readmission rates were examined. Results A total of 209 patients were identified. Mean age was 52 (SD +/-11.4), 59.8% were male, and 87.0% had synchronous disease. A total of 65.1% of patients underwent PVE, and 27.3% underwent hepatic artery infusion pump placement. 88.3% of cases underwent neoadjuvant chemotherapy. Following the first stage, 30-day morbidity was 24.4%, with 4.8% major (Clavien-Dindo grade ≥3) complications, and 30-day readmission was 6.7%. Mean time between first and second stage was 4.1 months (S.D. +/-3.1), and 57.5% received systemic chemotherapy between the two resections. Following the second stage, overall complications were 47.4% with 23.9% major complications, and 30-day readmission was 9.7%. Mortality following second stage was 3.8% at 30 days, and 5.3% at 90-days. Following the second stage, RFS at 1-, 3-, and 5-years was 80%, 46%, and 29% respectively. OS at 1-, 3-, and 5-years was 87%, 64%, and 45% respectively. Conclusion Two-stage hepatectomy for CRLM provides acceptable recurrence-free and overall survival in the context of advanced bilobar disease. Major complications and readmission following the first stage are rare. Following the second stage, short-term major morbidity, mortality, and readmissions are also acceptable. For well-selected patients, two-stage hepatectomy remains a safe and effective treatment for CRLM, with potential for more widespread adoption.

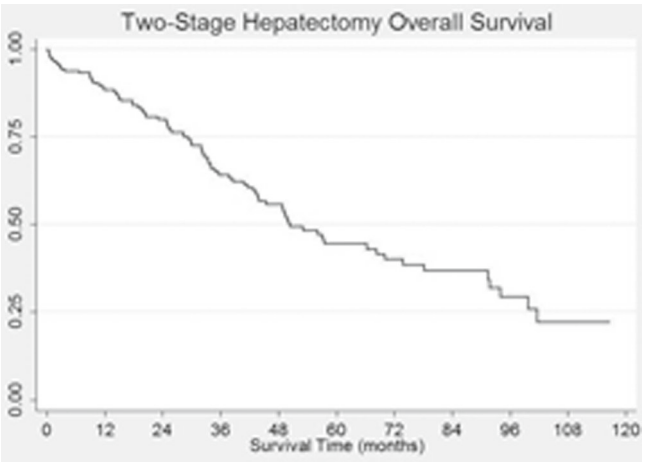


Figure 1: Overall Survival Following Successful Completion of Two-Stage Hepatectomy for Colorectal Liver Metastases

PT186

Comparative Effectiveness of a Virtual Tumor Board Versus Standard Care for Patients with Hepatocellular Cancer in a Regional Network A. Salami,[1]* P. Richardson,[2] M. Mason,[3] S. Sansgiry,[2] D. Castillo,[2] D. Anaya.[4] *1. Einstein Medical Center, Philadelphia, PA; 2. Houston VA Center for Innovations in Quality, Effectiveness and Safety, Michael E DeBakey VA Medical Center, Houston, TX; 3. Michael E DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 4. Section of Hepatobiliary Tumors, Department of Gastrointestinal Oncology, H. Lee Moffitt Cancer Center & Research Institute, Houston, TX.*

Introduction: Virtual tumor board (VTB) evaluation is associated with improved quality of care for patients with hepatocellular carcinoma (HCC). The impact of VTBs on treatment and survival is unknown. We sought to examine the comparative effectiveness of a regional VTB program on treatment and overall survival in patients with HCC. Methods: A regional VTB program was implemented at the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC – year 2010) to link providers at 9 remote Veterans Affairs Medical Centers (VAMC) within a VA-designated region (VISN16) with the weekly MEDVAMC HCC tumor board. VTB was available at all sites during the study period and allocation to VTB-led management was at the discretion of the treating provider (natural allocation, non-randomized). A retrospective cohort study including all patients diagnosed with HCC in VISN16 was performed (2010-2013). Treatment and survival outcomes were compared between the VTB group (intervention) and non-VTB patients (concurrent controls). Propensity score stratification was used to examine associations between VTB and outcomes. Results: 242 regional HCC patients were identified; 52 (21%) managed with VTB and the remainder 190 with standard non-VTB strategies. A total of 158 patients (65.3%) received treatment, with VTB patients having higher rates of treatment receipt than non-VTB patients (94.2% vs. 57.4%, p<0.01). Median OS was higher for patients in the VTB group as compared to the non-VTB group (1.8 years vs. 0.7 years, p<0.01). After propensity score stratification VTB-led management was found to be associated with increased likelihood of treatment receipt (OR 12.9 [95%CI 1.4-120], p=0.02) and decreased mortality (HR 0.4 [0.14-0.92], p=0.03) (Figure 1). Conclusion: Implementation of a VTB program at a regional level and within an integrated healthcare system is associated with increased treatment and improved overall survival in patients with HCC. These findings highlight the substantial effect of a delivery of care intervention, and represent a novel model of care to improve overall outcomes for patients with primary liver cancer at a larger scale.

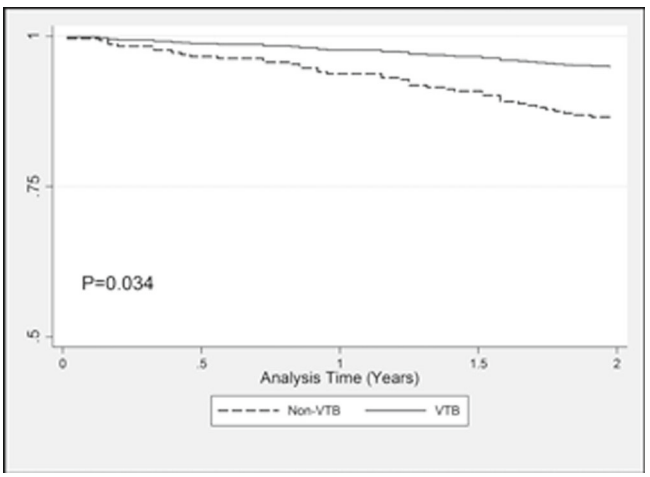
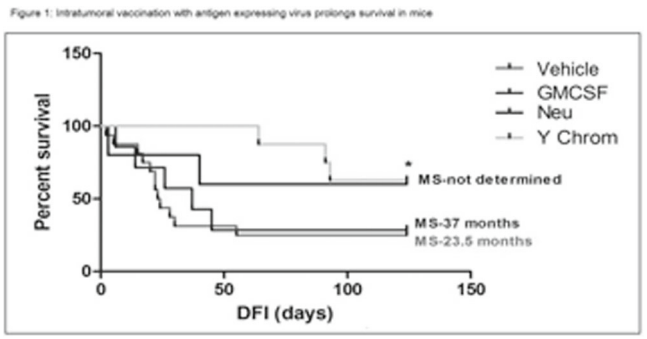


Figure 1. Propensity score-adjusted survival estimates comparing Non-VTB to VTB regional patients (N=242).

PT187

Intratumoral Vaccination Can Overcome Barriers to Immune Cell Recruitment in a Murine Model of PDAC K. Donohue,[2]* C. Dudgeon,[1] C. Monken,[1] E. Lattime,[1] D. Carpizo.[2] *1. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 2. Department of Surgery, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ.*

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy (5-year 6% survival rate) due to its propensity to metastasize via mechanisms of immunosuppression, including a desmoplastic response and inhibitory immune cell activation. We have previously shown that intratumoral injection of oncolytic viral vaccines expressing tumor antigen can overcome these mechanisms in pre-clinical models. In a Phase I clinical trial, patients with PDAC were treated by tumor injection and systemic boost using a PANVAC vaccine (NCT00669734). None of the 8 patients without metastatic disease developed distant metastases. This was associated with induction of tumor-specific immunity (unpublished). We hypothesize that a systemic immune response prevented metastatic disease. To test this hypothesis, we used an orthotopic mouse model of PDAC with the cell line Ink4a.1 luciferase/mcherry. Mice received intratumoral injection of a vaccinia virus engineered with tumor antigen (Neu or Y chromosome (Y)) and GMCSF at day 4 and day 18, and distal pancreatectomy at day 28. They were followed for overall survival. Primary tumors were examined for immune cell infiltration by flow cytometry (FC) and immunohistochemistry (IHC). There was a higher incidence of intratumoral CD3+ and CD8+ T cells in the antigen vaccines compared to controls by both FC and IHC. While the median survival of the GMCSF group was higher than the control (37 vs 23.5 days, p=0.55), this was not significant. The median survival in both the antigen groups was significantly higher than the vehicle and GMCSF control groups (Neu and Y median survival not reached, p=0.01 Her2 and Y vs. vehicle, p=0.05 Neu and Y vs. GMCSF). We conclude that intratumoral vaccination with tumor antigen expressing virus in this model can induce an anti-tumor effect, increase intratumoral T-cell infiltration and prolong survival. This evidence is consistent with intratumoral vaccination overcoming one of the barriers of PDAC immunosuppression, the prevention of recruitment of lymphocytes into the tumor. This model will be useful for studying the mechanisms by which intratumoral vaccination abrogates tumor immunosuppression in PDAC.



Immunocompetent Female FVB Mice were injected orthotopically with murine pancreatic cancer cells (Ink4a$^{-/-}$, Kras$^{G12D/+}$) and then were administered intratumoral vaccine containing GMCSF or GMCSF and a tumor expressing antigen (Neu, Y chromosome). 28 days later mice underwent distal pancreatectomy and splenectomy and were followed for overall survival.

PT188

Dysregulation of Hippo Signaling Pathway is a Prognostic Biomarker for Human Intrahepatic Cholangiocarcinoma K. Sugimachi,[1]* M. Nishio,[4] S. Aishima,[3] Y. Bekki,[1] K. Takenaka,[1] A. Suzuki,[4] K. Mimori.[2] *1. Surgery, Fukuoka City Hospital, Fukuoka, Japan; 2. Kyushu University Beppu Hospital, Beppu, Japan; 3. Saga University, Saga, Japan; 4. Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan.*

Background Intrahepatic cholangiocarcinoma (ICC) is known to be an aggressive malignant tumor with high mortality, although the oncogenic signaling of ICC has not been well studied. Yes-associated protein (YAP) and Mob1 are the key components of Hippo signaling pathway, YAP is a positive regulator of cell proliferation that is suppressed by Hippo signaling.

However Mob1 phosphorylates and draws YAP into the cytoplasm, preventing it from activating, thus suppresses cell proliferation. We recently reported Mob1 liver conditional knock out mice develop combined hepatocellular and cholangiocarcinoma and ICC (Nishio M et al. Proc Natl Acad Sci USA, 2016). The aim of this study is to reveal clinical significance of the dysregulation of the Hippo and TGF-β pathways in human ICC. Methods Expressions of Mob1, YAP, Smad2, and TGF-β2 were analyzed in 88 ICC cases. Protein expressions by immunohistochemistry were graded by the scoring system based on signal intensity and distribution. The clinicopathological factors including prognosis were analyzed based on protein expression. Results Nuclear overexpression of YAP was seen in 28 cases (31.8%) and it was significantly associated with poor overall survival rate (p=0.01). Mob1 nuclear expression decreased in 42 cases (47.7%) and associated with poor overall survival rate (p=0.02). YAP overexpression tended to correlate with decreased expression of Mob1. SMAD2 nuclear localization was significantly correlated with YAP overexpression independent of TGF-β. Cox- regression multivariate analysis revealed that YAP overexpression (p<0.01), low Mob1 expression (p<0.01), and lymphatic permeation (p<0.01) were the independent risk factors for the overall survival of ICC. Conclusions These results indicated that the nuclear YAP overexpression and decreased Mob1 expression were associated with malignant potential of ICC. Dysregulation of Hippo signaling could be a prognostic biomarker and potential therapeutic targets in human ICC.

PT189

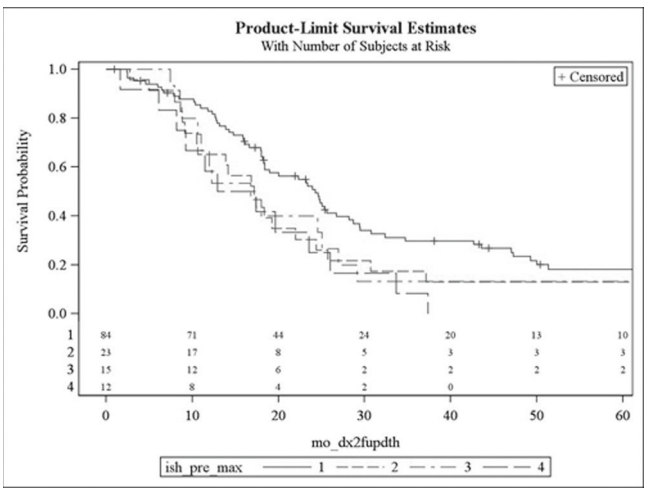
Vitamin D Supplementation Will Bring Promising Benefit to the Patients with Pancreatic Ductal Adenocarcinoma Y. Mukai,[2]* D. Yamada,[1] H. Eguchi,[1] Y. Iwagami,[1] T. Asaoka,[1] T. Noda,[1] H. Wada,[1] K. Kawamoto,[1] K. Gotoh,[1] M. Mori,[1] Y. Doki.[1] *1. Department of Gastroenterological Surgery, Osaka University, Suita, Japan; 2. Osaka university, Suita, Japan.*

Background: Pancreatic ductal adenocarcinoma (PDAC) is characterized with abundant activated-fibroblasts, called cancer associated fibroblasts (CAFs), which expresses alpha-SMA and promotes distant metastasis. Recently, it has been revealed that stromal cells in PDAC express abundant vitamin D receptor (VDR), and CAFs were perceptively inactivated with Vitamin D supplementation in a murine model. In this time, we investigated the relationships among the prognosis, the presence of CAFs, VDR expression in stromal cells and the amount of Vitamin D. Materials and Methods: From April 2007 to August 2012, a total of 86 PDAC patients receiving R0 resection (with preoperative therapy: 52 patients, and without preoperative therapy: 34 patients) were investigated. Alpha-SMA and VDR expressions were examined with immunohistochemical analysis, and the expressions were evaluated with semi-quantitative method. The level of vitamin D in patient's plasma was calculated using ELISA. Results: The expression of Alpha-SMA in stromal cell were detected all PDAC patients. When the patients were divided into two groups according to the number of alpha-SMA positive cells, the rich Alpha-SMA group showed significantly shorter distant metastasis free survival (35.4 vs 11.9 months, p=0.019). Clinicopathological backgrounds of these two groups did not show any significant differences except the presence of preoperative therapy (p<0.01) or Vitamin D level (high group vs low group, 31.7 vs 20.0 ng/ml, p<0.01). Meanwhile, VDR expressions were not changed between 2 groups with or without preoperative therapy (84.6 or 76.5%; p=0.29), indicating that Vitamin D supplementation would be effective without regard to the presence of preoperative therapy. Conclusion: The plenty presence of CAFs facilitate distant metastasis, and the patients with PDAC having rich CAFs showed significantly low level of Vitamin D. Although preoperative therapy may induce the fibroblast activation in PDAC, preoperative therapy did not have any influence on VDR in PDAC stroma. Vitamin D supplement therapy can be an effective tool for all PDAC patients, inhibiting metastasis through inactivation of CAFs.

PT190

Preoperative Vascular Grading in Pancreatic Surgery: Does Radiologic Vascular Involvement Predict Margin Status? S.S. Reddy,* A. Karachristos, J. Hoffman. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

INTRO:The use of neoadjuvant therapy has been used for treatment of borderline resectable pancreatic cancer(BLRPC). Controversy exists on this definition, and because of this, we examined the association of vascular involvement and margin status in patients who had initial resection. METHODS:Records of 137 patients who underwent surgery for resectable or BLRPC were collected. Included were radiologist grading of vascular involvement. For patients with both staging, we categorized vascular involvement as none, arterial/venous only, or both. We examined the association of vascular involvement and margin status using Chi-square tests and logistic regression. RESULTS: Of 137 patients, 55% were women and the median age was 70. All patients underwent surgery first, and 85% had a Whipple without vascular resection, and 13% with. Of 134 patients with Ishikawa staging, there were 63% stage I, 17% stage II, 11% stage III, and 9% stage IV. Of 96 patients with arterial staging, there were 74% stage i, 16% stage ii, and 10% stage iii. Of 93 patients with both Ishikawa and arterial staging, 61% had no vascular involvement, 7% arterial only, 14% venous only, and 17% had both. Ishikawa stage I-IV was associated with a positive SMA margin in 14%, 44%, 53%, and 58%, respectively(p<0.001). However, for arterial staging the association was weaker, and for arterial i-iii, a positive SMA margin was seen in 20%, 40%, and 40%, respectively(p=0.06). Therefore, Ishikawa staging was more predicative of arterial involvement. Higher Ishikawa staging was associated with positive SMV margins in 5%, 26%, 33%, and 33%, respectively (p<0.001), while preoperative arterial staging was not predictive(p=0.63). In logistic regression for any positive margin with both venous and arterial staging, only venous staging remained statistically significant in predicting a positive margin. CONCLUSION:The use of diagnostic imaging in predicting margins is more accurate when using a venous grading system as opposed to an arterial one. With a more standard approach of designating degree of vein involvement, and better preoperative imaging, further studies will be needed to substantiate these findings.

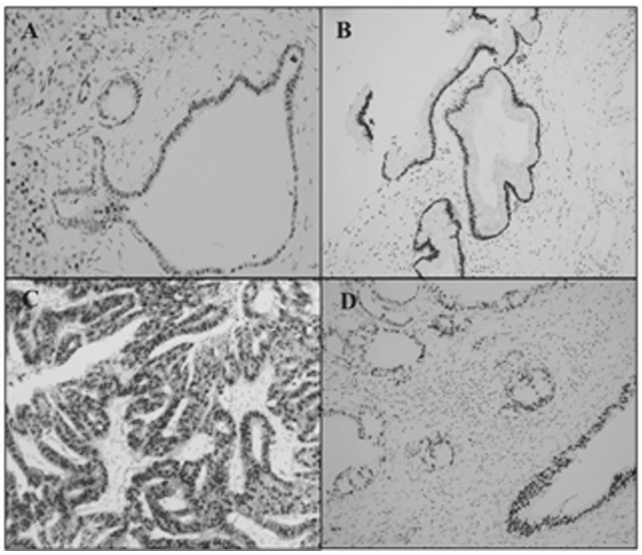


PT191

Increased SOX9 Expression in Premalignant and Malignant Pancreatic Neoplasms J.L. Gnerlich,* X. Ding, C. Joyce, K. Turner, G. Abood, G.V. Aranha, S.G. Pappas. *Surgery, Loyola University Medical Center, Maywood, IL.*

Background: SOX9, a progenitor cell marker important for normal pancreatic ductal development, is also implicated in malignant tissue transformation. Our aim was to examine differences in expression of SOX9 in intraductal papillary mucinous neoplasms (IPMNs) and ductal adenocarcinoma (PDAC) compared with benign pancreatic ducts (BP). Methods: SOX9 expression was evaluated by immunohistochemistry performed on 45 specimens including 37 BP, 24 low grade (LG) IPMN, 12 high grade (HG) IPMN, and 20 PDAC. A linear mixed model was used to compare the percentage of cells expressing SOX9 by specimen type. Repeated measures MANOVA was used to evaluate differences in SOX9 expression by staining intensity (weak, moderate, and strong) in pancreatic epithelial cells. Results: Nuclear SOX9 expression was detected in the epithelial cells of 98% HG IPMN, 93% LG IPMN, 81% PDAC, and 60% BP. Compared with BP, SOX9 was expressed from a significantly greater percentage of cells in LG IMPN, HG IMPN, and PDAC (P<0.001 for each). BP and PDAC showed greater variability in SOX9 expression in epithelial cells (BP: 4% strong, 25% moderate, 23% weak staining; PDAC: 22% strong, 44% moderate, 13% weak staining) compared with IPMNs which showed strong, homogenous SOX9 expression in almost all cells (HG

IPMN: 99% strong staining; LG IPMN: 94% strong staining). Compared with BP, both LG and HG IPMN showed significantly greater SOX9 expression ($P<0.001$ for each in strong staining intensity), but there was no significant difference in SOX9 expression between LG and HG IPMN ($P>0.05$). PDAC had significantly higher expression of SOX9 compared to BP, driven primarily by differences in moderate staining intensity ($P=0.02$), but significantly lower SOX9 expression compared with LG or HG IPMN ($P<0.001$ for strong staining intensity). Conclusions: IPMNs demonstrated the highest expression levels of SOX9, irrespective of grade. SOX9 expression patterns in BP and PDAC demonstrated much more heterogeneity when compared with the strong, uniform SOX9 expression in LG and HG IPMN. Further investigation is needed to evaluate the role of SOX9 as a marker in premalignant lesions and pancreatic cancer development.

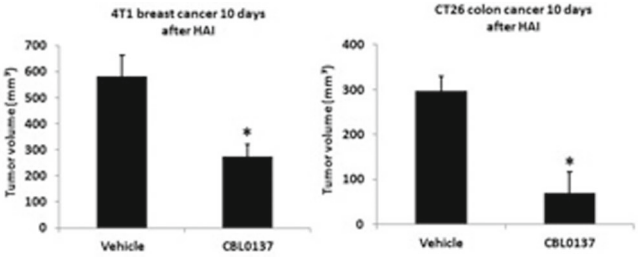


Representative micrographs demonstrating variability of SOX9 expression in different pancreatic tissue. (A) Benign pancreatic epithelial cells show heterogeneous expression of SOX9. (B) Low grade IPMN and (C) high grade IPMN show strong, uniform SOX9 expression. (D) Pancreatic ductal adenocarcinoma has higher levels of SOX9 expression compared with benign pancreatic ducts, but lower levels of SOX9 expression when compared with IPMN. Magnification, 100x.

PT192

Hepatic Arterial Infusion (HAI) with CBL0137 for Unresectable Liver Metastatic Murine Tumors M. Kim,* N. Neznanov, D. Fisher, C. Powers, D. Fleyshman, K. Gurova, J. Skitzki. *Surgical Oncology, Roswell Parck Cancer Institute, Buffalo, NY.*

Background: DNA binding of CBL0137 in tumor cells leads to global chromatin disassembly, inhibition of DNA replication, disorganization of transcription, and inhibition of the chromatin remodeling complex FACT (facilitates chromatin transcription) as measured by loss of the subunit SSRP1. Downstream consequences of FACT inhibition by CBL0137 include activation of p53 and inhibition of NF-κB. This completely new anti-cancer mechanism of action is not dependent upon the genetic landscape of tumors and has broad applications. Methods: In vitro cell survival studies used 4T1 breast or CT26 colon cancer; cells (10^5/well) were treated with vehicle or escalating doses of CBL0137. Mice were injected either with 2×10^5 4T1 or CT26 cells with a hemisplenectomy procedure. After 10 (4T1) and 7 (CT26) days of tumor establishment, mice were infused for 15 minutes with either vehicle or 0.6mg of CBL0137 via HAI. Tumor volume, apoptosis, SSRP1 loss, NF-κB, liver enzyme levels, and survival were analyzed. Results: Significant dose-dependent decreases in tumor cell viability were observed in both cell lines ($p<0.03$) starting at 100μg of CBL0137 treatment. Significant tumor growth delays were observed 5 and 10 days after single HAI therapy measured by luciferin activity and MRI, respectively. In CBL0137 treated animals, increased numbers of apoptotic cells in cancers ($p<0.05$) were detected by TUNEL, and western blot analysis for SSRP1 and Ki67 showed markedly decreased signals. The CBL0137 group showed higher AST/ALT levels 1 day after HAI compared to the vehicle group, but the levels returned to the normal range after 2 days. A significant survival benefit was noted in 4T1-bearing mice ($p<0.01$). Conclusion: This work provides strong rationale for further investigation of HAI with CBL0137 for treatment of primary or metastatic cancers. CBL0137 may be an ideal, low-toxicity drug for unresectable liver tumors.

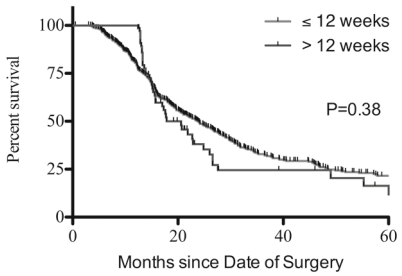


PT193

Time to Initiation of Adjuvant Chemotherapy: A Multi-Institutional Experience B.T. Xia,[1]* S.A. Ahmad,[1] A.H. Al Humaidi,[1] D.J. Hanseman,[1] C.G. Ethun,[2] S.K. Maithel,[2] D. Kooby,[2] A. Salem,[3] C. Cho,[4] S.M. Weber,[3] S.J. Stocker,[5] M.S. Talamonti,[5] D. Bentrem,[6] D.E. Abbott.[3] *1. Surgery, University of Cincinnati, Cincinnati, OH; 2. Emory University, Atlanta, GA; 3. University of Wisconsin, Madison, WI; 4. University of Michigan, Ann Arbor, MI; 5. NorthShore University Health System, Evanston, IL; 6. Northwestern Memorial Hospital, Chicago, IL.*

Introduction: The ESPAC-3 study demonstrated that time to initiation of adjuvant chemotherapy did not impact overall survival (OS) for patients with pancreatic cancer. We sought to determine if a similar relationship exists outside of a clinical trial, with different chemotherapy regimens. Methods: Perioperative data for patients who underwent pancreatectomy for ductal adenocarcinoma from five institutions (2005-2015) was assessed. Delay in adjuvant therapy (AT) was defined as initiating chemotherapy more than twelve weeks after surgery. Multivariate analysis was performed to identify predictors of delay in AT. Recurrence-free survival (RFS) and OS analyses were calculated using Kaplan-Meier methods. Results: Of 607 patients, 139 (22.9%) experienced omission of AT. Among 468 patients who received AT, 401 (85.7%) received chemotherapy prior to twelve weeks (median 7.3 weeks) post resection, and 67 (14.3%) were delayed in starting chemotherapy (median 15.7 weeks). The majority of patients were treated with single-agent gemcitabine (n= 370, 79.1%) or gemcitabine combination regimens (n= 51, 10.9%). Improved OS was observed in patients who received AT compared to patients who did not (22.7 vs. 15.8 months, P= 0.0001). There were no differences in the treatment duration (P= 0.22), RFS (P= 0.10) or OS (P= 0.38) observed between the timely and delayed AT groups. Similarly, no differences in RFS and OS were observed between the two groups when stratified by stage (stage I: P= 0.79 and 0.87, respectively; stage II: P= 0.11 and 0.14, respectively), and chemotherapy regimen (single-agent gemcitabine: P= 0.47 and 0.13, respectively; gemcitabine combination: P= 0.36 and 0.85, respectively). Preoperative malnutrition (serum albumin < 3.4 g/dL) and postoperative Clavien-Dindo Grade III/IV complications were significant predictors of delay in AT on multivariate analysis. Conclusion: In a multi-institutional experience of patients with resected pancreatic cancer, delayed initiation of AT did not negatively impact treatment duration, DFS and OS. Patients who do not receive AT within twelve weeks after surgery are still appropriate candidates for multi-modal therapy and its associated survival benefit.

Overall 5-year survival stratified by time to initiation of adjuvant chemotherapy.



Overall 5-year survival stratified by time to initiation of adjuvant chemotherapy.

PT194

IL-33, Released with Hepatectomy, Facilitated Recurrence of Cholangiocarcinoma Not through Direct Influence S. Nagaoka,* D. Yamada, H. Eguchi, Y. Iwagami, T. Asaoka, T. Noda, H. Wada, K. Kawamoto, K. Gotoh, Y. Doki, M. Mori. *Gastroenterological Surgery, Osaka University, Suita, Japan.*

Background and Purpose: Cholangiocarcinoma (CCA) is a lethal neoplasm because of frequent recurrence after surgery. IL-33 has been shown to facilitate the development of CCA in a murine model, and IL-33 is an alarmin released during tissue injury. Based on this information, we postulated that IL-33 may be released during liver surgery for CCA, and facilitate recurrent disease. Methods: The expressions of IL-33 in background liver of 50 CCA patients who underwent curative surgery in our institute were evaluated by immunohistochemistry (IHC). IL-33 was measured by ELISA in 24 paired plasma collections obtained immediately before and after surgery. To evaluate the direct influence of IL-33 to tumor progression, we performed proliferation assay, wound healing assay, MTT assay. Results: IL-33 expression in background liver of CCA varied widely (5.6-181.2 positive cells /HPF). However, IL-33 released into the plasma during hepatectomy directly correlated with the background liver expression assessed by IHC (The median ratio of IL-33 level in plasma, after to prior surgery, low vs high IL-33 IHC expression group, 1.02 vs 1.44, p<0.001). The recurrence free survival time (RFS) of the high expression group were significantly shorter than that of the low expression group (Median survival time (months), high vs low expression group, 11.1 vs 33.0 months, p=0.0149). The exposure of IL-33 did not change any malignant ability in CCA cell lines (HuCCT-1, CCLP-1) as follows; Proliferation: p=0.51 (HuCCT-1), p=0.42 (CCLP-1), Migration assay: p=0.61 (HuCCT-1), p=0.57 (CCLP-1), MTT assay for GEM: p=0.70 (HuCCT-1), p=0.93 (CCLP-1), p-value of the difference between with and without IL-33 supplement. Conclusions: Hepatic IL-33 is released during hepatic surgery into the circulation, and the high expression is a risk factor for CCA recurrence following surgery. IL-33 does not have any direct influence to CCA cell line, and we need to do further investigation assuming indirect influence.

PT195

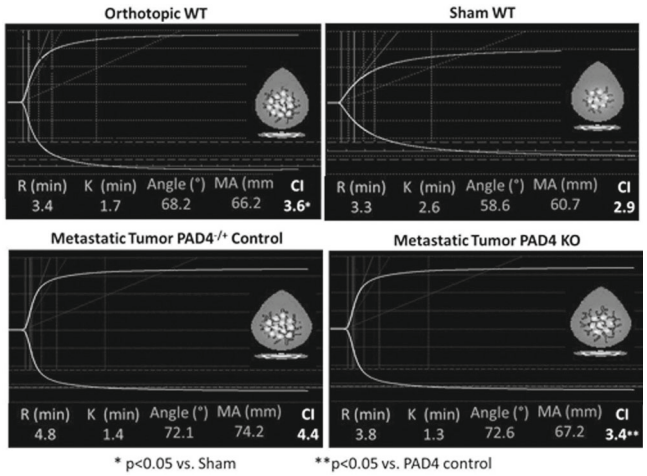
The Impact of Extrahepatic Disease Among Patients Undergoing Liver-Directed Therapy for Neuroendocrine Liver Metastasis: A Multi-Institutional Analysis A. Ejaz,[2]* B. Reames,[2] S.K. Maithel,[4] G. Poultsides,[6] T.W. Bauer,[5] R. Fields,[7] M. Weiss,[2] H.P. Marques,[8] L. Aldrighetti,[3] T. Pawlik.[1] *1. Surgery, The Ohio State University, Columbus, OH; 2. Johns Hopkins University, Baltimore, MD; 3. Ospedale San Raffaele, Milan, Italy; 4. Emory University, Atlanta, GA; 5. University of Virginia, Charlottesville, VA; 6. Stanford University, Stanford, CA; 7. Washington University, St. Louis, MO; 8. Curry Cabral Hospital, Lisbon, Portugal.*

Introduction: Management of neuroendocrine liver metastasis (NELM) in the presence of synchronous extrahepatic disease (EHD) is controversial. We sought to examine the outcomes of patients undergoing liver-directed therapy for NELM in the presence of EHD using a large multicenter international cohort of patients. Methods: 612 patients who underwent liver-directed therapy were identified from 8 participating institutions. Postoperative outcomes, as well as overall (OS) and progression-free survival (PFS) were compared between patients with (N=70, 11.4%) and without (N=542, 88.6%) EHD. Results: Median age of the cohort was 57 years (IQR: 48, 65) with a slight majority of patients being male (N=326, 53.3%). The majority of primary tumors were located in the pancreas (N=254, 41.8%) followed by the small bowel (N=188, 30.9%). At the time of liver-directed surgery, patients underwent surgery alone (N=471, 77.0%), ablation alone (N=15, 2.5%), or a combined approach (N=126, 20.6%). Most patients underwent a non-anatomic wedge resection (N=404, 66.0%). Patients with EHD had more aggressive high-grade tumors (EHD: 44.4% vs. no EHD: 16.1%; P<0.001). EHD was most commonly located in the peritoneum (N=29, 41.4%) and lung (N=19, 27.1%). Among the 70 patients with EHD, 20.0% (N=14) underwent concurrent resection for the EHD. After a median follow-up of 51 months, 174 (28.4%) patients died with a median OS of 140.4 months among the entire cohort. Patients with EHD had a shorter median OS versus patients who did not have EHD (EHD: 87 months vs. no EHD: not reached; P=0.002). Similarly, PFS was shorter among patients with EHD compared with patients without EHD (EHD: 46.8 months vs. no EHD: 68.6 months; P=0.005). In the cox regression model, the presence of EHD was independently associated with an increased risk of death (HR: 2.56, 95%CI 1.16-5.62; P=0.02). Conclusion: Patients with NELM and EHD had more aggressive tumors, which conferred over a 2-fold increased risk of death compared with patients who did not have EHD. Surgical treatment of NELM among patients with EHD should be individualized.

PT196

Neutrophil Extracellular Traps Promote Hypercoagulability in Cancer Through Release of Tissue Factor and Platelet Aggregation B.A. Boone,* J.L. Miller-Ocuin, W. Doerfler, J.T. Ellis, M.T. Lotze, M.D. Neal, H.J. Zeh. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

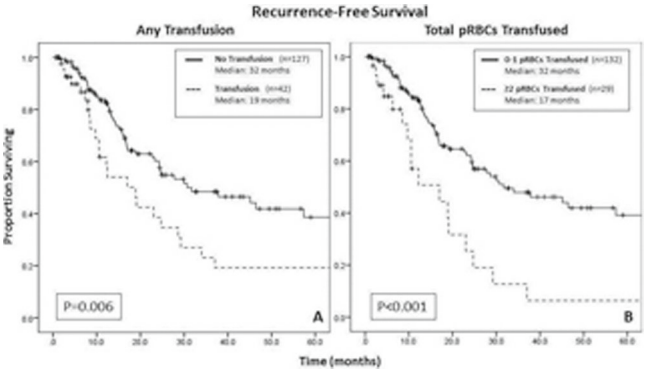
Introduction: Activated neutrophils release their contents containing DNA, histones, granules, and tissue factor through a process known as neutrophil extracellular trap formation (NETs). We have demonstrated that neutrophils from cancer bearing mice have increased propensity to form NETs through an autophagy dependent pathway. We hypothesize that upregulation of NETs in tumor bearing mice will lead to a hypercoagulable state. Methods: We compared metrics of coagulation in two different murine tumor models treated with the autophagy inhibitor chloroquine (CQ) to prevent NET formation and in mice genetically deficient in PAD 4, an enzyme critically important to NET formation. Thromboelastograms (TEG) were performed to assess dynamic clot formation. Platelet aggregation in whole blood was assessed using impedance aggregometry. Tissue factor, a critical initiator of the coagulation cascade, was measured in the plasma by ELISA. Data is reported as mean±SD and analyzed using student's t-test. Results: WT mice bearing orthotopic pancreatic tumors were hypercoagulable on TEG compared to sham controls (Figure, p<0.05). Blocking NETs with CQ partially reversed this effect. In a metastatic liver model, PAD4 KO mice, unable to form NETs, were less hypercoagulable than controls (Figure, p<0.05). Tumor bearing WT mice had increased platelet aggregation compared with sham controls (AUC 8.4±2.4 vs. 1.8±2.6, p<0.05). CQ treatment of mice and of whole blood led to a significant reduction in platelet aggregation. Tumor bearing PAD4 KO mice had significant reduction in platelet aggregation compared with tumor bearing WT mice (AUC 3.7±1.7 vs. 8.4±2.4, p<0.05). Circulating tissue factor was elevated in orthotopic WT mice (228±7 vs 207±6 ng/mL, p<0.05) and significantly decreased following treatment with CQ (187±2 vs. 228±7 ng/mL, p<0.05). Conclusion: NETs promote hypercoagulability in murine cancer models through release of tissue factor and platelet aggregation. Inhibiting NETs by treatment with CQ or genetic deletion of PAD4 reverses these effects. A similar mechanism may explain the hypercoagulable state commonly seen in human malignancy.



PT197

Effect of Perioperative Transfusion on Recurrence and Survival After Resection of Distal Cholangiocarcinoma: A 10-Institution Study from the U.S. Extrahepatic Biliary Malignancy Consortium A.G. Lopez-Aguiar,[1]* C.G. Ethun,[1] N. Le,[1] T.M. Pawlik,[2] G. Poultsides,[3] T.B. Tran,[3] K. Idrees,[4] C.A. Isom,[4] R. Fields,[5] B. Krasnick,[5] S.M. Weber,[6] A. Salem,[6] R.C.G. Martin,[7] C. Scoggins,[7] P. Shen,[8] H.D. Mogal,[8] C. Schmidt,[9] E. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] K. Cardona,[1] S.K. Maithel.[1] *1. Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 2. The Johns Hopkins Hospital, Baltimore, MD; 3. Stanford University Medical Center, Stanford, CA; 4. Vanderbilt Unversity Medical Center, Nashville, TN; 5. Washington University School of Medicine, St. Louis, MO; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State Universtiy Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

BACKGROUND: Perioperative allogeneic blood transfusion is associated with poor oncologic outcomes in several malignancies. Its effect on recurrence and survival in distal cholangiocarcinoma (DCC) is unknown. METHODS: All patients with DCC who underwent curative-intent pancreaticoduodenectomy at 10 institutions from 2000-2015 were included. 30-day mortalities were excluded. Primary outcomes were recurrence-free (RFS) and overall survival (OS). RESULTS: Of 314 pts with DCC, 206 (66%) underwent curative-intent pancreaticoduodenectomy. Median age was 67yrs, and 53 pts (28%) received perioperative blood transfusions, with a median of 2 units. There were no differences in baseline demographics or operative data between transfusion and no-transfusion groups. Compared to no-transfusion, patients who received a transfusion were more likely to have (+)margins (28vs14%; p<0.03) and major complications (46vs16%; p<0.001). Receipt of neoadjuvant or adjuvant therapy was similar between groups. Transfusion was associated with lower median RFS (19vs32mos; p=0.006; Figure1A) and OS (15vs29mos; p=0.003), which persisted on multivariable (MV) analysis for both RFS (HR 1.8; 95%CI 1.1-3.1; p=0.03) and OS (HR 1.9; 95%CI 1.1-3.2; p=0.03), after controlling for portal vein resection, EBL, margin status, grade, LVI, LN status, and major complications. Similarly, transfusion of ≥2 pRBC units was associated with lower RFS (17vs32mos; p<0.001; Figure1B) and OS (14vs29mos; p<0.001), which again persisted on MV analysis for both RFS (HR 2.6; 95%CI 1.4-4.6; p=0.002) and OS (HR 3.9; 95%CI 2.1-7.5; p<0.001). The RFS and OS of patients transfused 1 unit was similar to those not transfused. CONCLUSION: Perioperative blood transfusion is associated with decreased RFS and OS after resection for distal cholangiocarcinoma, after accounting for known adverse pathologic factors. Volume of transfusion seems to exert an independent effect, as 1 unit is not associated with the same adverse effects as ≥2units. This supports the judicious use of perioperative transfusion; protocols should be developed and followed.



PT198

Proteomic Analysis of Saliva in Patients with Pancreatic Adenocarcinoma C. Trajtenberg,[2] D. Roife,[3]* Y. Kang,[1] K. Lundberg,[2] E. Yohannes,[2] J. Fleming.[1] *1. The University of Texas M. D. Anderson Cancer Center, Houston, TX; 2. Case Western Reserve University, Cleveland, OH; 3. McGovern Medical School, Houston, TX.*

Introduction: Pancreatic cancer continues to be a lethal disease. There is currently no strategy available for its early diagnosis. Proteomic technology provides an excellent means for analysis of body fluids, cataloging protein constituents. This technology has been helpful in the identification of biomarkers for early detection of other cancers. In this study, we carried out a comprehensive characterization of the "salivary proteome" in patients with pancreatic cancer. We hypothesized that there are differences in the expression of proteins in saliva in patients with pancreatic cancer when compared to normal subjects. Methods: Whole stimulated salivary glandular secretions were collected, processed and stored from ten patients with pancreatic adenocarcinoma (PDAC) and compared to samples from ten healthy volunteers. Saliva specimens were treated, digested with trypsin, and proteins/peptides were separated by reversed phase liquid chromatography (RPLC) and analyzed by tandem mass spectrometry (MS/MS) using a shotgun label-free expression proteomics platform. Results: A total of 1575 peptides, mapping to 316 proteins were quantified and identified. Of those 153 peptides (belonging to 53 proteins) were found to be significantly different from controls at p<0.05. Twenty-one non-redundant proteins were up-regulated (P/C ratio >1.5), including Deleted in malignant brain tumor (DMBT1, involved in epithelial differentiation), Galectin-3 binding protein (mac-2 binding protein, involved in adhesion to matrix proteins), and Ly6-neurotoxin 1 (LYNX1, involved in nerve conduction). Thirty-two non-redundant proteins were down-regulated (P/C ratio <2), many of which were involved with the innate immune response, such as lactoferrin, lysozyme, and lactoperoxidase. Conclusion: There are differences in the expression protein profile in saliva in patients with pancreatic cancer when compared to age-matched controls. Further investigation is warranted to assess the diagnostic accuracy of these proteins and their prognostic implications.

PT199

Tailored Treatment of Patients with Hepatocellular Carcinoma with Portal Vein Invasion S. Walcott-Sapp,* J. Wagner, S. Orloff, S. Naugler, K. Farsad, K. Kolbeck, C.K. Enestvedt, S. Mayo, K. Billingsley. *Surgery, Oregon Health & Science University, Portland, OR.*

Introduction Advanced hepatocellular carcinoma (HCC) with portal vein invasion (PVI) has historically carried an extremely poor prognosis. Treatment options are limited by patients' tolerance of liver-directed therapy. Our multidisciplinary team has focused on the use of highly selective liver-directed treatments whenever safely possible. The aim of this study is to report survival and safety associated with this approach. Methods Thirty seven patients with HCC with PVI treated at our institution between 2008 and 2014 were identified in a prospectively collected, retrospectively reviewed liver tumor database. Additional data on treatment, degree of portal vein invasion, and presence of extrahepatic metastases were collected from medical records. Statistical analysis was performed with unpaired t-test, Welch's test, and single factor ANOVA. Statistical significance was defined as p<0.05. All survival times are reported in months with mean±standard deviation. Results The majority of

patients (59%) were diagnosed with PVI at the time of initial HCC diagnosis. The remainder had a mean time from diagnosis of HCC to diagnosis of PVI of 7.1±7.0 months. In all cases, treatment decisions were made after review by a multidisciplinary team. There were no differences between the treatment groups related to degree of portal vein invasion or maximum diameter of primary tumor at the time of diagnosis. The liver-directed therapy group (n=22) had significantly greater survival than the systemic (n=7) or supportive care (n=7) groups (25.7±16.1 vs. 9.5±4.9 vs. 4.7±2.1; p=0.0002). There was no difference in survival between the transarterial Y90 radioembolization (n=15) and chemoembolization (n=7) groups (29.7±16.4 vs. 17.0±11.5). All patients tolerated liver-directed therapy without acute liver failure or other complications requiring prolonged hospitalization. Conclusion Our data indicate patients with PVI may be safely treated with significant extension of life by using meticulous patient selection and a judicious technique of liver-directed treatment. These findings support a strategy of liver-directed therapy when deemed feasible and safe by multidisciplinary team assessment.

PT200

Targeted Pancreatic Cancer Drug-Delivery Utilizing Sigma-2 Ligand/Receptor Internalization is Energy-Dependent L.X. Jin,[1]* S. Vangveravong,[1] D. Cullinan,[1] P. Goedegebuure,[1] A. Loza,[1] R.H. Mach,[2] D. Spitzer,[1] W. Hawkins.[1] *1. Surgery, Washington University in St. Louis, St. Louis, MO; 2. University of Pennsylvania, Philadelphia, PA.*

Background: Pancreatic cancer is a devastating disease that is poorly responsive to traditional systemic therapies. Cancer-selective drug delivery can improve survival and reduce systemic toxicities. We have developed a pancreatic cancer drug delivery platform based on sigma-2 receptor ligands conjugated to small molecule drug cargos, which improves delivery and efficacy through efficient drug internalization. However, the mechanism of drug internalization via the sigma-2 receptor/ligand interaction remains unclear. Methods: Uptake of fluorescently conjugated sigma-2 ligand SW120 was studied in ASPC-1 human pancreatic cancer cells. Uptake was measured at 37C, 4C, after competitive inhibition with sigma-2 ligand SW43, and after pretreatment with Pitstop 2 (Abcam), an inhibiter of clathrin-mediated endocytosis. Uptake was visualized using live-cell imaging using A1Rsi confocal laser scanning microscope (Nikon). Image analysis was performed using FIJI (NIH) and Matlab (Mathworks). Results: SW120 (10 nM) was rapidly internalized into ASPC-1 cells at 37C with maximal fluorescence at 12 minutes. As a negative control, incubation of ASPC-1 cells with the unconjugated flourophore NBD Cl demonstrated no uptake after 15 minutes, indicating that uptake of SW120 depends on the specific sigma-2 receptor/ligand interaction. Fluorescence at 15 minutes was reduced by 85% in ASPC-1 cells incubated at 4C, indicating uptake of SW120 into cells is an energy dependent process. Pretreatment of cells with Pitstop 2 decreased total flourescence at 15 minutes by 76%, suggesting an important role of clathrin-mediated endocytosis in sigma-2 receptor uptake, while pretreatment with competitive inhibitor SW43 reduced uptake by 84%, suggesting that sigma-2 ligands are internalized via a specific receptor capable of saturation. Conclusion: Sigma-2 receptor ligands are rapidly internalized into pancreatic cancer cells via a specific, targetable, energy-dependent pathway that appears to rely on clathrin-mediated endocytosis. Further understanding of sigma-2 mediated drug internalization can help optimize targeted drug development and delivery for pancreatic cancer patients.

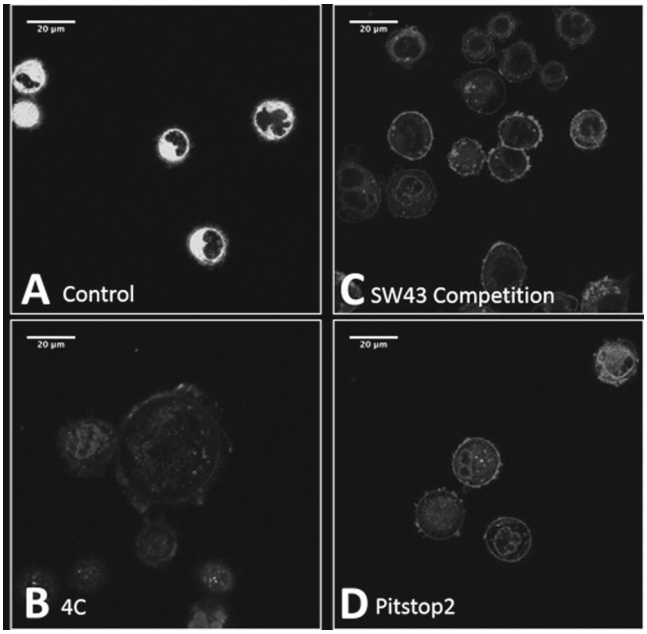


Figure. ASPC-1 pancreatic cancer cells after 15-minute incubation with SW120, a fluorescently labeled sigma-2 receptor ligand at A) 37C with no uptake inhibition; B) after incubation for 30 minutes at 4C prior to drug application; C) in the presence of 1 hour of pre-incubation with competitive inhibitor sigma-2 ligand SW43; D) after 30 minutes of treatment with Pitstop 2 cell permeable clathrin inhibitor prior to drug application. (Blue Hoescht stained nuclei; Red Cellmask stained plasma membrane; Green NBD-Cl flourophore conjugated sigma-2 ligand SW120. Magnification 100x. Scale bar corresponds to 20 mm.)

PT201

Surgical Management of Recurrent Neuroendocrine Liver Metastasis: An International Multi-Institutional Analysis G. Spolverato,[2]* F. Bagante,[2] L. Aldrighetti,[3] G. Poultsides,[4] T.W. Bauer,[5] R. Fields,[6] H.P. Marques,[7] S.K. Maithel,[8] T. Pawlik.[1] *1. Surgery, The Ohio State University, Columbus, OH; 2. University of Verona, Verona, Italy; 3. Scientific Institute San Raffaele, Milan, Italy; 4. Stanford University, Stanford, CA; 5. University of Virginia, Charlottesville, VA; 6. Washington University, School of Medicine, St Louis, MO; 7. Curry Cabral Hospital, Lisbon, Lisbon, Portugal; 8. Emory University, Atlanta, GA.*

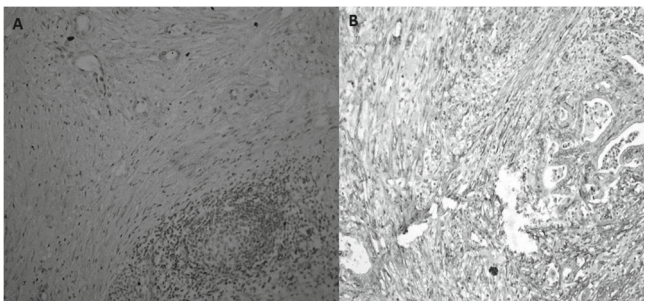
Background: The management and outcome of patients with recurrent neuroendocrine liver metastasis (NELM) are not well defined. We sought to characterize the treatment, as well as define the long-term outcomes, of patients with recurrent NELM. Methods: Between 1990-2014, 397 patients undergoing curative intent liver surgery for NELM were identified from a multi-institutional database. Recurrences were classified as intrahepatic, extrahepatic and both intra- and extra-hepatic. Overall survival (OS) was defined using Kaplan-Meir estimates and factors associated with survival were identified using Cox regression analyses. Results: At the time of initial surgery, the majority (79.3%) of patients had >50% liver involvement. NELM was well-differentiated in 164 (54.1%) patients, moderately-differentiated in 85 (28.1%), and poorly-differentiated in 54 (17.8%). While 10-year OS was 67.8% (95% CI, 61.2-73.5), 193 (48.6%) patients developed a recurrence within a median time of 4.7 years. Among patients who recurred, 128 (68.1%) patients experienced an intra-hepatic recurrence, 20 (10.6%) patients extra-hepatic recurrence, and 40 (21.3%) patients had both an intra- and extra-hepatic recurrence. 10-year OS among patients who did versus did not experience a recurrence was 82.9% and 54.4%, respectively)(p<0.001). Of note, 10-year OS varied according to the different recurrence patterns (intra-hepatic: 60.6% vs. extra-hepatic: 58.4% vs. intra- and extra-hepatic: 33.8%)(p=0.038). A subset of patients who had a recurrence underwent repeat surgery (n=53, 36.6%), while 34 (23.5%) patients were treated with a somatostatin analogue, 27 (18.6%) with systemic chemotherapy, and 31 (21.4%) with intra-arterial therapy. The 5-year OS of patients who

underwent a repeat surgery was 72.1%, which was better than patients treated with somatostatin analogues (53.5%), chemotherapy (24.8%), or intra-arterial therapy (68.5%)(p=0.006). Conclusion: Recurrence after surgery for NELM was common, occurring in up to half of patients. When feasible, repeat liver resection for recurrence offered a reasonable 5-year survival benefit and should be considered.

PT202

Characterization of the Desmoplasia in Lymph Nodes Metastases of Pancreatic Adenocarcinoma Patients Reveals Activation of a Cancer-Associated Fibroblasts Pattern E. Nizri,* S. Bar-David, G. Lahat, J. Klausner. *Tel Aviv medical center, Tel Aviv, Israel.*

Background: Desmoplasia in primary tumor is extensively studied in pancreatic adenocarcinoma (PDAC) primary tumor. Desmoplasia is also present around PDAC metastases, such as lymph nodes (LN) metastases. The cells of origin of this desmoplastic reaction and its molecular characterization are currently unknown. Our aims were to phenotype the molecular pathways and markers of this desmoplasia in the LN metastatic niche. Methods: We analyzed histological sections of patients with PDAC and LN metastases in which desmoplasia was present around tumor. We performed immunohistochemical analysis for various cancer associated fibroblasts markers and compared them to LN without desmoplasia. In addition, we analyzed mRNA from desmoplastic LN for various molecular signaling pathways known to be involved in desmoplasia of primary tumors. Results: Desmoplasia in the LN metastases was associated with α-SMA and GFAP in the peri-tumoral fibroblast, in contrast to patients without desmoplasia, in which it was present only in the reticular region and in the LN capsule. In addition, desmoplasia was associated with peri-tumoral expression of COL11A1, a known CAF marker and constituent of the peri-tumoral extra-cellular matrix. The expression of COL11A1 was restricted to fibroblasts around $CK7^+$ tumoral cells and was absent in LN without metastases or LN with metastases but without desmoplasia (LN-). mRNA quantification revealed robust COL11A1 expression in LN with metastases and desmoplasia (LN+) compared to LN- (5.2±1.3 vs. 1.1±0.8, p=0.02). We found that TGF-β is highly expressed in LN+ compared to LN- (2.6±0.4 vs. 1.2±0.3). Interestingly, molecular pattern of desmoplasia in LN is reminiscent of pancreatic stellate cells activation, raising the possibility that these cells migrate with PDAC cells to the LN. Conclusions: Desmoplasia in metastatic LN reveals a similar pattern to that of the primary tumor, which is associated with TGF-β expression and CAF markers. Thus, desmoplasia takes part in the creation of the metastatic niche and may serve as therapeutic target in advanced PDAC.



PT203

Impact of Major Vascular Resection on Short- and Long-term Outcomes in Patients with Intrahepatic Cholangiocarcinoma: A Multi-Institutional Analysis B. Reames,[2]* A. Ejaz,[2] H.P. Marques,[3] L. Aldrighetti,[4] T. Gamblin,[5] S.K. Maithel,[6] T.W. Bauer,[7] F. Shen,[8] G. Poultsides,[9] J. Marsh,[10] I. Popescu,[11] C. Sandroussi,[12] T. Pawlik.[1]
1. Surgery, The Ohio State University, Columbus, OH; 2. Johns Hopkins Hospital, Baltimore, MD; 3. Curry Cabral Hospital, Lisbon, Portugal; 4. Ospedale San Raffaele, Milan, Italy; 5. Medical College of Wisconsin, Milwaukee, WI; 6. Emory University, Atlanta, GA; 7. University of Virginia, Charlottesville, VA; 8. Eastern Hepatobiliary Surgery Hospital, Shanghai, China; 9. Stanford University, Stanford, CA; 10. University of Pittsburgh Medical Center, Pittsburgh, PA; 11. Fundei Hospital, Bucharest, Romania; 12. University of Sydney, Sydney, NSW, Australia.

Background: Major vascular (IVC or portal vein) resection for Intrahepatic Cholangiocarcinoma (ICC) has traditionally been considered a relative contraindication to resection. We sought to define perioperative outcomes and survival of ICC patients undergoing liver surgery with major vascular resection using a multi-institutional database. Methods: 1,087 ICC patients who underwent liver resection between 1990-2016 were identified from 13 participating institutions. Multivariable logistic and cox regressions were used to determine the impact of major vascular resection on perioperative outcomes and long-term overall survival. Results: Of 1,087 patients who underwent resection, 128(11.8%) also underwent major vascular resection [21(16.4%)IVC resections, 98(76.6%)PV resections, 9(7.0%)combined resections]. One hundred eighty-seven(17.2%) patients received neoadjuvant therapy. Most patients underwent a major hepatectomy involving ≥3 liver segments(n=664,61.1%). On final pathology, the majority of patients had T1(40.4%) or T2(35.5%) tumors; 194(17.8%) had lymph node metastasis. Patients undergoing major vascular resection had more advanced T3/T4 tumors [44(34.4%) vs. 137(14.3%) without resection;P<0.001]. Of note, major vascular resection was not associated with the risk of any complication (OR .680,95%CI 0.32-1.45) or major complication (OR 0.69,95%CI 0.35-1.33); post-operative mortality was also comparable between groups (OR 1.06, 95%CI 0.32-3.48). In addition, median recurrence-free (14.0 months vs.14.7 months, HR.737,95%CI .49-1.10) and overall (33.4 months vs.40.2 months, HR .709,95%CI.36-1.40) survival were similar among patients who did and did not undergo major vascular resection, respectively(both P>0.05). Conclusion: Among patients with ICC, major vascular resection was not associated with increased peri-operative morbidity or mortality at major centers. Long-term outcomes following resection of ICC requiring vascular resection were also comparable to outcomes following resection of tumors without vascular involvement. Concurrent major vascular resection should be considered in appropriately selected ICC patients.

PT204

A Short-term Preoperative Diet Decreases Bleeding in Liver Surgery: Results from a Multi-Institutional, Randomized Controlled Trial R.J. Barth,[1]* J. Mills,[1] A. Suriawinata,[1] J. Putra,[1] T. Tosteson,[1] G.F. Whalen,[2] J. LaFemina,[2] W. Kinlaw,[1] S. Tarczewski.[1]
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Introduction: We previously showed in a case series study that a one week, low calorie, low fat diet was associated with less blood loss and less steatosis in patients undergoing liver surgery. Our objective is now to evaluate the effect of this diet in a randomized controlled trial. Methods: We randomly assigned 60 patients with a BMI > 25 kg/m^2 to either no special diet or a 800 kcal, 20 gm fat, 70 gm protein diet for 1 week prior to liver resection. Participating surgeons were blinded to the diet assignment. Hepatic glycogen stores were evaluated using Periodic acid-Schiff (PAS) stains. Results: There was no difference between groups in baseline patient characteristics, extent of surgery, platelet counts or use of anti-platelet medications. 94% of the patients complied with the diet. The diet group consumed less daily total calories (807 kcal vs 1968 kcal, $p < 0.001$) and fat (21 gm vs 86 gm, $p < 0.001$) than the no diet group. Intra-operative blood loss was less in the diet group: mean blood loss 452 ml vs 862 ml, p= 0.021; median blood loss 250 ml vs 500 ml. The surgeon judged the liver to be easier to manipulate (scale 1-5, where 1 was "easy") in the diet group: 1.86 vs 2.90, p= 0.004. The complication rate (20% vs 17%), median length of stay (5 days vs 4 days) and mortality (none) did not

differ between the diet and no-diet groups. There was no difference between groups in hepatic steatosis, but there was less glycogen in hepatocytes in the diet group (PAS stain score 1.61 vs 2.46, $p < 0.0001$). Conclusions: A short course, low fat, low calorie diet significantly decreases bleeding and makes the liver easier to manipulate in hepatic surgery.

PT206

A Propensity-Matched Analysis of Laparoscopic Versus Open Distal Pancreatectomy for Pancreatic Adenocarcinoma M. Raoof,* S. Dumitra, P.H.G. Ituarte, Y. Woo, S. Warner, G. Singh, Y. Fong, L. Melstrom. *Surgery, City of Hope National Medical Center, Duarte, CA.*

Background: Laparoscopic-assisted distal pancreatectomy (LDP) has improved perioperative outcomes over open distal pancreatectomy (ODP). Concerns regarding failure to achieve proper oncologic resection and compromised survival remain. Methods: Using the National Cancer Database (NCDB), we analyzed patients undergoing distal pancreatectomy for resectable pancreatic adenocarcinoma over a four-year period (2010-2014). Propensity score nearest-neighbor 1:1 matching (PSM) was performed between LDP and ODP patients based on age, sex, race, insurance, hospital volume, comorbidities, T-stage, N-stage, grade, neoadjuvant therapy, adjuvant therapy. Primary outcome was overall survival. Results: Of the 1,947 eligible patients, 605 (31%) underwent LDP. After PSM two well-balanced groups of 544 patients each were analyzed. There was a trend towards improved overall survival (OS) in patients undergoing LDP as compared to ODP (HR: 0.83, 95% CI 0.68-1.0; Median OS 29 vs. 23 months, p=0.06). Patients undergoing ODP had a higher margin positive rate compared to those undergoing LDP (21.1% vs. 14.9%, p-value=0.007). Overall conversion rate was 27%. Patients undergoing ODP had comparable outcomes to LDP in regards to median time to chemotherapy (50 vs. 48 days, p-value=0.96); median nodes examined (12 vs. 12, p-value=0.61); 30-day mortality (1.6% vs. 1.1%, p-value=0.43); 90-day mortality (3.5% vs. 2.4%, p-value=0.28); 30-day readmission rate (8.6% vs. 9.4%, p-value=0.67). However, the median length of stay was shorter in the LDP group (6 vs. 7 days, p=0.0001). Conclusion: In the absence of randomized trials, this is the largest comparative study demonstrating LDP as an acceptable alternative ODP, associated with a lower margin positive rate and shorter length of stay, and with no detriment in long term survival.

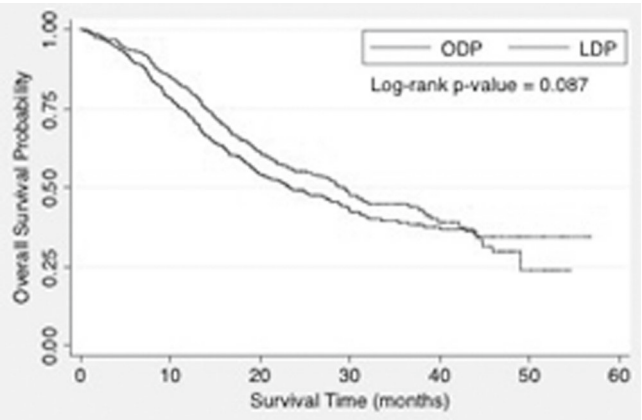
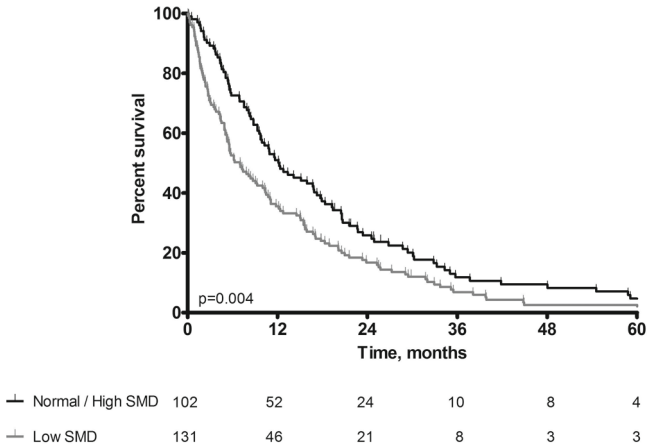


Figure 1. Kaplan-Meier Overall Survival Estimates of patients undergoing LDP vs. ODP in a propensity-matched, population-based cohort.

PT207

Low Skeletal Muscle Density is Associated with Early Death in Patients with Suspected Perihilar Cholangiocarcinoma J. van Vugt,[1]* M. Gaspersz,[1] J. Vugts,[1] S. Buettner,[1] S. Levolger,[1] R. de Bruin,[1] W. Polak,[1] J. de Jonge,[1] F. Willemssen,[2] B. Groot Koerkamp,[1] J. IJzermans.[1] *1. Dept of Surgery, Erasmus MC University Medical Center, Rotterdam, Netherlands; 2. Dept of Radiology, Erasmus MC University Medical Center, Rotterdam, Netherlands.*

INTRODUCTION: Low skeletal muscle mass is associated with increased postoperative morbidity and impaired survival following liver resection for perihilar cholangiocarcinoma (PHC). However, the majority of patients do not undergo surgery. The aim of this study was to investigate skeletal muscle mass and density as biomarkers to predict the outcome of all patients with suspected PHC, regardless of treatment. METHODS: All consecutive patients with suspected PHC treated in a tertiary center were included. Baseline characteristics and parameters regarding disease and treatment were collected. Skeletal muscle mass and skeletal muscle density, reflecting intramuscular adipose tissue infiltration and muscle quality (in Hounsfield units [HU]), were measured on the level of the third lumbar vertebra (L3) on abdominal computed tomography scans. RESULTS: In total, 233 patients were identified with a median follow-up of 25.3 months. In total, 221 (94.8%) patients died during the study period. The 3-month, 6-month, 1-year, 3-year and 5-year survival rates in the entire cohort were 79.0%, 60.9%, 42.1%, 7.7%, and 3.0%, respectively. The median survival did not differ between patients with (11.6 months, 95% CI 9.2-14.1) and without (11.1, 95% CI 7.4-14.8) low skeletal muscle mass (p=0.375), whereas a significantly lower median survival was observed in patients with low (7.0 months, 95% CI 4.7-9.3) compared with patients with high (12.1, 95% CI 8.1-16.1) skeletal muscle density (p=0.004, figure). After adjusting for age, tumor size, and suspected peritoneal or other distant metastases on imaging, low skeletal muscle density was independently associated with decreased survival (HR 1.78, 95% CI 1.03-3.07, p=0.04) within the first six months, but not after six months (HR 0.68, 95% CI 0.44-1.07, p=0.093). CONCLUSION: A time-dependent effect of skeletal muscle density on mortality was found in patients with PHC, regardless of subsequent treatment. Low skeletal muscle density may identify patients with PHC at risk for early death.



PT209

CD73 as a Novel Prognostic Marker of Pancreatic Adenocarcinoma E. Katsuta,* S. Hochwald, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: CD73 degrades AMP to adenosine, and it is involved in the generation of an immunosuppressed and pro-angiogenic tumor microenvironment that promotes the onset and progression of cancer. CD73 is also known as one of the essential mesenchymal stem cell markers. Given these roles, we hypothesized that CD73 expression in pancreatic ductal adenocarcinoma (PDAC) is associated with worse survival. METHODS: 170 cases of PDAC in the Cancer Genome Atlas (TCGA) dataset were classified as either high or low expression of CD73. Clinicopathological features, overall survival (OS) and Disease-free survival (DFS) were compared between these two groups. Then the factors that contribute their prognosis were analyzed.

RESULTS: High expression of CD73 in the tumor was significantly associated with larger tumor size (p=0.021). CD73 highly expressed cases demonstrated significantly worse survival in both OS (median 15.8 vs 21.4 months; p=0.004) and DFS (median 9.6 vs 17.3 months; p<0.001). On univariate analysis, residual tumor (R1, 2; p=0.008) and CD73 high expression (p<0.001) had a significant association with worse DFS. Multivariate analysis demonstrated that the independent factors negatively impacting DFS were residual tumor (p=0.045) and CD73 high expression (p=0.011). Lymph node metastasis (p=0.017), residual tumor (p=0.011) and CD73 high expression (p= 0.004) had a significant association with worse OS on univariate analysis. Multivariate analysis demonstrated that residual tumor (p=0.025) and CD73 high expression (p=0.007) were also related with poor OS. Correlation analysis revealed that CD73 expression was correlated with cell cycle related genes such as E2F7 (R=0.65) and cancer stem cell related genes such as MET (R=0.63). Only weak correlation was seen with epithelial–mesenchymal transition (EMT) related genes such as SNAI2 (R=0.42) and TMEM132A (R=0.42). No correlation was seen between CD73 and immune system nor angiogenesis related genes. CONCLUSIONS: CD73 high expression tumors were larger tumors and had worse OS and DFS in PDAC. CD73 expression levels correlated with cell cycle related genes and cancer stem cell related genes, but not with immune system or angiogenesis factors.

PT210

Histologic Classification and Grading Enhances Gallbladder Cancer Staging: A Population-Based Prognostic Score Validated by the U.S. Extrahepatic Biliary Malignancy Consortium

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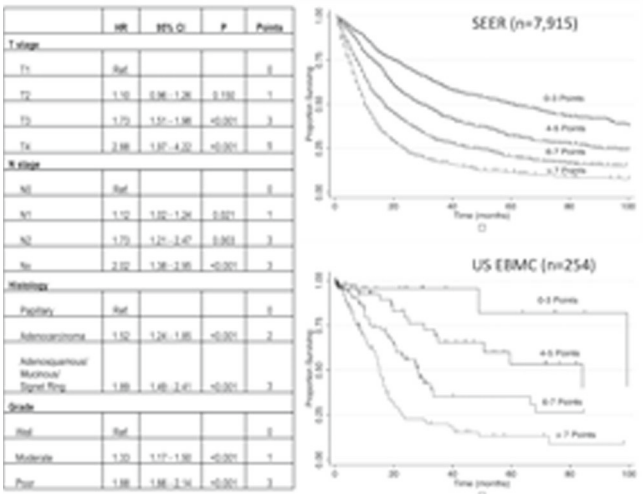
Background: Beyond the most common standard adenocarcinoma type, several gallbladder cancer (GBC) histologic types have been described as being associated with more favorable (papillary) or less favorable outcome (adenosquamous, mucinous, signet ring). We sought to examine the added value of histologic type and grade on the existing AJCC staging system for resected GBC. Methods: Patients who underwent resection of GBC from 1988 to 2013 were identified using the Surveillance Epidemiology End Results (SEER) registry. A prognostic score was created by assigning points for T stage, N stage, grade and histologic type, based on the regression coefficient in multivariate survival analysis. The score was externally validated using the US Extrahepatic Biliary Malignancy Consortium (USEBMC) database (2000-2015) and compared with the current AJCC staging system. Results: Of 7,915 patients identified in the SEER database, 83% had adenocarcinoma, 7% papillary, 4% adenosquamous, 4% mucinous, and 2% signet ring. In the USEBMC database, the frequencies of the respective histologies were 86%, 9%, 2%, 1% and 2%. Median survival per histologic type, for SEER and USEBMC respectively, were 45 and 110 mos for papillary, 16 and 24 mos for adenocarcinoma, 14 and 12 mos for mucinous, 8 and 4 mos for adenosquamous, and 9 and 15 mos for signet ring (P between histologies <0.001 for both cohorts). On multivariate analysis, T stage, N stage, grade and histologic type were all independent predictors of overall survival (Figure). The developed prognostic score, based on points for each of these 4 variables, showed excellent discriminatory ability both in the SEER as well as the USEBMC cohorts (Figure). The Area Under Curve (AUC) for the prognostic score was significantly improved compared with the AJCC system (0.69 vs. 0.64, both P<0.001 using SEER data, and 0.76 vs. 0.66, both P<0.001 using USEBMC data). Conclusion: The incorporation of histologic type and grade into the current TNM system allows for a simple and more accurate tool to determine prognosis following surgical resection of gallbladder cancer.



PT212

Assessing Relative Cost of Complications Following Bile Duct Surgery

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Introduction: While advances in surgical technique have improved the safety and decreased the complications associated with bile duct surgery, post-operative complications continue to impose both a clinical and financial burden on patients and the healthcare system. This study sought to identify the frequency and economic impact of complications following bile duct surgery. Methods: The Premier Hospital Database was queried for patients undergoing bile duct surgery between 2008 and 2015. Complications were identified based on ICD-9 code and grouped based on complication type. Complication frequency as well as impact on clinical and economic outcomes was calculated. Cost differences were calculated with respect to patients undergoing bile duct surgery who did not experience each given complication. Differences were averaged within complication types. Complication frequency and effect on cost were ranked, with ranks summed to evaluate relative economic impact of complication types. Results: A total of 2,087 patients met inclusion criteria. The most common groups of complications following bile duct surgery were pulmonary, gastrointestinal, and infectious (Table 1). Specifically, respiratory insufficiency (16.16%), bleeding (14.19%), and ileus (10.59%) occurred most often. The complications with the greatest average percent effect on treatment-related costs were neurologic, psychiatric, and cardiac. With respect to specific complications, methicillin resistant Staphlococcus aureus pneumonia (1.65%), stroke (1.54%), and pyelonephritis (1.19%) had the greatest impact on cost. After combining the ranks of complication frequency and percent of effect on cost, infectious, pulmonary, and gastrointestinal complications had the greatest cumulative effect on cost related to bile duct surgery. Conclusions: Financially significant complications following bile duct surgery stem from a combination of peri-procedural factors. Minimizing sources of infection including urinary and central venous catheters, improving post-operative pulmonary toilet and mobilization, and decreasing post-operative narcotic use can help improve cost-effectiveness of bile duct surgery for benign and malignant conditions.

Table 1. Most Frequent and Financially Significant Complications following Bile Duct Surgery

Complication Group	Percent	Ranks of Frequency	Average $ Medicare Cost Pct	Ranks of Effect on Cost	Combined Rank
Infectious	26.22	3	0.26	1	4
Pulmonary	25.38	1	0.18	4	5
Gastrointestinal	25.33	2	0.18	5	7
Iatrogenic	21.47	4	0.07	6	10
Bleeding	14.19	5	0.07	6	11
Psychiatric	1.11	10	0.26	1	11
Neurologic	0.72	11	0.26	1	12
Cardiac	12.39	6	0.00	9	15
Hepatic	1.58	9	0.06	8	17
Renal	7.33	7	-0.02	10	17
Deep Vein Thrombosis/Pulmonary Embolus	1.84	8	-0.21	11	19

PT213

Over-utilization of Routine Screening in Pancreas Cancer: An Opportunity to Minimize Cost and Unnecessary Testing
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Introduction: Pancreas cancer is the 3rd leading cause of cancer death in the US with only 8% five-year survival. Given this poor prognosis, performance of routine preventative health screening tests should be carefully scrutinized. We sought to define the frequency and cost associated with routine screening after the diagnosis of pancreas cancer. Methods: The MarketScan® database (years 2012-14) was used to identify patients with new pancreas cancer diagnoses. Patients were followed for a minimum of one year, with a one year retrospective evaluation of comorbidities. Subsequent to diagnosis, we defined the frequency of several routine screening tests including colonoscopy, mammography, PSA, and cholesterol measurements using CPT and ICD-9 codes. Procedures were excluded if performed for diagnostic or therapeutic purposes. Total cost (payment) and patient out-of-pocket costs were determined. Results: Of 10,433 patients with a new pancreas cancer diagnoses, 1,788 patients (17.1%) underwent at least one of four screening tests. 591 (5.7%) patients underwent colonoscopy, 168 (1.6%) mammography, 904 (8.7%) had a PSA lab test, and 395 (3.8%) had cholesterol screening. 1,023 patients (9.8%) underwent potentially curative resection, yet these patients accounted for only 13% of the screening test volume. The remaining 87% of screening tests occurred in unresected patients. Median costs for screening tests were $921/colonoscopy, $96/mammogram, $19/PSA, and $8/cholesterol test. Average out-of-pocket costs were under $5 for cholesterol, PSA, and mammography, but were $57 for colonoscopy. The total cost of screening in this cohort was $803,298, or $449 per screened patient. Conclusion: In this cohort of patients with pancreas cancer, screening tests were common and expensive. When considering limited life expectancy after the diagnosis of pancreas cancer, it is difficult to recommend the use of routine screening tests for other disease processes, especially given their debated cost-effectiveness in healthy individuals. For malignancies with poor long-term survival, the health care system should be refined to eliminate this wasteful screening.

PF214

A Nomogram to Predict Pathologic Lymph Node Positivity in Clinical Stage I-II Pancreatic Adenocarcinoma D.S. Swords,[1]* C. Zhang,[2] A.P. Presson,[2] M.A. Firpo,[1] S.J. Mulvihill,[1] C.L. Scaife.[1]
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Introduction: Clinical nodal staging in pancreatic adenocarcinoma (PDAC) is inaccurate. Most patients are clinically node negative, but > 70% are node positive on pathologic evaluation. We hypothesize that readily available preoperative variables are associated with node positivity, and could be used to create a predictive nomogram. Methods: The National Cancer Database was reviewed from 2010-2013 for patients with clinical stage I-II PDAC. Exclusions were neoadjuvant therapy, < 12 nodes examined, and missing data for clinical or pathologic stage, size, and number of nodes examined or positive. Multivariate logistic regression assessed factors associated with nodal positivity, and an interaction was included for extrapancreatic extension and clinical N stage. A logistic regression based nomogram was constructed and 10-fold cross validation was used to evaluate model discrimination. Results: Of 7,475 patients, 2,126 (28%) were clinically node positive vs. 5,498 (74%) after pathologic evaluation (P<0.001). The associations of preoperative factors with node positivity are displayed (Table). Size was an important predictor, and the size-dependent rates of node positivity were 53% for < 2 cm, 77% for 2-4 cm, and 74% for > 4 cm. Importantly, tumor size was pathology-based. We recommend multiplying cross sectional imaging-based size estimates by 1.33 for use in this nomogram based on studies showing that imaging underestimates actual size by 25%. Interestingly, extrapancreatic extension was protective for cN0 patients, but associated with increased odds of pathologic node positivity for cN1 relative to cN0 patients. A nomogram was created to predict node positivity using the variables in the table. The 10-fold cross validated AUC was 0.77. Conclusion: Our nomogram has good discrimination to preoperatively predict lymph node positivity for patients with resectable PDAC. It could potentially be useful in identifying biologically aggressive resectable PDAC patients at higher risk of nodal involvement in order to select patients for neoadjuvant therapy.

Results of multivariate logistic regression analysis of preoperative factors associated with node positivity in Stage I-II Pancreatic Adenocarcinoma

Variable	Adjusted Odds Ratio (95% Confidence Interval)	P Value
Age (Reference 18-59)		
60-69	0.83 (0.71, 0.97)	0.019
70-79	0.87 (0.75, 1.03)	0.1
> 80	0.77 (0.63, 0.95)	0.016
Sex (Reference Male)		
Female	1.1 (0.98, 1.23)	0.12
Race (Reference Hispanic)		
Non-Hispanic White	1.24 (0.92, 1.66)	0.15
Non-Hispanic Black	1.31 (0.93, 1.84)	0.12
Charlson-Deyo Comorbidity Index (Reference 0)		
1	0.98 (0.86, 1.12)	0.73
≥ 2	1.05 (0.85, 1.32)	0.64
Tumor Location (Reference Body)		
Head	2.5 (2.02, 3.09)	<0.001
Tail	1.37 (1.05, 1.8)	0.02
Tumor Size (Reference < 2 cm)		
2-4 cm	2.34 (1.96, 2.79)	<0.001
> 4 cm	3.16 (2.58, 3.89)	<0.001
Extrapancreatic Extension and Clinical Nodal Status		
Extrapancreatic extension and cN0	0.71 (0.63, 0.81	<0.001
Extrapancreatic extension and cN1	3.83 (2.34, 6.27)	<0.001
No extrapancreatic extension and cN0	1 (Reference)	-----
No extrapancreatic extension and cN1	7.75(5.57,11.1)	<0.001
Grade (Reference Low)		
Moderate	1.83 (1.5, 2.24)	<0.001
High	2.31 (1.87, 2.86)	<0.001
CA 19-9 (Reference Normal, i.e. <37 U/mL)		
Elevated	1.6 (1.36, 1.88)	<0.001
Unknown	1.21 (1.03, 1.43)	0.019

PF215

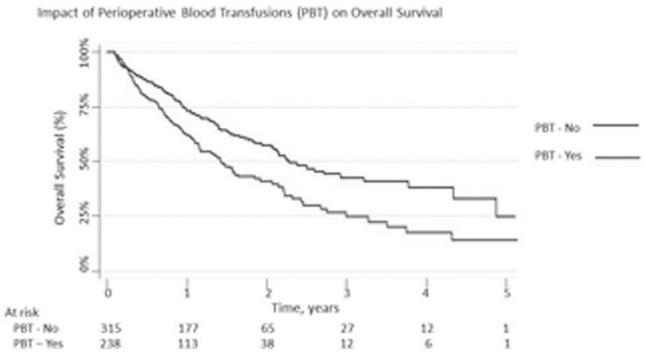
C6 Ceramide Potentiates Chemotoxicity of Gemcitabine against Chemo Resistant Pancreatic Cancer Cell Lines H. Wanebo,[1]* W. Bowen,[2] A. Liss.[3] *1. Surgery/ Surgical Oncology, Roger Williams Medical Center, Providence, RI; 2. Brown University, Providence, RI; 3. Mass General Hospital, Boston, MA.*

INTRODUCTION: Pancreatic cancer is a highly chemo-resistant malignancy with 5% overall survival, and limited treatment options with chemotherapy (Gemcitabine) and surgical resection possible in <20% of patients with post resection survival of only 15-20%. OBJECTIVE: Our studies suggest potential value of C6 Ceramide as a chemo enhancing biologic in therapy of chemoresistant pancreatic cancer. C6 Ceramide is an active sphingomyelin end product that has the major biologic function of inducing apoptosis in cells compromised or damaged by injury or malignancy, and appears to have potential value in therapy of malignancy. We and others have demonstrated C6 Ceramide inhibition of pro survival (AKT/PI3K/mTOR) and KRAS mutant pathways, which promote pancreatic cancer growth and metastases. METHODS/MATERIALS: Cell lines obtained from 4 freshly cultured pancreatic cancers, and 3 well established cancer cell lines (ATCC) were cultured in 96 well plates, 4000 cells/well, and were treated at 24 hours with Gemcitabine in 0.9% NaCl (1,2,5,10 ug/ml), alone and with C6 Ceramide in DMSO (2.5, 5.0, 10 ug/ml) and two liposomal formulations of C6 Ceramide: (galloyl) DPC6: D0PC: C6 Ceramide (0.5, 1.0, 2.0 ug/ml), and (pegylated) 180 PEG 2PE: D0PC: C6 Ceramide (0.5, 1.0, 2.0 ug/ml), and included vehicle controls. Cell viability was assessed by resazurin assay, 48 hour post drug infusion. RESULTS: As noted in Figure 1, the effect of treatment on freshly cultured cell lines (722, 1108, 1312, and 1513) showed marked cell growth inhibition with combination C6 Ceramide and Gemcitabine (cell death 60-80%). This result was also replicated in all of the 3 ATC based cells (long term cultured). CONCLUSION: C6 Ceramide appears to potentiate chemotoxicity of Gemcitabine against all (freshly cultured and long term cultured) pancreatic cancer cell lines, suggesting clinical value in continued development of C6 Ceramide as an anti-cancer biologic.

PF217

Blood Transfusion is Associated with Worse Outcomes Following Pancreatic Resection for Pancreatic Adenocarcinoma A. Javed,* S. Ronnekleiv-Kelly, R. Burkhart, M. Makary, J. He, J. Cameron, C. Wolfgang, S. Frank, M. Weiss. *Surgical Oncology, Johns Hopkins Hospital, Baltimore, MD.*

Introduction. Pancreatectomy remains the only potentially curative therapy for patients with pancreatic ductal adenocarcinoma (PDAC). Existing literature suggests that 27-68 % of patients require perioperative allogeneic blood transfusion (PBT). An historical practice of liberal PBT use is being questioned as data emerges documenting a detrimental long-term oncologic effect. The impact of transfusion in an era of restrictive PBT is incompletely described. Methods. A single-institution, prospectively-maintained database identified 553 patients who underwent resection for PDAC from 2009-2015. Patients were stratified by PBT and clinicopathological variables were analyzed. Perioperative mortalities were excluded. Primary outcome measure was median overall survival (OS). Results. A total of 238 patients (43.0%) received PBT. Those receiving PBT were more likely to be elderly or have a history of coagulopathy and anemia. PBT was also more common with rising ASA class, neoadjuvant therapy administration, higher estimated blood loss (EBL), positive margin status, and need for concomitant vascular resection. The median OS for the entire cohort was 24.8 months. PBT was associated with a poorer median OS (17.2 vs. 27.4 months, p<0.001) (Figure 1). Univariate analysis identified age, AJCC T-stage, number of harvested nodes, tumor size, lymphovascular invasion, EBL and margin status as factors associated with OS. In the multivariable analysis, PBT was independently associated with poorer OS (HR=1.6, p=0.001). Receipt of two or more blood units was associated with a shorter survival (16.2 vs. 26.8 months, p<0.001). Conclusion. Patients are more apt to require PBT with increasing comorbidities, locally-advanced/borderline-resectable tumors, and neoadjuvant therapy. PBT is associated with decreased survival, while increasing transfusion requirements are associated with poorer outcome. This is the largest single-institution study confirming the effects of PBT on long-term outcomes after pancreatectomy for PDAC.



PF218

Modified Fukuoka Guidelines Improves Detection of High Grade Dysplasia and Invasive Cancer in Patients with Pancreatic Mucinous Cystic Neoplasms B.C. Chapman,* A. Gleisner, D.M. Overbey, A. Paniccia, C. Bartsch, C. Gajdos, S. Wani, M.D. McCarter, R. Schulick, B. Edil. *Surgery, University of Colorado School of Medicine, Denver, CO.*

Introduction: The purpose of this study is to compare the accuracy of the American Gastroenterological Association (AGA) 2015 guidelines, Fukuoka Consensus 2012 guidelines, and a modified Fukuoka guideline including a cyst ≥3 cm as indication for pancreatectomy in the management of pancreatic mucinous cystic neoplasms (PMCNs). Methods: We retrospectively identified patients at our institution undergoing pancreatectomy for PMCNs (2012-2016). The AGA, Fukuoka, and modified Fukuoka criteria were applied and the incidence of missed high grade dysplasia (HGD) and invasive cancer (presence on surgical pathology in a patient not meeting criteria for surgery using each guideline) were evaluated. Results: We identified 92 patients with PMCNs: 11 (11%) MD-IPMN, 28 (27%) SB-IPMN, 37 (35%) mixed-IPMN, and 16 (15%) MCNs. Among all patients, 48 (52%) were symptomatic, 22 (24%) had high risk features, 80 (88%) had worrisome features, and 13 (14%) had suspicious or positive cytology. On surgical pathology, HGD or invasive cancer was found in 82% of MD-IPMN, 10% of SB-IPMN, 81% of mixed-IPMN, and 25% of MCNs. Using the AGA guidelines, 20 (22%) patients did not meet criteria for pancreatectomy and among these, 7 patients had a missed diagnosis of HGD (n=6) or invasive cancer (n=1). Using the Fukuoka guidelines, 18 (20%) patients did not meet criteria and among these, 9 patients had a missed diagnosis of HGD (n=7) or invasive cancer (n=2). Using the modified Fukuoka guidelines, 4 (4%) patients did not meet criteria and among these, 3 patients had a missed diagnosis of HGD (n=2) or invasive cancer (n=1). Overall, HGD and/or invasive cancer was present in 58% (n=53) of patients and the rate of missed HGD or invasive cancer was 13% (n=7), 17% (n=9), and 6% (n=3) using the AGA, Fukuoka, and modified Fukuoka guidelines, respectively. Conclusions: The addition of a cyst size ≥3 cm as an indication for pancreatectomy in patients with mucinous neoplasms reduced the percentage of missed HGD or invasive cancer from 13% using the AGA guidelines and 17% using the Fukuoka guidelines to less than 6%.

PF219

The Role of Surgery and Adjuvant Therapy in Node-Positive Biliary Tract Cancer H.S. Tran Cao,* Q. Zhang, Y. Sada, C. Chai, S.A. Curley, N. Massarweh. *Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Bellaire, TX.*

INTRODUCTION: Node positivity is a poor prognostic factor in patients with biliary tract cancers. Optimal management of biliary tract cancers with positive regional nodes, specifically the impact of surgery and adjuvant therapy on survival, is unclear. METHODS: This was a retrospective cohort study of patients with T1-3N1 gallbladder cancer (GBC) and intrahepatic cholangiocarcinoma (IHC) in the National Cancer Data Base (2004-2012). Patients were classified by treatment approach (non-operative, surgery, surgery + adjuvant therapy). Adjuvant therapy was further categorized as chemotherapy or (chemo)radiation. Overall survival (OS) was the primary outcome; the association between risk of death and treatment approach was evaluated using multivariable Cox regression. RESULTS: Among patients with GBC (n=1,335) and IHC (n=1,009), rates of surgical resection were 84.1% and 36.6%, respectively. Non-operative therapy, surgery, and surgery + adjuvant therapy were associated with median OS of 11.6 months, 13.3 months, and 19.6 months for GBC (log-rank, p<0.001) and 12.7 months, 16.2 months, and 22.6 months for IHC (log-rank, p<0.001), respectively. Compared to non-operative therapy, surgery was associated with a lower risk of death for GBC (HR 0.71, 95% CI [0.56-0.89]) and IHC (0.70 [0.56-0.87]). Addition of (chemo)radiation was associated with a survival benefit over surgery alone for both GBC (0.66 [0.55-0.79]) and IHC (0.71 [0.51-0.99]). This benefit persisted among patients with R0 resection for GBC (0.69 [0.56-0.87]), but not IHC (0.89 [0.58-1.36]). Adjuvant chemotherapy was not associated with a survival advantage for either cancer over surgery alone. CONCLUSIONS: Although regional node positivity is associated with poor OS for GBC and IHC, a multimodal approach based on surgery and adjuvant (chemo)radiation, but not chemotherapy, confers a survival benefit. Optimal management of node-positive disease includes margin negative resection and addition of (chemo)radiation for all GBC patients and for IHC patients with positive resection margins. Future studies of biliary tract cancers with clinical node positivity evaluating the impact of preoperative radiation on survival may be of value.

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Predictors of Early Recurrence and Omission of Adjuvant Therapy after Pancreatectomy for Pancreas Cancer: A Case for Neoadjuvant Therapy in High-risk Patients B.T. Xia,[1]* D.E. Abbott,[2] A.H. Al Humaidi,[1] D.J. Hanseman,[1] C.G. Ethun,[3] S.K. Maithel,[3] D. Kooby,[3] A. Salem,[2] C. Cho,[6] S.M. Weber,[2] S.J. Stocker,[4] M.S. Talamonti,[4] D. Bentrem,[5] S.A. Ahmad.[1] *1. Surgery, University of Cincinnati, Cincinnati, OH; 2. University of Wisconsin, Madison, WI; 3. Emory University, Atlanta, GA; 4. NorthShore University Health System, Evanston, IL; 5. Northwestern Memorial Hospital, Chicago, IL; 6. University of Michigan, Ann Arbor, MI.*

Introduction: A substantial group of patients with resected pancreatic cancer demonstrate early recurrence (ER) or fail to receive adjuvant therapy, negatively impacting survival. We sought to determine if an at-risk patient population can be identified preoperatively, to select patients who would particularly benefit from neoadjuvant therapy. Methods: Perioperative data for patients who underwent pancreatectomy for ductal adenocarcinoma from five academic institutions (2005-2015) was assessed. The primary endpoint was

early failure, defined as ER (within six months after surgery) and omission of adjuvant therapy (OAT). Multivariate analysis was used to identify predictors of early failure, and survival analysis was performed using the Kaplan-Meier method and compared using the log-rank test. Results: Pancreaticoduodenectomy (n=674, 85.6%) was the most common resection performed. Of 787 patients, 236 (30%) experienced early failure post resection. This was associated with a significant survival disadvantage compared to patients who did not have ER/OAT (median overall survival 13.4 vs. 27.5 months, P<0.0001). Advanced age, race, age adjusted Charlson comorbidity index, Eastern Cooperative Oncology Group (ECOG) performance status, and elevated preoperative carbohydrate antigen 19-9 (CA 19-9) were associated with increased likelihood of ER/OAT post resection (all P<0.05). Race (Black vs. White; odds ratio [OR] 1.81; P=0.03), ECOG score (≥2 vs. 0; OR 2.91; P=0.02), and CA 19-9 (≥180 vs. <180; OR 2.02; P=0.01) persisted as preoperative predictors of ER/OAT on multivariate analysis. Conclusions: Nearly one-third of patients with resected pancreatic cancer demonstrate early recurrence or omission of adjuvant therapy. This cohort of vulnerable patients may be better served by neoadjuvant therapy, to ensure completion of multimodal therapy, as well as to select out patients with poor tumor biology and occult metastatic disease at the time of diagnosis. Further research should be focused on developing a prognostic nomogram for prediction of early failure post pancreatectomy to aid in sequence of therapy decisions.

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Local Recurrence After Laparoscopic Microwave Thermosphere Ablation of Malignant Liver Tumors H. Takahashi,* H. Pournik, E. Berber. *General Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Introduction: Thermosphere ablation uses a new generation microwave technology that creates spherical ablation zones with a single antenna. We previously reported on the safety and feasibility of this technology. The aim of this study is to analyze local recurrence (LR) associated with this new treatment modality in patients with malignant liver tumors. Methods: This was a prospective study of 76 patients with 217 malignant liver tumors who underwent microwave thermosphere ablation (MTA) between September 2014 and September 2016. The patients were followed up with tri-phasic CT scans or MRIs at 2 weeks postoperative and then quarterly. Clinical, operative and oncologic data were analyzed. Kaplan-Meier and Cox proportional hazard model were used to study the incidence of LR and predictive parameters. Results: Tumor type included colorectal cancer (n=85, 39.2%), neuroendocrine (n=83, 38.2%), hepatocellular cancer (n=12, 5.5%) and others (n=37, 17.1%). Procedures were performed laparoscopically in 65 (86.7%) and open in 11 (13.3%) patients. Morbidity was 8.9% and there was one 90-day non-procedure related mortality. Median follow-up was 11 months with half of patients completing at least 1-year follow-up. Local recurrence rate was 13/207(6.2%) per lesion and 9/74(12.2%) per patient. New liver and extrahepatic recurrences were detected in 33.8% and 35.1% of patients, respectively. LR rate was 9.4% for colorectal cancer and 13.5% for other tumor types, while no LR was identified in patients with hepatocellular or neuroendocrine cancer. Forty-six percent of LR demonstrated contiguous recurrence while 54% of LR were adjacent recurrence pattern. On univariate analysis, parameters affecting LR were tumor type, tumor size, and ablation margin less than 1 cm. Tumor size was the only independent parameter predicting LR after MTA, with > 3 cm tumors having a 8.4-fold increased risk of LR (p=0.001). Conclusions: To our knowledge, this is the first study to report LR after MTA of malignant liver tumors. The short-term local tumor control rate achieved in this study compares favorably with that reported for radiofrequency and other microwave ablation technologies in the literature.

Multivariable analysis (Cox proportional hazard model)

	Hazard Ratio	95% confidence interval	P value
Tumor size (>3cm vs. <3cm)	8.4	2.29 – 30.5	0.001
Ablation margin (<1.0 cm vs. > 1.0 cm)	3.5	0.92- 15.3	0.06
Blood vessel proximity (Near vs. Not near)	1.4	0.40- 4.61	0.62

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CA19-9 on Surveillance May be More Sensitive for Recurrence than Radiographic Evidence in Pancreas Cancer C. Rieser,* M.S. Zenati, A. Hamad, J. Steve, S. Kowalsky, N.S. Bahary, A.H. Zureikat, H.J. Zeh, M. Hogg. *Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

BACKGROUND: Decrease in CA19-9 has been shown to predict response to neoadjuvant therapy. Perioperative CA19-9 levels have also been shown to predict overall survival (OS). The objective of this study is to define the chronologic relationship between changes in CA19-9 and radiographic recurrence and assess the utility of CA19-9 to predict the risk of recurrence (RFS) during interval surveillance. METHODS: A retrospective review was performed on patients resected for pancreas cancer from 1/2010-5/2016. CA19-9 levels were classified at diagnosis, postoperative, and 6-month intervals. MDCT scans were obtained to assess for recurrence. CA19-9 levels were correlated with RFS and OS. RESULTS: A total of 572 patients were identified: 47 (8%) had insufficient levels for analysis and 97 (17%) never had CA19-9 elevation. On surveillance, 180 (31%) had elevated CA19-9 throughout follow up, 98 (17%) had normal CA19-9 throughout follow up, 124 (22%) had persistent normalization of CA19-9, and 26 (5%) normalized with eventual elevation of CA19-9. Median follow up was 46 months (95%CI 33-40). Median RFS was 12.2 months (95%CI 10.8-13.5) and median OS was 26.7 months (95%CI 23.2-29.4). Elevated postoperative CA19-9 had a good PPV of 73% (95%CI 69-77%) and a NPV of 46% (95%CI 40-51%) for eventual recurrence. Subsequent elevation of CA19-9 at 6-month intervals had poor PPV (average 35%) but high NPV (average 90%) for recurrence. MVA demonstrated that CA19-9 elevations at diagnosis, first postoperative, and 6-month intervals were independently predictive of RFS. However, in relation to patients never having CA19-9 elevation, Cox MVA shows persistently normalized CA19-9 has a HR=0.527 (p=0.005), while persistently elevated CA19-9 has a HR=3.112 (p<0.0001) and relapsing CA19-9 a HR=2.269 (p=0.002) for OS. CONCLUSIONS: These data suggests elevation in CA19-9 on surveillance may precede radiographic evidence of recurrence. Additionally, normal CA19-9 on surveillance, when elevated at diagnosis, is a good indicator of disease free survival. Furthermore, classification of CA19-9 pattern on surveillance may help counsel patients and demonstrate salvage chemotherapy efficacy.

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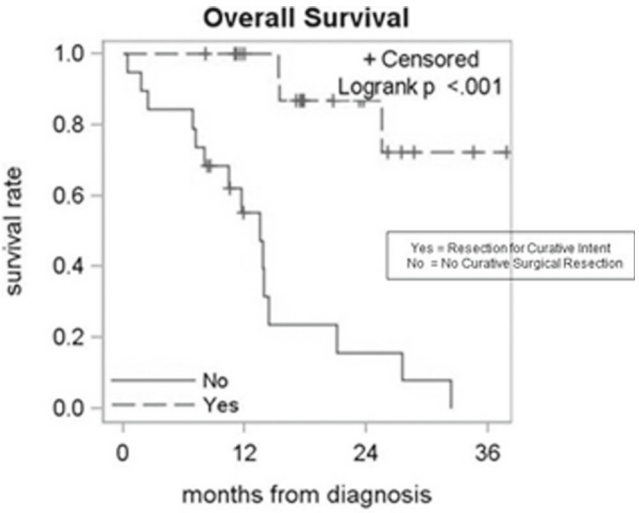
Neoadjuvant FOLFIRINOX and/or Gemcitabine/Abraxane for Advanced Pancreatic Adenocarcinoma K. Turner,* S. Narayanan, K. Attwood, R. Iyer, B. Kuvshinoff, S. Hochwald, M. Kukar. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Neoadjuvant chemotherapy is increasingly being utilized for locally advanced (LAPC)/borderline resectable pancreatic cancer (BRPC); however long term follow up data is sparse. At our institution, we use FOLFIRINOX as the regimen of choice. Gemcitabine (Gem) and Abraxane is utilized in patients not suited for FOLFIRINOX or if they have poor radiographic response and/or develop significant toxicities to FOLFIRINOX. The aim of this study was to report our institutional experience with neoadjuvant therapy for patients with advanced pancreatic cancer. A retrospective review was performed of all patients with BRPC or LAPC who received FOLFIRINOX, Gem/Abraxane, or both prior to surgical resection. FOLFIRINOX was typically given for 4 – 6 cycles while gem/Abraxane was given for 2 cycles. From January 2011 to December 2015, 39 patients were identified who met the study criteria. Eight patients received FOLFIRINOX alone (median age 62), 20 patients received FOLFIRINOX + Gem/Abraxane, and 11 received only Gem/Abraxane (median age 72). Eighteen patients (46%) completed the intended cycles of chemotherapy. Twenty two patients had a radiologic and/or biomarker response. Exploration was performed in 25 of 39 (64%) patients of whom 20 (51%) underwent curative resection. Of the 20 resected patients, there were no post-operative deaths. The median tumor size, median lymph node ratio, and R0 resection rates were 2.4 cm, 0, and 85% for the entire cohort. Median follow up was 20.7 months. The median overall survival for the resected cohort was not reached vs 13.5 months in the no resection group; two year overall survival for resection vs. no resection groups was 87% vs 16% (Figure 1). FOLFIRINOX and/or Gemcitabine/Abraxane as neoadjuvant therapy for LAPC/BRPC is fairly well tolerated, leads to appreciable rates of margin negative surgical resection, and a significant overall survival advantage.



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Air-Fluid Test: A Novel Technique in Preventing Post-Hepatectomy Biliary Leak G. Stoduto,[1] P. Sousa,[1]* R. Albagli,[1] R. Vasconcelos,[2] K. Steinbruck,[4] T. Auel,[4] R. Fernandes,[4] G. Bento,[4] L. Pacheco.[3] *1. Brazilian National Cancer Institute, Rio de Janeiro, Brazil; 2. Child's State Hospital, Rio de Janeiro, Brazil; 3. Quinta D'or Hospital, Rio de Janeiro, Brazil; 4. Bonsucesso Federal Hospital, Rio de Janeiro, Brazil.*

Background: Dissection of the liver parenchyma may cause various complications including blood loss, infection, liver failure and bile leakage. The latter remain a common cause of major morbidity after hepatic resection. Therefore, many methods have been introduced to prevent bile leakage after liver transection. Objectives: This study was performed to evaluate the value of air-fluid test in identifying intraoperative biliary leakage and avoiding postoperative complications. Material and Methods: One hundred and three patients submitted to hepatic resection were consecutive evaluated between February 2011 and February 2016. The surgeries were performed due malign and benign diseases and 82 (79,6%) were major hepatectomies while in 21 (20,4%) less than 4 segments were resected. Air-fluid test was performed in all procedures. Liver resection technique used was kellyclasia in 67 (65%) of the cases and ultrasonic aspirator in 36 (35%). Pringle maneuver was made in 7 (6,8%) patients with median time of 13 minutes and blood transfusion was needed in 6 (5,8%) patients. Results: The main endpoint of this case series was the ocurrency of biliary fistula and none of the 103 patients presented with it. The absence of biliary leakage was documented through normal bilirubin dosage in the abdominal drain. Postoperative morbidity occurred in 26 (25,2%) of surgeries using Clavien-Dindo classification and liver failure was diagnosed in 14 (13,6%) patients according to ISGLS classification and the latter had been presented as a single complication in 9 (8,7%) patients. Postoperative mortality was not observed. The median hospital length of stay was 6,3 days. Conclusions: The bile leakage test proved to be useful for preventing post-operative bile leakage with low cost-effectiveness. Air-fluid test is a simple procedure that can be realized in any type of hepatic surgery with no increase of the likelihood of other complications. We suggest that this technique should be performed in liver resections.

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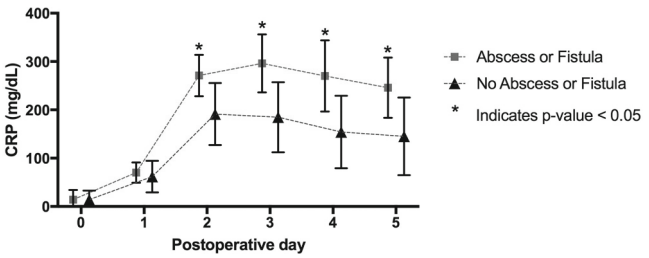
C-Reactive Protein Measurement Identifies Pancreatic Fistula or Abscess Formation Following Pancreaticoduodenectomy J.W. Kunstman,* J.M. Healy, T.D. Murtha, R.R. Salem. *Yale University School of Medicine, New Haven, CT.*

Background: Serious morbidity following pancreaticoduodectomy (PD) is often due to abscess or pancreatic fistula (PF) formation related to leakage of pancreatic secretions. C-reactive protein (CRP) has been advocated as a predictive marker for anastomotic leakage following gastrointestinal surgery. We hypothesized that CRP could be predictive for the development of PF or abscess following PD. Methods: All patients undergoing PD at an academic tertiary center by an experienced pancreatic surgeon from January, 2013 to June, 2016 were enrolled. Serum CRP was assessed daily until discharge, but did not alter treatment plans. The primary outcome measure was development of PF or intraabdominal abscess. Data was collected prospectively and analyzed retrospectively. Results: 161 patients underwent PD and 27 (16.7%) cases of PF or abscess were noted. CRP in patients with PF/abscess was significantly elevated after POD#1 (figure). Of patients with CRP≥250mg/dL each day from POD#2-4, 53.8% had PF/abscess while only 4.4% of those without PF/abscess were similarly elevated (HR=25.1, 95% C.I.=8.1-77.2). If CRP≤170 for any day between POD#2-4, the negative predictive value for PF/abscess formation was 96.9% (95% C.I.=91.3-99.2); this applied to 60.2% of patients who underwent surgery. CRP was superior to fever, leukocytosis, or platelet count in predicting PF/abscess. Among assessed patients requiring readmission (N = 20), CRP≥125 had a positive predictive value for PF/abscess of 92.3% (95% C.I.=66.7-99.6). Discussion: Early post-operative elevation in CRP is highly predictive for clinically-relevant PF or abscess development following PD. Conversely, low CRP levels are even more highly predictive of the absence of either PF or abscess. Measuring CRP could facilitate earlier diagnosis of PF or intraabdominal abscess following PD and enable timely discharge or intervention in appropriate patients. These interesting findings should be further validated in future clinical trials.



Serum CRP following pancreaticoduodenectomy in patients that develop pancreatic fistula or intraabdominal abscess during their postoperative course versus those that do not.

PF226

What is the Rate of Malignancy in Resected IPMN? An Analysis of Over 100 U.S. Institutions in a Single Year R. Elkhoury,* M. Banulescu, C. Kabir, P. Wasserman, V.K. Maker, A.V. Maker. *University of Illinois at Chicago and the Creticos Cancer Center at Advocate Illinois Masonic Medical Center, Chicago, IL.*

Introduction: A subset of IPMN will progress to invasive pancreatic adenocarcinoma, however, as we have previously reported, identifying invasive from non-invasive disease remains challenging. The decision to operate is based primarily on worrisome or high-risk radiographic international criteria. National IPMN databases have heretofore been unavailable, therefore, the rate of malignancy in resected IPMN in the USA remained unclear. Methods: More than 5000 pancreatectomies from >100 institutions were evaluated from the ACS National Surgical Quality Improvement Program 2014 database. Continuous and categorical variables were compared using Student's t-tests or chi-square. P <0.05 was used for entry criteria for the adjusted model. Results: Of 478 patients that underwent pancreatectomy for IPMN, 232 were males and 246 were females; aged 66 ± 11 years. Malignant disease was identified in 108, or 23% of resected lesions. There was no difference in sex, age, BMI, diabetes, pre-operative albumin, or type of resection performed (proximal vs. distal) in patients with invasive vs. non-invasive pathology. Patients with invasive IPMN did present significantly more often with higher liver function tests, >10% weight loss (15 vs. 6%), clinical jaundice (18 vs. 3%), and increased incidence of stent placement (18 vs. 5%). These patients were also more likely to undergo an open surgical approach (p=0.03). There were no differences in post-operative complications including fistula, delayed gastric emptying, reoperation, LOS, or readmission. Adjusted logistic regression identified an association of invasive disease with increased alkaline phosphatase levels (OR=1.01[1.00-1.02],p<0.01) and decreased likelihood of soft pancreatic gland texture (OR=0.19[0.05-0.68],p<0.01), but not with pancreatic duct size. Conclusions: Only 23% of IPMN resected at >100 U.S. institutions contained malignant histology, while the vast majority were non-invasive. Resections carried similar morbidity regardless of pathology. Improved biomarkers for high-risk lesions are necessary, and we add new information to supplement associations with malignancy for this disease.

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The Role of Routine Diagnostic Laparoscopy for Resectable Pancreatic Cancer J.S. Peng,* S. Chalikonda, J. Wey, R. Walsh, G. Morris-Stiff. *Cleveland Clinic Foundation, Cleveland, OH.*

Introduction Diagnostic laparoscopy (DL) at the time of resection for pancreatic cancer can detect occult metastatic disease and alter surgical management. We examined the yield of DL in the current era of high quality computed tomography (CT) and routine review by a multidisciplinary tumor board. Methods Patients undergoing exploration from January 2014 to December 2015 for resectable pancreatic ductal adenocarcinoma (PDAC) were included. Data regarding demographics, operative details, and pathology were collected. Patients with anatomically borderline lesions, or those who underwent neoadjuvant therapy as part of clinical trials were excluded. DL proceeded with placement of one port and visual examination using a 5 mm, 30 degree laparoscope without mobilization. A second 5 mm port was placed as needed to perform a biopsy if a lesion was visualized. Patients with asymptomatic metastatic disease did not undergo prophylactic surgical palliation. Results A total of 86 patients were included with 68 head/uncinate lesions and 18 body/tail lesions. Fifty patients (58%) had prior abdominal surgery. Seventy-six patients (88%) underwent DL while 10 patients (12%) did not due to need for palliation (3), prior surgery (4), or surgeon preference (3). Two DLs were unsuccessful. Of the 74 successful DLs, 23 patients (31%) underwent at least one biopsy. Eight (11%) showed positive findings (3 of 58 head/uncinate, 5 of 18 body/tail). Eleven resections (15%) were completed robotically or laparoscopically. Six-seven patients underwent laparotomy (57 after DL, 10 without DL) and five were found to have distant metastatic disease: two had DLs without biopsy, one had an unsuccessful DL, and two did not have DL. Two patients had a positive celiac axis node and six patients had locally unresectable disease without metastasis. Overall, 65 patients underwent successful resection, with 52 of 68 proximal (76%) and 13 of 18 distal lesions (72%). Pathologic outcomes are shown in Table 1. Conclusions DL is safe and successful even in patients with prior surgeries and should be performed for resectable PDAC. DL currently has a detection rate of 11% overall for occult metastasis and 28% in body and tail lesions.

	Overall	Head/Uncinate	Body/Tail
	86	68	18
DL	76	58	18
Positive	8 (11)	3 (5)	5 (28)
Negative	66 (87)	53 (92)	13 (72)
Failed	2 (3)	2 (3)	0
Exlap	67	60	7
Metastatic	7 (10)	7 (12)	0
Locally Advanced	6 (9)	6 (10)	0
Resected	65 (76)	52 (76)	13 (72)
Open	54	47	7
Minimally Invasive	11	5	6
Pathology			
PDAC	59		
Ampullary	3		
Cholangiocarcinoma	2		
Duodenal	1		
PDAC			
Size (cm)	3.0		
R0	37 (63)		
R1	22 (37)		
T1	2 (3)		
T2	11 (19)		
T3	46 (78)		
T4	0		
N0	11 (19)		
N1	48 (81)		

Expressed as number (percentage) or median.

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Chemokine Receptor 3 and Platelet Factor 4 Axis Promotes Survival and Metastasis of Pancreatic Cancer Cells B. Hall,* A. Cannon, B.A. Lueck, C. Are, S. Kumar, S.K. Batra. *General Surgery, University of Nebraska Medical Center, Omaha, NE.*

Introduction Metastasis is the principal cause of cancer-related mortality. Multiple studies have demonstrated the essential requirement of platelets in cancer cell dissemination. Platelets are the predominant source of platelet factor 4 (PF4), a ligand for CXCR3. Pancreatic cancer (PC) cells overexpress CXCR3; however, its role in PC survival and metastasis has not been investigated. Methods Immunohistochemistry and immunofluorescence analysis were performed to analyze the expression of CXCR3, CK19, and MUC4 in the autochthonous murine models and human PC tissues. The role of PF4 in oncogene (MUC4) regulation and endothelial adhesion was analyzed using qRT-PCR, western blots, luciferase reporter and adhesion assay. The impact of PF4 on anoikis was analyzed under low adhesion conditions. Results Human PC tissues showed significantly higher ductal expression of CXCR3 compared to normal pancreas with a composite score of 11.3 (n=22). Autochthonous murine models (K-rasG12D; TP53R172H; Pdx-1cre) of PC also demonstrated high CXCR3 expression in the ductal and migratory cells in 7 and 25 weeks old animals, as validated by co-expression of CXCR3 and CK19 by immunofluorescence analysis. qRT-PCR analysis of RNA isolated from PC cell lines demonstrated significantly higher expression of CXCR3A and B isoforms compared to immortalized non-cancerous ductal cells. However, 82% of PC patients (n=17) showed higher expression of CXCR3B preferentially binding to PF4. PF4 treatment increased the expression of MUC4, an oncogene implicated in the PC cell survival and metastasis. Luciferase reporter assay demonstrated that MUC4 distal promoter carries elements responsive to PF4 treatment. In addition, PF4 treatment in the PC cell line Capan 1 significantly increased its adhesion with the endothelial cells from 13% to 28% ($p<0.001$), which was abrogated by AMG487, an inhibitor of CXCR3. The presence of PF4 also increased the survival of Capan1 cells under low adhesion conditions. Conclusions PF4/CXCR3 axis facilitates the PC cell survival and metastasis by upregulating MUC4 expression and enhancing cancer-endothelial cell interactions.

PF229

Frailty: A Major Consideration for Short- and Long-term Outcomes in Resected Pancreatic Cancer I.T. Konstantinidis,* A. Lewis, F. Tozzi, P.H.G. Ituarte, S. Warner, Y. Woo, G. Singh, Y. Fong, L. Melstrom. *Surgical Oncology, City of Hope Medical Center, Duarte, CA.*

Introduction: Frailty has been associated with adverse postoperative outcomes. However, little is known about its correlation with survival in resected pancreatic cancer. This study examined the correlation of frailty with postoperative outcomes and survival after pancreatectomy for cancer. Methods: Data from National Surgical Quality Improvement Program (NSQIP) patients (n=7400) who underwent pancreatectomy between 2011 to 2013 were reviewed. A modified frailty index (mFI) validated for use in NSQIP was used to examine correlations between frailty and postoperative outcomes. In order to examine correlations between frailty and survival, California Cancer Registry (CCR) data for patients (n=4959) who underwent pancreatectomy for cancer between 2000 to 2012 was used to assess the association between the Charlson Comorbidity Index (CCI), as a surrogate for frailty, and overall survival. Results: The distribution of NSQIP patients according to the mFI was 0, 1, 2, 3, 4 in 2797 (37.8%), 3422 (46.2), 1074 (14.5), 104 (1.4) and 3 (0.04) respectively. The patients were divided to non frail (mFI=0), mildly frail (mFI=1-2), or severely frail (mFI3≥3). Overall, 8.7% of patients experienced a grade 4 Clavien complication and 3.1% experienced postoperative mortality. Worsening frailty correlated with an increase in grade 4 Clavien complications (non-frail: 6.3% vs. mildly frail: 9.7% vs. severely frail: 26.2%; $p<0.001$) and mortality (1.9% vs. 3.8% vs. 4.7% respectively; $p<0.001$). The majority of CCR patients had similarly few comorbidities: CCI: 0, 1, ≥2 in 3869 (77.8%), 861 (17.31%) and 243 (4.89%) respectively. Median survival decreased as CCI increased (for CCI 0, 1 and ≥2 was 23 vs. 19 vs. 15 months respectively; $p<0.001$; Figure 1). Conclusions: Frailty is a powerful correlate of postoperative outcome and survival for resected pancreatic cancer patients and is an important consideration in planning for surgical intervention.

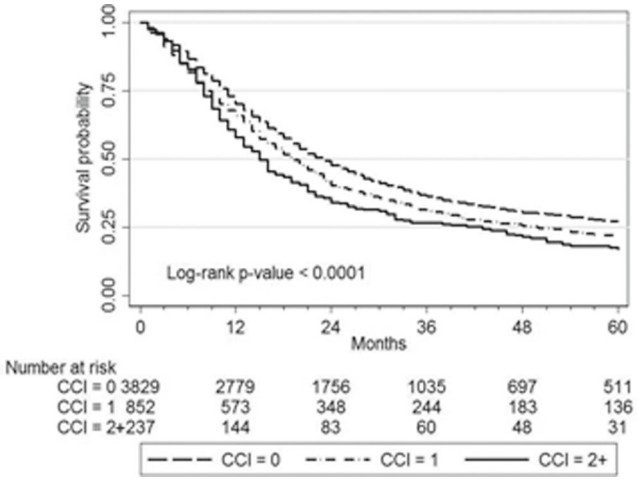

Figure 1. Relationship between patient survival and frailty (estimated by CCI grades)

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Affordable Care Organizations: Is Laparoscopic Liver Resection for Adenoma Cost-effective? D.T. Pointer,[1]* A. Volk,[1] A. Hauch,[1] L. Boehm,[5] M. Darden,[2] G. Parker,[3] J. Sulzer,[4] J.F. Buell.[1] *1. Tulane University, Dept. of Surgery, New Orleans, LA; 2. Tulane University, Dept. of Economics, New Orleans, LA; 3. Dartmouth, School of Business, Hanover, NH; 4. Louisiana State University, Dept. of Surgery, New Orleans, LA; 5. Tulane University, School of Medicine, New Orleans, LA.*

The introduction of laparoscopic surgery has revolutionized general surgery altering the indications for cholecystectomy, adrenalectomy and even splenectomy. The current management of hepatic adenoma remains controversial. Methods: Utilizing our surgical experience of hepatic adenomas (n=43), we evaluated the cost impact of expectant observation compared to laparoscopic resection. To evaluate the impact of clinical decisions on an ACO model, we estimated lifetime cost of observation versus elective laparoscopic intervention in a 50 patient cohort. Using the published hemorrhage and rupture rate of 27.2% and a malignant degeneration rate of 8.2%, we calculated cost data for analysis. Results: Outcomes for the laparoscopic (n=38) versus open (n=5) group were used to establish the operative times, transfusion, and length of stay data to calculate the cost of management. Cost data demonstrated the efficacy of laparoscopic resection ($846,700) over open resection ($1,607,500). The sum cost of yearly observation with contrast MRI and open resection for acute hemorrhage, rupture or malignant transformation comes to $1,658,700. Conclusions: Elective laparoscopic resection for isolated or limited hepatic adenomas appears to be safe and cost effective. With emerging data that tumors as small as three centimeters may contain a hepatocellular cancer, the traditional indication for resection at 5 centimeters may be too conservative.

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Radioembolization for Hepatocellular Carcinoma: A Nationwide 10-Year Experience of 1,222 Cases S. Tohme,* A. Chidi, A. Tsung. *University of Pittsburgh, Pittsburgh, PA.*

Background: Radioembolization (RE) has emerged over the past decade as an effective and safe modality for treatment of patients with hepatocellular carcinoma (HCC). We aimed to examine the United States nationwide experience with RE for HCC and validate the efficacy of this treatment. Methods: We conducted a retrospective cohort study from the National Cancer Database. We included all adult patients diagnosed with HCC between 2003 and 2012. Our primary outcome of interest was mortality after treatment. Univariate and multivariate analyses for factors predicting mortality were performed. Overall survival by different variables of interest were estimated by the Kaplan-Meier method and Cox regression models. Results: We identified 137,731 patients who were diagnosed with HCC. A total of 1,222 (0.9%) received liver-directed RE and the number of patients receiving RE has been steadily increasing in the past decade. Of those who received RE, 77.7% were male, 77.1% were Caucasian, and the median age was 63 years. Mortality data were available for 926 (76%) patients. Median overall survival for all patients who received radioembolization was 13.3 months (95% CI 12.0-14.6 months). In unadjusted analysis, patients who died were more likely to be older than 75 years, lower educational levels, larger tumor sizes at diagnosis, have metastatic disease at time of treatment and did not receive or were not recommended to undergo surgery. There was no difference in mortality among patients who received their treatment at an academic or a community hospital. In our adjusted analysis, there was no difference in mortality across gender or across the different age categories. Patients were more than 3-fold more likely to die if they had tumors larger than 5cm or had metastatic disease at the time of treatment. Conclusions: We identified several prognostic factors for patients with HCC receiving RE with large tumors and extrahepatic disease benefiting the least. This is imperative to know in order to optimize the selection of patients who will benefit most in an effort to improve outcomes and decrease patients' unnecessary toxicity, morbidity and cost.

PF232

Adjuvant Chemoradiation is Associated with Improved Survival for Node-positive Pancreatic Adenocarcinoma M. Raoof,* L. Melstrom, S. Warner, Y. Woo, G. Singh, Y. Chen, Y. Fong. *Surgery, City of Hope National Medical Center, Duarte, CA.*

Background: American Society of Clinical Oncology guidelines recommend adjuvant chemoradiation (ACR) for margin-positive(R1) and/or node-positive(N+) pancreatic cancers. However, randomized trials and meta-analyses have have not shown superiority of ACR over AC. Methods: National Cancer Database (NCDB) was used to analyze patients with N+ and/or R1 pancreatic adenocarcinoma who underwent ACR or AC over a ten-year period (2004-2014). Patients who received neoadjuvant radiation, no adjuvant treatment or adjuvant radiation alone were excluded. Propensity score nearest-neighbor 1:1 matching (PSM) was performed between ACR and AC groups based on age, sex, race, insurance, comorbidities, T-stage, nodal status, margin status, grade, and neoadjuvant chemotherapy. Primary outcome was overall survival (OS). Results: A total of 9,732 patients were eligible. After PSM two well-balanced groups of 4000 patients each were analyzed. ACR resulted in superior OS in patients with N+ and/or R1 disease as compared to AC alone (HR: 0.83, 95% CI 0.78-0.87; Median OS 22 vs. 19 months, p<0.001). Subset analyses demonstrated overall survival benefit of ACR compared to AC in N+, margin-negative patients (HR: 0.82, 95% CI 0.77-0.88; Median OS 24 vs. 20 months, p<0.001), as well as N+, R1 patients (HR: 0.77, 95% CI 0.68-0.87; Median OS 17 vs. 15 months, p<0.001); but no benefit in node-negative, R1 patients (HR: 1.12, 95% CI 0.84-1.48; Median OS 18 vs. 22 months, p=0.43) Conclusion: This is the largest study to date that shows superiority of ACR over AC in N+ patients irrespective of margin status. The study failed to show a survival benefit in R1, node-negative patients.

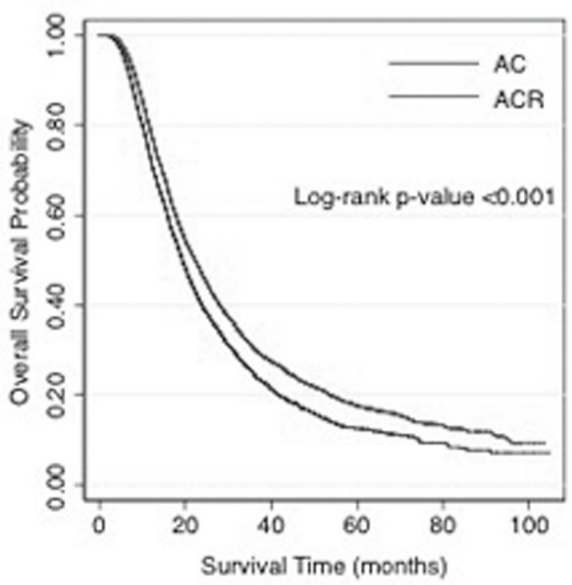

Figure 1. Kaplan-Meier Overall Survival Estimates of N+ and/or R1 patients undergoing ACR vs. AC in a propensity-matched, population-based cohort.

PF233

Intra-Arterial Therapy for Multifocal Intrahepatic Cholangiocarcinoma Results in Equivalent Survival Compared with Surgical Resection G. Wright,* S.J. Perkins, H.L. Jones, A.H. Zureikat, J. Marsh, M.P. Holtzman, H.J. Zeh, D. Bartlett, J.F. Pingpank. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Multifocal intrahepatic cholangiocarcinoma (mICC) has been traditionally treated with surgical resection when amenable. Intra-arterial therapy (IAT) for mICC has not been directly compared with surgical resection. Methods: A retrospective review of mICC treated from 2004-2015 was performed. Patients with solitary tumors, distant metastases, or treatment with systemic chemotherapy alone were excluded. Patients were divided into two groups: surgical resection vs. IAT. IAT included transarterial chemoembolization (TACE), transarterial radioembolization (TARE), and hepatic arterial infusion (HAI) pump therapy. Patients treated with surgery+IAT were analyzed in the surgical resection group. A Cox proportional hazards model included age, co-morbidities, tumor size and number, bilobar disease, grade, vascular invasion, nodal disease, and treatment strategy. Results: 118 patients with mICC are included; 60 surgical resection and 58 IAT (TACE=42, HAI pump=13, TARE=3). There was a higher incidence of bilobar disease among IAT (84.9% vs. 51.7%, p<0.001). The incidence of vascular invasion was higher in the surgical resection group (70.0% vs. 46.6%, p=0.015). There was a trend toward increased use of systemic chemotherapy in the surgical resection group (73.3% vs. 55.2%, p=0.054). Among those treated with surgical resection, the R0 resection rate, 90-day morbidity, and mortality were 54.2%, 21.7%, and 8.3%, respectively. Median overall survival for surgical resection was 20m vs 16m for IAT (p=0.078). Treatment strategy was not an independent predictor of survival on multivariate analysis (p=0.257 – Fig. 1). When removing the 8 patients treated with surgery+IAT (4 neoadjuvant; 4 salvage therapy) from the surgical resection group and analyzing in 3 arms, the median survival is 39, 17, and 16m for surgery+IAT, surgical resection alone, and IAT alone, respectively (p=0.023). Median survival for patients with R1 resection was 14m. Conclusion: Despite selection bias for use of surgical resection compared with IAT, there was no difference in overall survival between these two therapeutic modalities in the treatment of mICC.

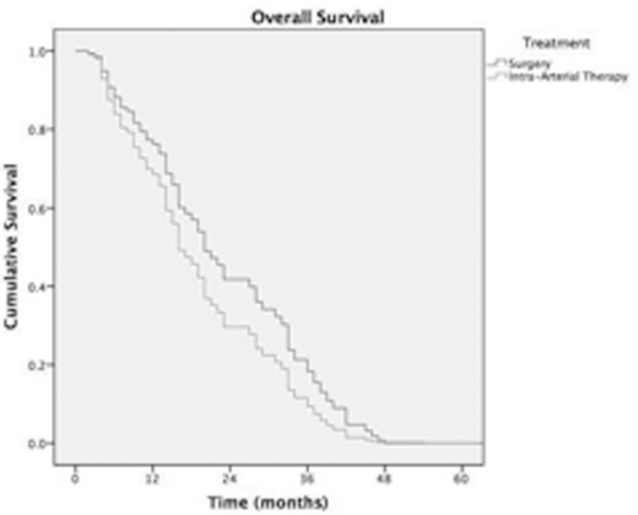

Figure 1. Overall survival in the treatment of multifocal intrahepatic cholangiocarcinoma.

PF234

Prognostic Significance of Chromogranin A in Small Pancreatic Neuroendocrine Tumors M. Raoof,* Z. Jutric, L. Melstrom, S. Warner, Y. Woo, Y. Fong, G. Singh. *Surgery, City of Hope National Medical Center, Duarte, CA.*

Background: The incidence of non-functional pancreatic neuroendocrine tumors (PNETs) ≤ 2 cm is rising. The biologic behavior of these tumors is variable and therefore their management remains controversial. We hypothesized that Chromogranin A (CgA) levels are prognostic in these patients and may help guide management. Methods: Patients with PNETs measuring ≤ 2 cm, without distant metastases were identified from the National Cancer Database (NCDB) over a ten-year period (2004-2014). Patients were categorized as CgA high (≥36.4 ng/ml) or CgA low (<36.4 ng/ml), and those lacking data on CgA levels were excluded from the study. Univariate and multivariate analyses were performed using Cox proportional Hazards Model. Results: Of the 445 eligible patients, 149 (33.5%) were CgA Low and 296 (66.5%) were CgA High. Median CgA level was 71 (Inter-quartile range, IQR 24-294) ng/ml. On multivariate analysis, CgA levels independently predicted overall survival after controlling for tumor size, grade, clinical nodal status and academic status of the facility (p=0.001). At a median follow up of 26.5 months there were no deaths in the CgA Low group whereas 8% of the patients in CgA High group had died (p=0.0068). Only CgA High patients benefited from surgical resection (HR 0.31, 95% CI 0.11-0.86, p-value=0.025) Conclusion: Serum CgA levels can be incorporated in surgical decision making for patients with small PNETs. Patients with a high CgA should be strongly considered for resection.

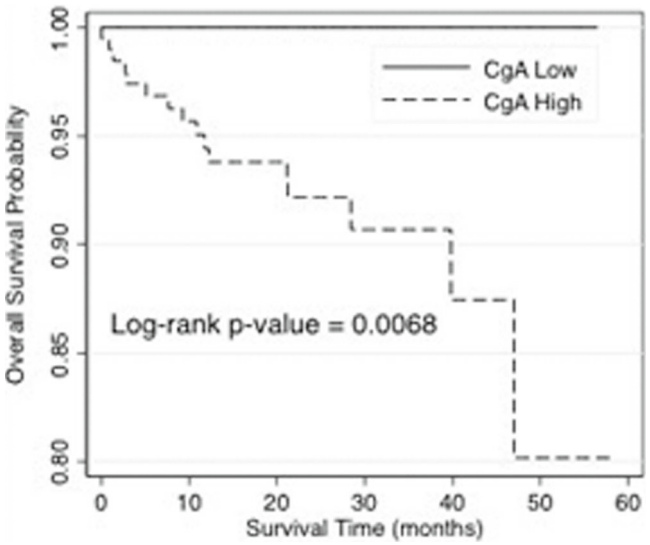

Figure 1. Kaplan-Meier Overall Survival Estimates of patients with a low vs. high Chromogranin A level (CgA) in a population-based cohort.

PF235

The Prognostic Value of Hepatic Arterial and Portal Venous Involvement in Patients with Perihilar Cholangiocarcinoma
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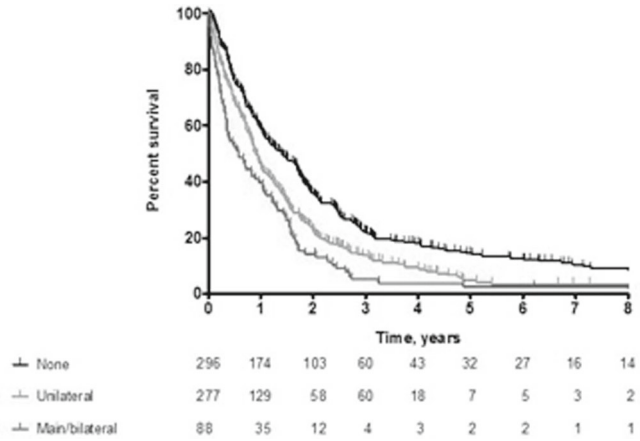
1. Dept of Surgery, Erasmus MC University Medical Center, Rotterdam, Netherlands; 2. Dept of Surgery, Academic Medical Center, Amsterdam, Netherlands; 3. Dept of Medical Oncology, Academic Medical Center, Amsterdam, Netherlands; 4. Dept of Radiology, Academic Medical Center, Amsterdam, Netherlands; 5. Dept of Radiology, Erasmus MC University Medical Center, Rotterdam, Netherlands.

INTRODUCTION: Vascular involvement is part of staging systems and prognostic models for patients with perihilar cholangiocarcinoma (PHC). For instance, the AJCC and DeOliveira/Clavien classification require detailed evaluation of both unilateral and main hepatic artery (HA) and PV involvement. We investigated the prognostic value of vascular involvement on imaging in patients with PHC. METHODS: All patients with suspected PHC in two tertiary referral centers between 2002 and 2014 were identified. Baseline patient and tumor characteristics were collected from medical records. Vascular involvement was defined as apparent tumor contact of ≥180 degrees to the PV or HA. The Kaplan Meier method with log-rank test was used to compare overall survival (OS) between groups. Cox regression analysis was used for multivariable analysis. RESULTS: In total, 674 patients were included with a median OS (95%CI) of 12.3 months (10.7-13.9). Patients with unilateral PV involvement (36.2%) had a median OS of 13.4 (10.9-15.8 months), similar to 14.2 (11.3-17.0) in patients without PV involvement (p=0.12). Patients with main/bilateral PV involvement (19.8%) had a median OS of 8.1 (5.4-10.9) months, inferior to patients with unilateral or no PV involvement (p<0.001). Median OS for patients with unilateral HA involvement (41.9%) was 10.9 (9.5-12.2) months compared with 16.9 (13.1-20.6) months in patients without HA involvement (p<0.001). Patients with main/bilateral HA involvement (13.3%) had a median OS of 6.9 (3.3-10.5) months, inferior to 10.9 (9.5-12.2) months for patients with unilateral or no HA involvement (p<0.001, figure). Independent prognostic factors included main/bilateral HA involvement (HR 1.83, 95%CI 1.37-2.47) as well as unilateral HA involvement (HR 1.34, 95%CI 1.11-1.61). PV involvement was not an independent prognostic factor. Other independent prognostic factors were suspected distant metastases, ECOG performance status 3-4, age ≥75 years and tumor size >3 cm. CONCLUSION: This study demonstrated that both unilateral and main HA involvement are independent poor prognostic factor for OS in patients presenting with PHC, whereas PV involvement is not.



PF236

Neoadjuvant Versus Adjuvant Chemotherapy for Resected Pancreatic Adenocarcinoma Patients: A National Cancer Data Base Comparison
Z. Kozick,* A. Hashmi, M. Fluck, M. Hunsinger, T. Arora, J. Wild, M. Shabahang, J. Blansfield. *Surgical Oncology, Geisinger Medical Center, Danville, PA.*

Introduction There is controversy with the benefits of neoadjuvant versus adjuvant chemotherapy for pancreatic cancer (PAC) patients. Neoadjuvant therapy has been touted to improve survival. This study's objective is to investigate predictors and potential benefits of neoadjuvant chemotherapy in resectable PAC patients. Methods The National Cancer Data Base was used to retrospectively analyze stage I and II surgically resected PAC patients receiving adjuvant or neoadjuvant chemotherapy from 2004-2012. Results A total of 12,983 patients fit eligibility criteria. Twelve percent of patients received neoadjuvant chemotherapy. A significant increase in neoadjuvant therapy was observed over time (p<0.0001) with 5% getting neoadjuvant therapy in 2004 versus 17% in 2012. Multivariate analysis showed that patients were more likely to receive neoadjuvant therapy if they were treated at an academic facility. Only 4% of patients from community cancer programs were treated neoadjuvantly versus 15% at academic centers. Private insurance was associated with higher odds of neoadjuvant chemotherapy (p<0.0001). Nine percent of the uninsured were treated with neoadjuvant therapy versus 13% with private insurance. Surgical outcomes were improved in neoadjuvant patients compared to adjuvant. Univariate analysis showed 84% of neoadjuvant patients had negative margins versus 76% of adjuvant. The number of lymph nodes examined were comparable in the two groups with a median of 14. However, more patients had negative nodes in the neoadjuvant group (56%) versus the adjuvant group (31%). These differences remained on multivariate analysis with higher rates of negative surgical margins (OR: 1.273, 95% CI: 1.099-1.474) and negative lymph nodes (OR: 2.852, 95% CI: 2.547-3.194) in patients receiving neoadjuvant compared to adjuvant chemotherapy. Conclusion Surgical outcomes are improved after neoadjuvant chemotherapy compared to adjuvant chemotherapy with more patients achieving negative margins and negative lymph nodes. Prospective studies will be needed to compare these two treatment modalities in a head to head comparison.

PF237

Neoadjuvant Therapy Should be Considered in all Resectable Pancreatic Cancer Patients
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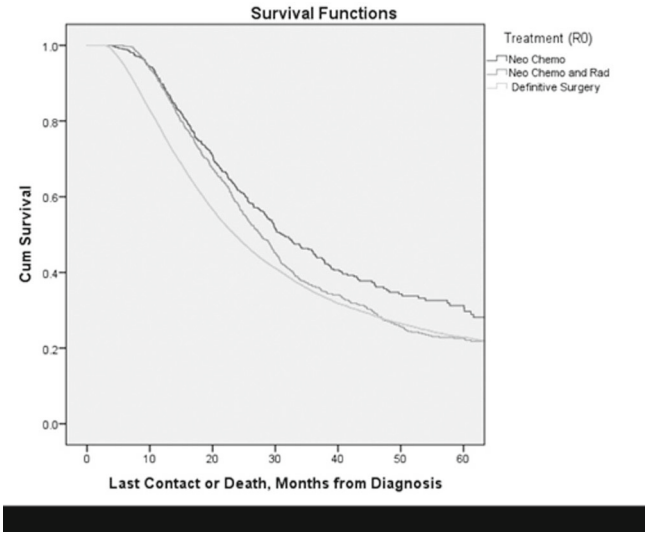
Purpose: Neoadjuvant therapy (NT) for resectable pancreatic cancer continues to be debated. There is little data to demonstrate survival benefit over patients who were treated with up front surgery (UFS) vs NT. We sought to examine the impact of neoadjuvant chemotherapy (NCT), neoadjuvant chemoradiation (NCRT), and UFS on survival in pancreatic cancer patients. Methods: Utilizing the National Cancer Database we identified patients who underwent pancreatic resection for adenocarcinoma. Baseline comparisons of patient characteristics were made for continuous and categorical variables using

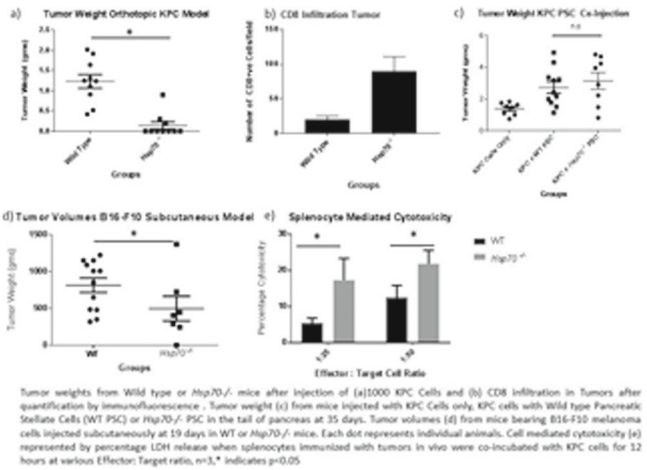
Mann-Whitney U, Kruskal Wallis and Pearson's Chi-square test as appropriate. Survival analyses were performed using the Kaplan-Meier method. Multivariable cox proportional hazard models (MVA) were developed to identify predictors of survival. All statistical tests were two-sided and α <0.05 was considered significant. Results: We identified 31,506 patients who underwent pancreatic resection: UFS=28,605, NCRT=1642, and NCT=1259 with a median age of 67 (18-90) years. The median tumor diameter was 3 cm (0.1-9.8) and nodes harvested were n=13 UFS, n=12 NCRT, and n=16 NCT, p<0.001. R0 resections were performed in 20,902(75.9%) UFS, 1252 (82.9%) NCRT, and 940 (79.6%) NCT, p<0.001. The pathologic complete response rates were n=39 (3.3%) NCRT and n=17 (1.8%), p=0.04. The median survival for patients who underwent R0 resection was 23.5 months UFS, 27.6 months NCRT, and 31.1 months NCT, p<0.001. Adjuvant therapy (chemotherapy (CT) or CRT) in the UFS did demonstrate a survival benefit 22.2 months vs 19.4 months, p<0.001, however this did not benefit NCT or NCRT, p=0.8 and p=0.8 respectively. Additionally survival in the UFS with adjuvant therapy either CT or CRT was still decreased compared to either NCT or NCRT, p<0.001 and p=0.001 respectively. MVA demonstrated that age, T-stage, lymph nodes positive, R0 resection, grade, NCT and NCRT were predictors of survival. Conclusions: NT improves survival in resectable pancreatic cancer patients. NCT and NCRT demonstrated survival benefit compared to UFS even with adjuvant therapy. Patients with resectable pancreatic cancer should be considered for NT.



PF239

Depletion of Heat Shock Protein 70 in Tumor Microenvironment Affects Cancer Growth in Pancreatic Cancer B. Giri,* B. Garg, V. Sethi, S. Modi, S. Banerjee, A. Saluja, V. Dudeja. *Surgery, University of Miami, Miami, FL.*

Introduction Heat shock protein 70 is known to be overexpressed in cancer cells and its inhibition results in apoptosis and cell death. However, the role of HSP70 in tumor microenvironment (TME) in supporting tumor growth is not known. Methods Cancer cells from Pdx1-Cre;K-Ras$^{+/LSLG12D}$;p53$^{R172H/+}$ (KPC) mice were injected orthotopically into C57BL/6(WT) or mice with deletion in Hspa1a and Hspa1b (Hsp70$^{-/-}$) thereby modeling an environment with intact HSP70 in the cancer cells but absent HSP70 in TME. Tumor immune infiltration was examined by immunofluorescence. Similarly, B16-F10 melanoma cells were implanted in WT or Hsp70$^{-/-}$mice. Pancreatic Stellate cells(PSCs) from Hsp70$^{-/-}$ or WT mice were co-injected with KPC cells in WT(ratio=9:1) mice to evaluate the effect of HSP70 in tumor stroma only. Cell mediated cytotoxicity was assessed after splenocytes obtained from mice immunized with KPC tumors were subsequently co-incubated with cancer cells. Results The growth of KPC pancreatic cancer cells as well as B16-F10 melanoma cells was markedly reduced when injected in Hsp70$^{-/-}$ mice compared to growth in WT mice, suggesting that absence of HSP70 in TME decreases tumor growth. Lack of HSP70 in tumor stroma, simulated by co-injection of HSP70$^{-/-}$ PSC with KPC pancreatic cancer cells, did not reduce tumor growth when compared to co-injection with WTPSC, hinting that the effect may not be stroma dependent. Interestingly, tumors forming in HSP70$^{-/-}$ mice had greater CD8 infiltration. Furthermore, HSP70$^{-/-}$ splenocytes were able to induce markedly increased cell mediated cytotoxicity when compared to WT splenocytes. Conclusion HSP70 depletion in the TME leads to tumor growth inhibition which is possibly immune mediated. Strategies to modulate HSP70 in immune cells could emerge as novel therapy against cancer, either alone or in combination with immune check point blockade.



Tumor weights from Wild type or *Hsp70-/-* mice after injection of (a)1000 KPC Cells and (b) CD8 infiltration in Tumors after quantification by immunofluorescence . Tumor weight (c) from mice injected with KPC Cells only, KPC cells with Wild type Pancreatic Stellate Cells (WT PSC) or *Hsp70-/-* PSC in the tail of pancreas at 35 days. Tumor volumes (d) from mice bearing B16-F10 melanoma cells injected subcutaneously at 19 days in WT or *Hsp70-/-* mice. Each dot represents individual animals. Cell mediated cytotoxicity (e) represented by percentage LDH release when splenocytes immunized with tumors in vivo were co-incubated with KPC cells for 12 hours at various Effector: Target ratio, n=3,* indicates p<0.05

PF241

Length of Stay and Discharge to Skilled Nursing Facility are the Strongest Modifiable Risk Factors for Readmission Following Pancreaticoduodenectomy K.A. Mirkin,* N. Gusani, C. Hollenbeak, A.B. Cooper. *Department of Surgery, Penn State, Hershey, PA.*

Background: Pancreaticoduodenectomy is a technically difficult and notoriously morbid procedure. As payers begin to link reimbursement to readmission rates, there is growing interest in understanding and preventing readmissions. The objective of this study was to evaluate factors contributing to 30-day readmission rates for patients undergoing pancreaticoduodenectomy. Methods: Data from the Pennsylvania Health Care Cost Containment Council (PHC4) were reviewed for patients undergoing pancreaticoduodenectomy from 2011-2014 (n=1,552). Outcomes included 30-day readmission and length of stay (LOS). Univariate comparisons were performed between characteristics of those readmitted (n=404) and not readmitted (n=1,148). Readmission and LOS were modeled using multivariate logistic regression and linear regression, respectively. Results: Of the 404 (26.0%) patients who were readmitted, the most common causes for readmission were post-operative infection (26.2%), anastomotic complications (8.0%), and dehydration (5.7%). Patients who were readmitted were more likely to be discharged to a skilled nursing facility (SNF) and were associated with a longer LOS of index admission (p<0.001, both). In multivariate analysis, black race (HR 1.96, p=0.001), discharge to a SNF (HR 1.73, p=0.006) and increased LOS (HR 1.36, p=0.019), were associated with increased odds of readmission. After controlling for patient, admission, and facility characteristics, black race, urgent and emergent admissions, and discharge to a SNF or home with home healthcare, were predictive of a longer LOS (p<0.05). High surgeon volume, and high hospital volume were associated with a shorter LOS (p<0.05). Conclusion: The most common causes of readmission following pancreaticoduodenectomy in Pennsylvania from 2011-2014 were post-operative infection, anastomotic complications, and dehydration. Patients with a longer initial hospital stay and those discharged to a SNF were associated with higher odds of readmission. Understanding the interplay of these factors may result in opportunities to improve outcomes in patients undergoing this complex surgery.

PF242

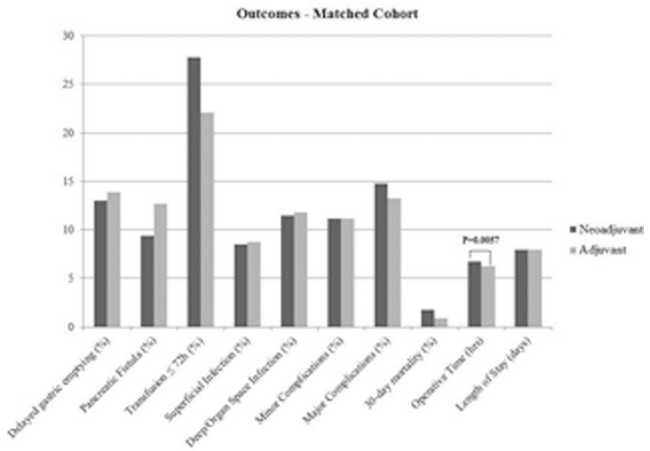
Integration of Public Genomics Datasets to Inform Predictive Molecular Pathology: A Case Study C.M. Court,[1]* S. Shonan,[1] P. Winograd,[1] D.W. Dawson,[3] T.G. Graeber,[2] J.S. Tomlinson.[1]
1. UCLA, Department of Surgery, Los Angeles, CA; 2. UCLA, Department of Molecular and Medical Pharmacology, Los Angeles, CA; 3. UCLA, Department of Pathology, Los Angeles, CA.

Introduction: Clinicopathologic variables such as lymph node status and metastatic disease have consistently proven to be the most predictive markers of patient outcomes and form the backbone of every staging system for pancreatic cancer. The completion of large-scale studies of the genetics of cancer such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Concortium (ICGC) has provided public access to datasets with the scale necessary to analyze the relationships between these clinicopathologic parameters and the underlying genetic changes that characterize cancer. As a case study in how to utilize these datasets to inform clinical decisions, we studied the relationship between somatic mutations and clinicopathologic variables as well as outcomes data. Methods: Data was obtained for 580 patients from both the TCGA (n=187 cases) and ICGC (n=395) consortiums. Clinical and somatic mutation data was standardized between the datasets, and patient's without adequate clinical data, tumor type other than adenocarcinoma or without somatic mutation data were removed (n=53). Data was reanalyzed using the R/Bioconductor package maftools. We then correlated the somatic mutation data with the standard tumor characteristics using Fisher exact tests. Results: After filtering out genes without annotation in the COSMIC database, a total of 11 genes were found to be more frequently mutated in patients with positive lymph nodes versus those with negative lymph nodes. Similarly, 10 genes were found to be more frequently mutated in patients with metastatic disease versus those with local or regional disease only. Combining these genes into a gene panel, resulted in a somatic mutation panel that was predictive of both lymph node positivity ($p < 0.0001$) and metastatic disease ($p < 0.001$). Conclusions: The combination and reanalysis of public genomic datasets has the potential to assist in predicting both clinicopathologic variables and, in turn, patient outcomes. We present a case study in how such data can be used to inform predictive molecular pathology and assist with clinical decision-making for patients diagnosed with pancreatic cancer.

PF243

Neoadjuvant Therapy Versus Upfront Surgery for Pancreatic Adenocarcinoma: A Propensity Score Matched Analysis of Short-term Outcomes G.G. Kasumova,* S.W.L. De Geus, O. Tabatabaie, A.B. Fadayomi, S. Ng, J.F. Tseng. *Beth Israel Deaconess Medical Center, Boston, MA.*

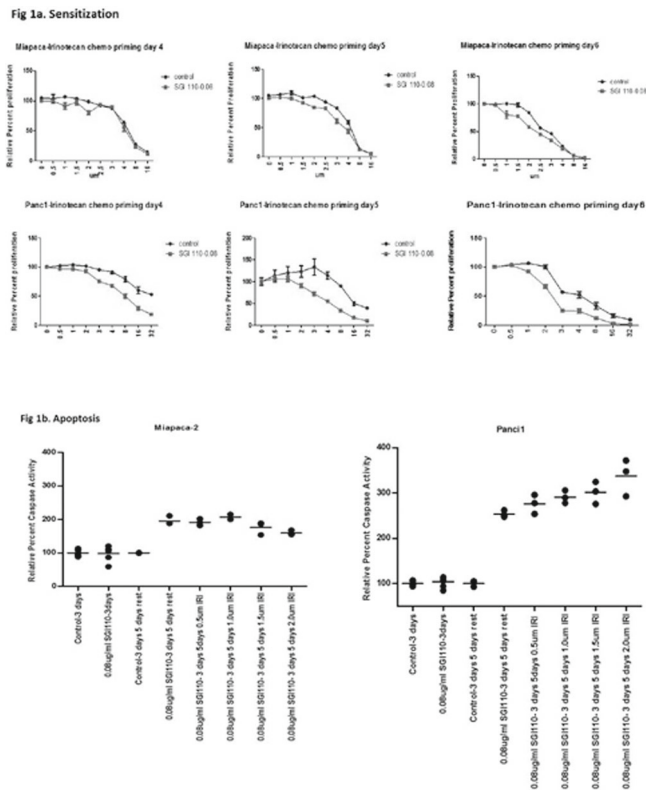
Background: Neoadjuvant therapy is increasingly utilized and has demonstrated a survival advantage in patients with borderline and locally advanced pancreatic cancer. However, many have feared that preoperative chemotherapy and radiation result in a more challenging operative field and subsequent increased morbidity. Methods: The ACS-NSQIP targeted pancreas database was queried for patients with adenocarcinoma who underwent elective pancreaticoduodenectomy in 2014. Propensity score matching was used to account for potential selection bias in pre-operative and intra-operative characteristics. Sensitivity analysis was performed to evaluate the impact of neoadjuvant radiation. Outcomes were compared by chi-square or Wilcoxon rank sum tests. Results: 1313 patients were identified, of whom 338 (25.7%) received neoadjuvant therapy. Patients who received neoadjuvant therapy vs upfront surgery were more likely to be: female (53.6% vs 47.2%; p=0.044), <65 years of age (53.0% vs 39.2%; p<0.0001), have BMI <25.0 (43.5% vs 36.6%; p=0.034), and require vascular resection (37.6% vs 19.6%; p<0.0001). Post-operatively, patients receiving neoadjuvant therapy were less likely to develop pancreatic fistulae (9.2% vs 14.0%; p=0.0231), more likely to require transfusion (27.8% vs 22.4%; p=0.0424), and have a longer operative time (median: 405 vs 371 mins; p<0.0001). The matched cohort consisted of 662 patients. After matching, there were no differences in baseline characteristics, including sex, age, race, ASA class, BMI, approach (open vs MIS), pre-operative biliary stenting, and vascular resection. After matching, the only significant difference in outcomes between the two groups was longer operative time (median 405 vs 377; p=0.0057) (see Figure). These results were robust on sensitivity analysis for the use of radiation. Conclusions: Neoadjuvant therapy is safe and, despite prolonged operative time, does not affect 30-day post-operative outcomes. Concern for increased morbidity should no longer preclude treatment with neoadjuvant chemotherapy and/or radiation in borderline, locally advanced, and resectable pancreatic tumors.



PF244

Guadecitabine (SGI110) Sensitizes Pancreatic Cell Lines to Irinotecan Treatment Y. Hu,* M. Thakar, M. Thakar, S. Saggi, N. Ahuja. *Surgical Oncology, Johns Hopkins University, Baltimore, MD.*

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer-related deaths in the USA. Although surgery is the only curative treatment, most patients present with advanced, inoperable disease at diagnosis. Response to chemotherapy remains meager at best. Irinotecan, a topoisomerase inhibitor, is used in combination regimens to treat locally advanced disease. In this study we aimed to sensitize pancreatic cell lines to irinotecan through pre-treatment with guadecitabine, a next generation hypomethylating agent. Methods: A modified MTT assay was used as a measure of cell viability following irinotecan treatment in Miapaca-2 and Panc1 cell lines pretreated with SGI 110. Apoptosis was quantified by proxy of Caspase-3 and -7 activity, following five days of irinotecan therapy with and without pretreatment with guadecitabine. Results: We demonstrated that pretreatment with guadecitabine sensitizes pancreatic cell lines to irinotecan treatment. This effect was more pronounced in Panc-1 than in Miapaca-2 cell lines (Fig 1a). Pretreatment of Panc-1 cells with 2 and 4 μM of guadecitabine resulted in a 50% decrease in mean cell viabilities following 5-day irinotecan therapy. In addition, the decrease in cell viability was paralleled with an increase in apoptotic cell death (Fig 1b). In addition, we were able to demonstrate that guadecitabine shows a delayed cell toxic effect. Treatment with 0.08ug/ml guadecitabine lead to higher caspase 3/7 activity following a 5-day hiatus (Fig. 1b), as compared to the uninterrupted treatment group. Furthermore, the addition of irinotecan lead to increased caspase 3/7 activity in Panc1, however it did not in Miapaca-2. Conclusion: Pretreatment with guadecitabine, a DNA-hypomethylating agent sensitizes pancreatic cancer cells to chemotherapeutic agents, such as Irinotecan. We believe that chemo-priming strategies represent a promising method for augmenting chemotherapy response rates in a clinical setting. Further studies are warranted to understand the mechanism of action responsible for this effect. *Funding supported by ASTEX Pharmaceuticals



PF245

Dynamics of the Immune Response in Cholangiocarcinoma

N.M. Figueroa,[1]* B.A. Belt,[1] A. Patel,[1] B. Han,[1] J. He,[1] S. Gerber,[1] M. Hill,[2] W. Alexander,[2] M. O'dell,[2] A. Hezel,[2] D.C. Linehan.[1]
1. Surgery, University of Rochester Medical Center, Rochester, NY; 2. James P. Wilmot Cancer Institute, Rochester, NY.

Background: Cholangiocarcinoma (CCA) is a highly metastatic disease with few treatment options. It is characterized by a prominent desmoplastic reaction in which stromal components, including inflammatory immune cells, greatly outnumber malignant cells. Little is known about the immune response to CCA and tools for studying its role in disease progression are lacking. Trangenic mice with targeted Kras activation and loss of p53 (Alb-Cre/LSL-Kras ^{G12D} /p53^{Lox}) in the liver spontaneously develop CCA. Here, we characterize the immune infiltrate in human CCA and Kras-p53 mutant mice in order to help identify immune pathways that will be susceptible to targeted immunotherapy. Methods: Immunohistochemistry (IHC) and digital imaging analysis was performed on human CCA and normal liver tissue sections from archived paraffin embedded tissue blocks for myeloid and T cell markers. CCA tumors from Kras-p53 mice and normal livers were excised and digested into single cell suspensions or embedded for histological analysis. Flow cytometry analysis and IHC were performed on single cell suspensions and tissue sections, respectively, to determine equivalent immune cell subsets in tumor bearing Kras-p53 mice. Results: Human CCA was characterized by a prominent inflammatory leukocyte infiltrate (CD45+) with increased levels of immature myeloid cells of both monocytic and granulocytic origin and immunosuppressive T cells (Foxp3+). Like human CCA, Kras-p53 murine hepatic tumors were highly desmoplastic with higher levels of tumor infiltrating inflammatory leukocytes compared to normal liver. Flow cytometry analysis of single cell suspensions from tumors of Kras-p53 mice and normal livers demonstrated the inflammatory immune reaction was dominated by bone marrow derived CD11b+ monocytic and granulocytic myeloid cells. These data suggest the abundant tumor immune response in CCA is predominantly immunosuppressive. Conclusions: Analysis of the immune reaction to CCA in a genetically defined mouse model revealed the presence of an immunosuppressive infiltrate recapitulating the features of human disease. As such, the transgenic Kras-p53 mouse provides an ideal model to test targeted immunotherapy for the treatment of CCA.

PF246

Occult Metastatic Pancreatic Cancer Cells Stimulate an Innate Immune Response in the Liver Microenvironment

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Background: The role of innate immunity in regulating the progression of pancreatic adenocarcinoma (PDAC) cells in the liver microenvironment has not been fully characterized. We hypothesized that occult metastatic PDAC cells in the liver stimulate an innate immune response, but are able to ultimately evade this response resulting in tumor progression. Methods: PDAC tumors were collected from patients, cell lines established, transduced with luciferase, injected into the spleens of nude mice to generate liver metastases, then primary tumors were removed. Time to progression (TTP) of occult liver metastases was measured with bioluminescent imaging. In vitro phagocytosis assays were performed on PDAC cells co-cultured with murine macrophages. Human (tumor cell) and murine (macrophage) cytokines were measured on the media from engulfment studies using Luminex bead-based assays. Results: Tumor 608 (T608) had a significantly shorter time to metastatic outgrowth compared to other tumors (Fig. 1A). Ablation of liver resident macrophages in vivo with clodronate halved TTP in T608 as compared to control, demonstrating their role in suppressing tumor outgrowth. Despite the shorter TTP, T608 cell engulfment by macrophages was 10-fold greater than T449 or T450. Macrophages stimulated a robust increase in T608 production of proinflammatory and chemotactic cytokines, such as TNF-a, MDC, IP-10, and MCP-1 (all $p<0.05$; Fig. 1b). T608 cells stimulated macrophages to release inflammatory cytokines such as MCP-1, MIP-2, IL-6, and IL-10 (all $p<0.05$; Fig. 1C). Conclusions: PDAC cells stimulate a local innate immune response within the liver metastatic microenvironment and the ability to evade the innate immune response is specific to a given patient's tumor resulting in differential TTP. Augmenting the innate immune response and blocking the tumor's ability to evade this response may delay metastatic outgrowth and improve survival from PDAC.

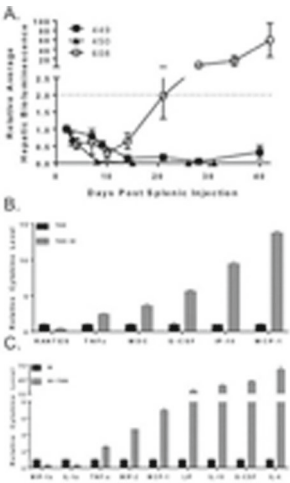

Figure 1: Metastatic PDAC cells in the liver stimulate a local innate immune response, however proliferative outgrowth is due to individual tumor biology. A. Tumor 608 (T608) had a significantly shorter time to metastatic outgrowth compared to T450 and T449 as defined by a twofold increase in relative average hepatic bioluminescence. B. 18 hours following the addition of murine macrophages to T608 cells, human cytokine analysis revealed at least a twofold increase in the secretion of proinflammatory cytokines (all $p<0.05$), except for a decrease in RANTES ($p=0.07$). C. 18 hours following the addition of T608 cells to murine macrophages, murine cytokine analysis resulted in at least a twofold increase in the production of chemotactic and proinflammatory cytokines (all $p<0.05$).

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Hepatocellular Carcinoma (HCC): Resection with Adjuvant Hepatic Artery Infusion Chemotherapy (HAIC) Versus Resection Alone: A Systematic Review and Meta-analysis

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BACKGROUND: HCC have a recurrence rate of up to 70% in 5 years after resection detrimentally lowering survival. The role of adjuvant HAIC in management of HCC in patients who are not candidates for transplantation is controversial. We aimed to evaluate overall and disease free survival in these patients. METHODS: A comprehensive online search of MEDLINE, EMBASE, PubMed, SCOPUS and the Cochrane database was conducted (Jan 1994 - August 2016). Comparative studies including patients with HCC, who are not transplant candidates, undergoing surgical resection and adjuvant

HAIC vs surgical resection alone were reviewed. Study quality was assessed using STROBE checklist. Pooled risk ratios and 95% confidence intervals (CI) for overall and disease-free survival at 1, 3 and 5 years were calculated. RESULTS: Overall, 10 studies with 595 HCC patients were included; 283 underwent resection followed by HAIC and 312 underwent resection alone. Mean age was 61 ± 10.1 years with a male/female ratio of 6/1. Meta-analysis of all included studies showed better overall survival in patients undergoing resection followed by HAIC compared with resection alone at 1-YR (Average: 90.1% vs 79.5%, RR:1.15, CI:1.07 – 1.24, p=0.095, NS), 3-YR (Average 72.1% vs 49.4%, RR:1.57, CI:1.34 – 1.77, p<0.01) and 5-YR (Average 51% vs 30.2%, RR:1.71, CI:1.33 – 2.20, p<0.01). Median survival time for the resection with HAIC group was 54.94 months compared to 31.5 months for the resection alone group. In addition, disease-free survival was better with HAIC at 1-YR (RR:1.36, CI:1.21 – 1.54, p<0.01), 3-YR (RR:1.59, CI:1.27 – 1.98, p<0.01) and 5-YR (RR:1.85, CI:132. – 2.61, p=0.011). The median disease-free survival time for the resection with HAIC group was 17.5 months compared to 7.35 months for the resection alone group. Subgroup analysis showed that this survival advantage was more significant in patients with tumors ≥7cm (p<0.05). CONCLUSION: Combination of HCC resection with HAIC improve overall and disease-free survival of patients with HCC who are not candidates for transplantation, especially in tumors ≥ 7cm.

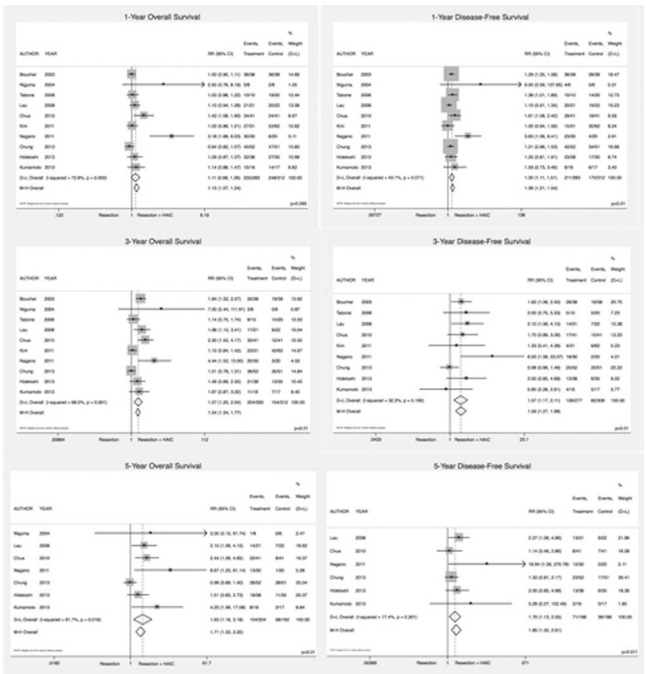

Figure 1

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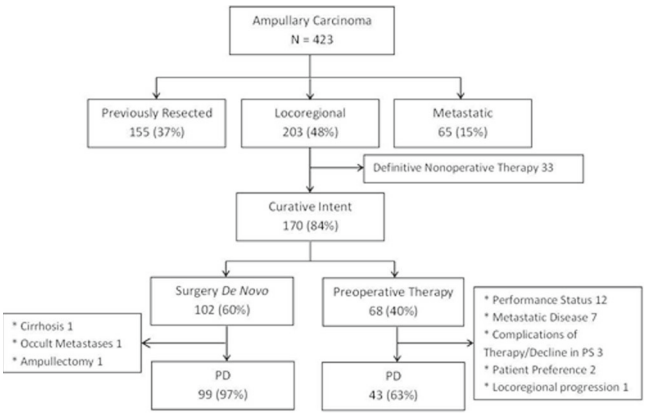
Influence of Preoperative Therapy on Outcomes of Patients with Adenocarcinoma of the Ampulla of Vater J. Cloyd,* H. Wang, Z. Jun, J. Denbo, M.J. Overman, G. Varadhachary, D. Fogelman, L. Prakash, M. Kim, T.A. Aloia, J. Vauthey, J.E. Lee, J. Fleming, M.H. Katz. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Although increasingly administered to patients with pancreatic ductal adenocarcinoma, the role of preoperative therapy for patients with adenocarcinoma of the ampulla of Vater is undefined. Methods: All patients with ampullary adenocarcinoma who were evaluated at a single institution between 1999-2014 were retrospectively reviewed (Figure). Differences in clinicopathologic characteristics, perioperative complications, locoregional recurrence (LR) and overall survival (OS) were compared between patients who underwent surgery de novo and patients who received preoperative chemotherapy or chemoradiation prior to pancreatoduodenectomy (PD). Results: 142 patients underwent PD, 43 (30.3%) who received preoperative therapy and 99 (69.7%) who did not. Preoperative therapy consisted of chemoradiation (65%), chemotherapy (7%) or both (28%). Tumors resected de novo were larger (p<0.01) and had a different subtype distribution (p<0.01) on final pathology than those resected following preoperative therapy. In addition, patients who underwent surgery first had a lower comorbidity index (p<0.05) and were more likely to receive postoperative chemotherapy (p<0.01) and chemoradiation (p < 0.0001). Nine (20.9%) specimens had <5% viable tumor cells following preoperative therapy, including 6 (14.0%) with a complete pathologic response. There were no differences in rates of postoperative complications, mortality, readmission, LR (9.1% vs 7.0%), median survival (107 vs 146 months) or 5-year OS (60.6% vs 70.4%). On multivariate cox regression analysis, the receipt of preoperative therapy was not associated with improved survival (OR 1.14, 95% CI 0.56-2.31). Conclusion: The delivery of preoperative therapy to patients with ampullary adenocarcinoma prior to pancreatoduodenectomy is safe, feasible and associated with excellent long term overall survival and locoregional recurrence rates. However, it was not associated with improved outcomes compared to a surgery first approach in this single institution retrospective review.



Flowchart of all patients with ampullary cancer seen at a single institution between 1999-2014. Percentages represent proportion of patients in the group immediately superior.

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Age-Related Differences in Presentation and Management of Pancreatic Neuroendocrine Tumors B.N. Miller,* P. Mehta, A. Morada, A. Hendifar, A. Annamalai, A. Wachsman, D. Dhall, N. Nissen. *Cedars-Sinai Medical Center, Los Angeles, CA.*

INTRODUCTION: Pancreatic neuroendocrine tumors (PNETs) have unique characteristics and management strategies. There is limited data on potential age-related differences in the incidence, presentation and management of these tumors. DESIGN: Retrospective review of all PNET patients treated at a 900-bed academic center from 2000 to 2016. Patients were divided into those with early-onset diagnosis (age < 50) or late-onset diagnosis (age ≥ 50). Univariate analyses performed using Chi-Square test. RESULTS: A total of 185 PNET patients were diagnosed at a mean age of 69.6 ± 14.5 years [16.8-92]. Early- and late-onset groups consisted of 45 and 140 patients, respectively. Mean tumor size was 3.6 ± 3.06 cm [0.3-17]. 128 patients (69%) underwent surgical resection of the primary tumor and 27% of these patients had metastases. Early-onset patients were more likely to have lesions in the head of the pancreas (p=.003) and to have symptoms on presentation, whereas late-onset patients were more lilkely to have tail lesions (p=.001) and to have incidentally discovered tumors (p=.002). Both groups had similar rates of stage 4 disease at presentation, but tumors in the early group were more likely to be Grade 2/3 (p=.046). Early-onset patients were more likely to undergo pancreatic resection than patients in the later group (p=.029) and were more likley to undergo pancreatic resection in the setting of metastatic disease (p=.014) or Grade 2/3 tumors (p=.027). In addition, early-onset patients with tumors in the head of the pancreas were comparatively more likely to undergo resection, while tumors in the body/tail were resected with no differences in frequency. There was no difference in location-specific metastatic potential between groups. Notably, only 2 of the 27 body lesions metastasized. All 12 functional tumors were resected. Conclusion: There are important age-related differences in the presentation of PNETs. Practice patterns of management of these tumors also seems to vary between groups, but the impact of selection or treatment bias

may be substantial and requires further analysis. Younger patients are more likely to have higher grade tumors and to require pancreaticoduodenectomy.

	Early-Onset (n=45)	Late-Onset (n=140)
Symptomatic Presentation	22 of 25 (88%)	38 of 71 (54%)
Incidental Presentation	3 of 25 (12%)	33 of 71 (46%)
STAGE		
Stage 4	17 of 41 (41%)	50 of 126 (40%)
Non-Stage 4	24 of 41 (59%)	76 of 126 (60%)
N/A	4 of 45 (9%)	14 of 140 (10%)
LOCATION		
Head	20 of 39 (51%)	31 of 119 (26%)
Resected	19/20 (95%)	22/31 (71%)
Metastatic	8/20 (40%)	8/31 (26%)
Body	8 of 39 (21%)	19 of 119 (16%)
Resected	5/8 (63%)	14/19 (74%)
Metastatic	0/8 (0%)	2/19 (11%)
Tail	11 of 39 (28%)	69 of 119 (58%)
Resected	10/11 (91%)	52/69 (75%)
Metastatic	7/11 (64%)	26/69 (38%)
GRADE		
Grade 1	19 of 37 (51%)	69 of 99 (70%)
Resected	15/19 (79%)	57/69 (81%)
Grade 2 or 3	18 of 37 (49%)	30 of 99 (30%)
Resected	18/19 (100%)	23/30 (77%)

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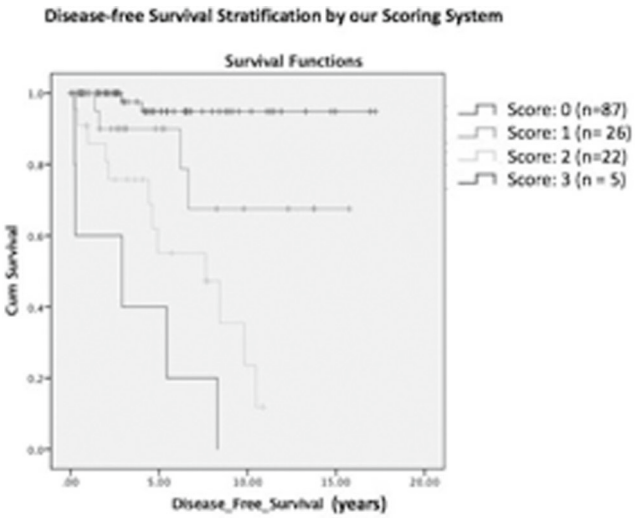
Development of a Scoring System Predictive of Distant Recurrence Following Curative Resection of Pancreatic Neuroendocrine Tumors S. Sho,* C.M. Court, P. Winograd, P.A. Toste, D.W. Dawson, T.R. Donahue, J.S. Tomlinson. *General Surgery, University of California, Los Angeles, Los Angeles, CA.*

Introduction Some patients suffer distant recurrence after intended curative surgical resection of localized pancreatic neuroendocrine tumors (pNET). Factors associated with development of metastastic disease remain poorly defined. We sought to identify factors predictive of distant tumor recurrence in surgically resected pNET and develop a scoring system prognostic for disease-free survival (DFS). Method Patients who underwent surgical resection for localized pNET between 1989 and 2015 were identified and clinical and pathologic factors, as well as outcome variables were recorded. Univariate and multivariate analysis were performed to identify factors predictive of metastatic recurrences. A scoring system was devised using the identified factors. Prognostic performance of the scoring system was assessed using ROC curve and Kaplan-Meier analyses. Result We identified 140 patients with localized, completely resected pNETs. Overall 5 and 10yr DFS were 84.6% and 67.1%, respectively. Distant recurrences were found in 23 (16.4%) patients. Multivariable analysis revealed tumor size ≥5cm (p=0.001, HR=7.48), positive lymph node (LN) status (p=0.011, HR=5.09) and Ki-67 index ≥8% (p<0.001, HR=12.3) as independent predictors of distant recurrence. Patients with these factors had a significantly worse 5yr DFS (tumor size>5cm: 70.2% vs. 90.1%, p<0.0001; positive LN: 56.4% vs. 92.1%, p<0.0001; Ki-67>8cm: 53.6% vs. 92.5%, p<0.0001). A scoring system based on these factors (1-point/factor present) was highly predictive of metastatic recurrences with area under the ROC curve of 0.882. Utilizing a score of ≥2 to predict disease recurrence yielded sensitivity and specificities of 74% and 90%, respectively. The 5yr DFS for scores of 0, 1, 2 and 3 were 95.1%, 90%, 62% and 25%, respectively. Conclusion The combination of tumor size>5cm, LN positivity and Ki-67>8% are highly predictive of metastatic recurrences in surgically resected pNET. Our proposed scoring system may help identify patients who would benefit from more vigilant follow-up, potential utilization of adjuvant therapies, and future trial stratification.



PF252

Pancreatic Adenocarcinoma with High Expression of CD31 Have Better Prognosis E. Katsuta,[1]* M.G. Dozmorov,[2] A.L. Olex,[2] L.J. Fernandez,[2] S. Hochwald,[1] K. Takabe.[1] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. Virginia Commonwealth University, Richmond, VA.*

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is known for its hypovascularity. A phase 3 study demonstrated no improvement in outcome with Bevacizumab, anti-angiogenic drug, added to standard chemotherapy for PDAC. Therefore, we hypothesized that PDAC with relatively high vascularity may be associated with better survival. METHODS: Using Level 3 gene expression data from The Cancer Genome Atlas (TCGA), patients were classified into either high or low CD31 expression group. Overall survival and related genes and pathways were compared between these two groups. RESULTS: First, we verified our dataset by confirming whether high expression of angiogenic factor and vascular signals associate with survival in colon cancer, which is known to respond to Bevacizumab. High expression of angiogenic gene (VEGF-A) as well as marker gene for vascular endothelial cells (CD31) was associated with poor overall survival (OS) in colon cancer. In the PDAC cohort, high expression of CD31, which indicate presence of vascular endothelial cells, was significantly associated with better OS (p=0.002). Multivariate analysis using Cox proportional hazard regression demonstrated that residual tumor (R1, 2; p=0.020) and CD31 high expression (p=0.009) were the only independent factors that negatively impacted on OS. Pathway analysis revealed that not only vascular epithelium stability pathways such as Cell adhesion molecules (p<0.001), Focal adhesion (p<0.001), ECM-receptor interaction (p=0.003) and adherens junction (p=0.005), but also immune reaction related pathways such as Cytokine-cytokine receptor interaction (p<0.001), Chemokine signaling pathway, Leukocyte transendothelial migration (p<0.001), T cell receptor signaling pathway (p<0.001) and Natural killer cell mediated cytotoxicity (p<0.001) were upregurated in CD31 high group. It implies that anti-tumor immune response works for better OS in CD31 high tumors. Interestingly, there was no survival difference by expression of HIF1-alpha, an ischemia marker. CONCLUSIONS: CD31 high expression PDACs have better overall survival, and related with not only mature vessels pathways but also immune reaction related pathways.

PF254

Perioperative Alpha-feto Protein Response is a Prognostic Marker in Patients with Hepatocellular Carcinoma S. Bhagwandin,* Q. Wang, S. Hiotis. *The Icahn School of Medicine at Mount Sinai, Long Island City, NY.*

Background The clinical value of α-fetoprotein (AFP) in patients with hepatocellular carcinoma (HCC) is its utility as a biomarker to predict disease recurrence after curative resection. Serial AFP monitoring has been common practice, and AFP 'response' has been empirically defined as a 50% decrease within four weeks post-operatively. The role of serum AFP as a prognostic

marker, however, has been limited by data supporting whether or not a perioperative drop of AFP suggests a survival advantage. This study aims to review the specific kinetics of serum AFP in patients with elevated preoperative levels (>400 ng/ml), and determine if certain patients are at higher risk for disease recurrence and worse overall survival. Methods Data was analyzed from sixty-two patients with an elevated serum pre-operative AFP (≥ 400 ng/mL) that underwent curative resection for HCC. Serum AFP was measured within 8-24 weeks of surgical resection, and patients were stratified according to whether the post-operative AFP level was ≤20 ng/ml or >20 ng/ml. Results 58 patients (94%) demonstrated a decrease in AFP perioperatively, whereas 4 patients had AFP levels that increased from baseline. 33 (53%) patients had a serum AFP measurement below 20 ng/ml within 8-24 weeks of surgery. Smaller tumors (5.0 +/- 3.2 vs. 8.0 +/- 4.3) were more likely to have a perioperative decrease in AFP ≤ 20 ng/ml (p=0.002). The 5-year overall survival was 88% vs. 31% (p<0.001) in patients with AFP levels ≤20 ng/ml and >20 ng/ml, respectively. HCC recurrence at five years was 48% in patients with post-operative AFP levels ≤20 ng/ml and 83% (p<0.001) if AFP >20 ng/ml. Conclusions Perioperative AFP response has not been directly correlated as a prognostic marker among patients with HCC in the literature prior to this study. This trend of AFP kinetics with a cut-off value of 400 ng/ml preoperatively may assist in monitoring and predicting treatment response among patients. Markedly elevated preoperative serum AFP (>400 ng/ml) that decreases ≤20 ng/ml within 8-24 weeks of surgery is associated with improved overall survival and lower HCC recurrence.

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Neoadjuvant Therapy Improves Fibrinolysis Resistance in Patients with Adenocarcinoma Undergoing Pancreatic Resection

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Introduction: Plasmin activation is a mechanism for malignant invasion via the fibrinolytic system. We hypothesize that patients undergoing pancreatic resection for adenocarcinoma (ACA) have increased fibrinolysis resistance compared to healthy volunteers and those with more benign pancreatic pathology. Methods: Patients undergoing pancreatic resection were prospectively enrolled. Blood was collected prior to surgery and assayed with conventional thrombelastography (n-TEG) and a modified assay (t-TEG) with exogenous tissue plasminogen activator (tPA) to quantify fibrinolysis resistance measured by the maximum clot strength (MA) and percent of clot lysis at 30 minutes (LY30). Results were compared to 160 health volunteers (HVS). Receiver operator characteristic (ROC) curves were developed to assess performance of the assays ability to correctly identify ACA. Results: Forty-one patients were enrolled with the diagnoses of ACA 29(71%), PNET 5(12%), IPMN 4(10%), inflammatory 3(7%). Compared to HVS, patients undergoing pancreatic resection had a higher median clot strength (MA) with n-TEG(63mm vs 55mm p<0.001) and t-TEG (56mm vs 39 mm p<0.001) and decreased fibrinolysis activity (LY30 n-TEG 0.6% vs 1.6% p<0.001, t-TEG 11.9% vs 52.9% p<0.001). Patients not undergoing neoadjuvant therapy n-TEG MA(p=0.017), t-TEG MA(p=0.003), and t-TEG LY30(p=0.015) were associated with ACA (figure 1). In patients with ACA, T stage correlated with t-TEG MA (0.399 p=0.048) and trended towards significance for overall cancer stage (0.343 p=0.068). Neoadjuvant therapy was associated with a decreased t-TEG MA (45mm vs 58mm p=0.042 figure 1) and increased t-TEG LY30 (24% vs 6% p=0.001). The t-TEG MA has an area under the curve of 0.717 for predicting ACA, which improved to 0.826 for patients whom had not received neoadjuvant therapy. Conclusion: The t-TEG has identified an association of ACA and resistance to fibrinolysis that improves with neoadjuvant therapy. These data also support a potential diagnostic role of TEG. Patients with adenocarcinoma with no prior treatment appear to carry the highest risk of thrombotic complications due to fibrinolysis resistance.

PF256

Evolution of Neoadjuvant Therapy in Borderline Resectable Pancreatic Cancer: Surgical and Long-term Outcomes in a Single Institution

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Neoadjuvant therapy (NT) regimens for borderline resectable pancreatic cancer (BRPC) have evolved to include multi-agent FOLFIRINOX/FOLFOX followed by 5FU and radiation. We report our experience and compare outcomes of initially resectable pancreatic cancer (IRPC) vs BRPC receiving NT. We retrospectively collected data on patients who underwent pancreaticoduodenectomy between January 2008 and October 2015. Demographics, surgical parameters, pathology, NT regimens, and surgical outcomes were compared between patients classified as either IRPC or BRPC according to the AHPBA/SSO/SSAT consensus definition. Further analysis was done comparing older gemcitabine chemotherapy regimens with newer multi-agent based treatments, pre-and post- neoadjuvant CA 19-9 serum measurements, and histologic response to neoadjuvant therapy on pathologic examination of resected specimens. A total of 195 patient records were included in our analysis comprising of 133 IRPC and 62 BRPC cases. The IRPC patients were older (67.6 vs 62.9, p=0.003), had fewer females (43% vs 60%, p=0.03), had a higher pre-operative BMI (27.7 vs 25.4, p=0.009) and lower albumin (3.14 vs 3.40, p=0.04). While IRPC operations were shorter (449 min vs 520 min, p=0.003), had less blood loss (663 ml vs 954 ml, p=0.002) and were less likely to include vascular resection (29% vs 76%, p=0.002) the rate of R0 resection was identical (82% for both, p=1) and the IRPC group had higher node-positive ratio (19.3% vs 7.2% p<0.0001). 15 patients received single agent chemotherapy regimens while 42 received multi-agent regimens. 90% received radiation therapy. BRPC and IRPC survival was similar (log-rank p=0.7) with median survival of 731d and 652d respectively. A high histopathologic response (CAP grade 0 or 1) to NT was not associated with increased survival (p=0.4), but completion of ≥4 cycles of multi-agent pre-operative chemotherapy was (p=0.001). While the effects of chemo- and radiotherapy in these BRPC tumors lead to more technically challenging surgeries in terms of blood loss and operative time, they have similar rates of R0 resection, perioperative outcomes and short-term survival.

PF259

The Effects of Peritoneal Carcinomatosis on the Prognosis of Patients with Advanced Midgut Neuroendocrine Tumors

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Introduction: Peritoneal carcinomatosis is generally associated with a poor prognosis. However, the clinical implication of peritoneal carcinomatosis from midgut neuroendocrine tumors (NETs) remains undefined. Given the indolent nature of midgut NETs, we hypothesized that carcinomatosis in these patients does not inherently translate into a poor prognosis. Methods: Four-hundred forty-eight consecutive midgut NET patients, operated on at our institution between December 1995 and September 2014, with distant metastatic disease were included. Patients were divided into three groups. Group 1 had peritoneal carcinomatosis only (n=14/448), group 2 had liver metastasis without carcinomatosis (n=350/448), and group 3 had carcinomatosis with liver metastasis (n=84/448). Kaplan-Meier analysis was performed and survival rates were compared among the three groups. Results: Survival data among the groups were as follows: group 1 (carcinomatosis only): 8/14 patients have died (57%), group 2 (liver metastasis only): 90/350 patients have died (26%) and group 3 (carcinomatosis and liver metastasis): 35/84 patients have died (42%). Group 1, 2, and 3 patients had a median survival of 87, 287, and 138 months, respectively. Conclusions: The presence of peritoneal carcinomatosis per se in patients with midgut NET portends an extremely poor prognosis. However, with a concurrent advanced disease in the liver the lethality has been curtailed. This intriguing and unexpected finding needs a more protract longitudinal follow up study to validate and the biologic explanation of this phenomenon warrant further exploration.

PF260

The Impact of Resected Liver Volume to Total Liver Volume Ratio on Survival After Resection for Colorectal Liver Metastases

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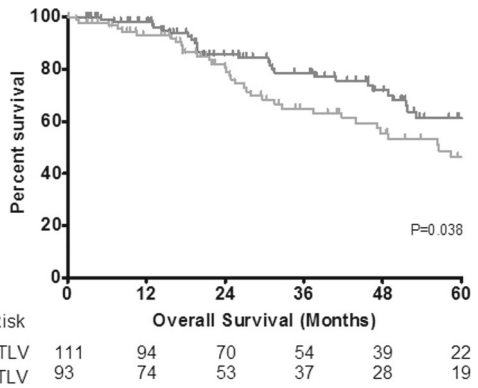
Introduction Liver resection remains the cornerstone of treatment for patients with colorectal liver metastases(CRLM). However, postoperative liver failure following major resections, remains a devastating risk. As such, parenchymal sparing hepatectomy(PSH) is increasingly utilized. The use of PSH for advanced CRLM remains somewhat controversial. Methods

Preoperative total liver volume(TLV) was measured by hand tracing of the liver outline on axial portal venous-phase images. Resected liver weight was considered equal to resected liver volume(RLV), since the liver has nearly the same density as water. In turn, the RLV/TLV ratio was used to characterize the extent of surgery. Using sensitivity analyses, a cut-off of 22% was determined, classifying patients into limited(<22%) and extended resection(≥22%) groups. Short and long-term outcomes of both groups were then compared. Results 204 patients were included; median age was 58 years(IQR:49-66). At surgery, 111 patients(54.4%) underwent a limited resection(<22% of the TLV); 93(45.6%) underwent an extended resection. Patients who underwent extended resection had greater tumor size(median: 13.0 cm^3, IQR:3.9-40.0 vs. 5.3 cm^3, IQR:1.7-16.6;p=0.004) and number(2, IQR:1-4 vs. 2, IQR:1-2;p=0.014). Patients with extended resection had a longer hospital stay(5, IQR:4-7 vs. 5, IQR:4-6;p=0.021) and greater frequency of severe complications, according to the Clavien-Dindo classification(23.7% vs 11.7%;p=0.024). Of note, patients with extended resection had significantly worse OS(56.6 months vs. 106.3 months;p=0.038; figure). In multivariate analysis, after adjusting for factors such as tumor volume and number, extended resection remained strongly associated with worse OS(Hazard ratio [HR]: 1.75; 95%CI:1.01-3.03;p=0.048). This effect was greater in patients with tumor volume<7.9 cm^3(HR: 2.56; 95%CI:1.10-5.98;p=0.030). Conclusion Patients who underwent extended resection(RLV / TLV ≥22%) fared worse than those who underwent limited resection, even after controlling for tumor volume and other prognostic factors. Given the better short-term outcomes of limited resection, its use should be strongly encouraged.



PF261

Assessing Relative Cost of Complications Following Hepatic Ablation N. Bhutiani,* P. Philips, C. Scoggins, K.M. McMasters, R.C.G. Martin. *University of Louisville Department of Surgery, Louisville, KY.*

Introduction: Despite the relatively good safety profile and patient tolerability associated with ablative modalities for treatment of primary and secondary hepatic malignancies, complications that do occur can significantly impact treatment costs. This study aimed to identify frequency and economic burden of complications following hepatic ablation. Methods: The Premier Hospital Database was queried for patients undergoing hepatic ablation between 2008 and 2015. Complications were identified based on ICD-9 code and grouped based on complication type. Complication frequency as well as impact on clinical and economic outcomes was calculated. Cost differences were calculated with respect to patients undergoing hepatic ablation who did not experience each given complication. Differences were averaged within complication types. Complication frequency and effect on cost were ranked, with ranks summed to evaluate relative economic impact of complication types. Results: A total of 1,943 patients met inclusion criteria. The most common groups of complications following hepatic ablation were pulmonary, gastrointestinal, and iatrogenic (Table 1). Specific complications with greatest frequency were bleeding (7.83%), ileus (6.6%), and atelectasis (5.05%). However, the complication groups with the greatest percent effect on treatment-related costs were infectious, cardiac, and pulmonary. Specific complications with the greatest impact on cost included intra-abdominal infection (1.53%) and bacteremia (1.28%). After combining the ranks of complication frequency and percent of effect on cost, pulmonary, gastrointestinal, and infectious complications had the greatest cumulative effect on cost related to hepatic ablation. Conclusions: Financially significant complications following hepatic ablation stem largely from post-procedure infection, respiratory failure, and gastrointestinal disturbance. Efforts focused on improving peri-procedural pulmonary toilet and post-operative mobilization as well as minimizing post-operative narcotics and sources of infection including indwelling catheters and central lines can help improve cost-effectiveness of hepatic ablation for primary and secondary liver malignancies.

Table 1: Most Frequent and Financially Significant Complications following Hepatic Ablation

Complication Group	Percent	Rank of Frequency	Average Effect on Cost (%)	Rank of Effect on Cost	Combined Rank
Pulmonary	16.11	1	0.22	5	6
Gastrointestinal	13.88	2	0.23	4	6
Infectious	8.78	6	0.50	1	7
Cardiac	7.19	8	0.24	3	11
Deep vein Thrombosis/Pulmonary Embolus	8.83	9	0.35	2	10
Bleeding	7.83	4	0.08	9	13
Iatrogenic	8.89	3	0.05	10	13
Psychiatric	8.51	10	0.21	6	16
Hepatic	1.36	9	0.17	8	16
Neurologic	8.20	11	0.21	6	16
Renal	4.89	7	-0.06	11	18

PF262

Factors Contributing to Readmission After Pancreaticoduodenectomy: An ACS-NSQIP Analysis R. Ramanathan,* T. Mason, B.J. Kaplan. *Virginia Commonwealth University Medical Center, Richmond, VA.*

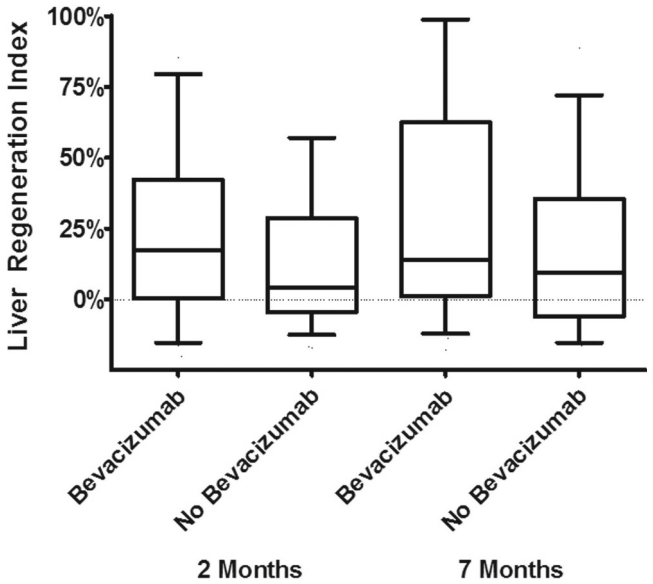
Background: Readmissions are gaining increased importance as a tracked metric affecting quality assessment, public reporting and reimbursement. Methods: Prospective ACS-NSQIP data were retrospectively reviewed and analyzed for patients who underwent PD from 2011-2014. Preoperative variables assessed included age, sex, BMI, malnutrition, medical comorbidities, smoking, ASA class, functional status, chemotherapy and radiation. Intraoperative variables included operative time, blood transfusion requirement, malignant histology and trainee involvement. Postoperative variables included morbidity, length of stay and discharge destination. Since 2014, targeted pancreas-specific data have been captured in ACS-NSQIP, and these data were separately analyzed for pancreas-specific contributors to readmissions. Results: Between 2011 and 2014, there were 13392 PD performed with a 16.6% readmission rate. Statistically significant ($p<0.05$) factors contributing to readmissions included absence of preoperative chemotherapy within 30 days (Odds Ratio [OR]: 2.88, $p<0.05$), presence of radiation therapy (OR 3.78, $p<0.01$), malignant pathology (OR: 1.47, $p<0.05$), increased hospital stay ($p<0.05$) and any morbidity ($p<0.05$). Specific morbidities associated with significance included sepsis and organ space infection. In 2014, 3,207 patients had targeted pancreas-specific data recorded. When evaluating the contribution of preoperative obstructive jaundice, biliary stent, chemotherapy and radiation, the lack of obstructive jaundice was a significant contributor to readmission. Of the following operative factors, approach, duct size, gland texture, reconstruction method and vascular resection, only duct size greater than 6mm was a significant positive independent contributor to readmission ($p<0.05$). Postoperatively, delayed gastric emptying and percutaneous drainage were associated with readmission while drain amylase values and pancreatic fistula were not. Conclusions: Most of the factors involved in readmission are non-modifiable factors, making readmission a poor quality measure. Reducing incidence of sepsis and organ space infection offer modifiable factors for physicians to reduce readmissions.

PF263

Preoperative Bevacizumab is Associated with Enhanced Liver Regeneration After Resection for Colorectal Liver Metastases G. Margonis,[1]* S. Buettner,[1] N. Andreatos,[1] M. Zargham Pour,[1] N. Shao,[1] M. Aliyari Ghasebeh,[1] K. Sasaki,[1] J. IJzermans,[2] J. He,[1] I. Kamel,[1] C. Wolfgang,[1] M. Weiss.[1] *1. The Johns Hopkins Hospital, Baltimore, MD; 2. Erasmus MC, University Medical Center, Rotterdam, Netherlands.*

Introduction Liver resection remains the only curative treatment for patients with colorectal liver metastases(CRLM). Neoadjuvant chemotherapy, with/without bevacizumab, is frequently administered to CRLM patients. However, the impact of preoperative chemotherapy and bevacizumab on liver regeneration and post-hepatectomy liver failure remains controversial. Methods Liver regeneration rates of patients who underwent hepatectomy for CRLM between 2003-2015 were assessed. The early and late regeneration indexes

were defined as the relative increase in liver volume(RLV) within 2[(RLV2m-RLVp)/RLVp] and 7 months[(RLV7m-RLVp)/RLVp] from surgery. Regeneration rates of the preoperative treatment groups(Chemotherapy +/- bevacizumab) were then compared. Results Preoperative chemotherapy details and liver volumetry data were available for 185 patients; 78(42.2%) received neoadjuvant chemotherapy with bevacizumab(BEVA+), 46(24.8%) received chemotherapy only(BEVA-) and 61(33%) received no chemotherapy. Patients in the BEVA+ and BEVA- groups received similar chemotherapy cycles[4 (3-6) vs. 4 (3.5-6);p=0.378] and regimens(p=0.353). Despite the comparable clinicopathological characteristics and RLVp /TLV at surgery (p=0.903) of both groups, we noted a marked increase of early and late liver regeneration in the BEVA+ group(17.2% vs. 4.3%;p=0.035 and 14.0% vs. 9.4%;p=0.091, respectively). Of note, early and late regeneration rates(3.73% and 10.89% vs. 4.3% and 9.4% respectively) were comparable between patients who did not receive chemotherapy and BEVA- patients(all p>0.05). In multivariable analysis –adjusted for gender, age, portal vein embolization, preoperative chemotherapy, resected liver volume, tumor number, postoperative chemotherapy, fibrosis, steatosis- bevacizumab remained an independent predictor of early liver regeneration(p=0.019). Conclusion Neoadjuvant chemotherapy did not impair liver regeneration. Perhaps more importantly, bevacizumab was associated with enhanced liver regeneration in our cohort. The validity and clinical implications of this finding warrant further investigation.



PF264

Preoperative Treatment with Biologic-Agent for Colorectal Liver Metastasis: Impact on the Association of Surgical Margin Status with Long-term Prognosis A. Hammad, K. Sasaki, C. Quintini, C. Miller, E. Berber, F. Aucejo.* *Surgery, Cleveland Clinic Foundation, Cleveland, OH.*

Background: While the prognostic role of surgical margin status after resection of colorectal liver metastasis (CRLM) has been previously explored, its impact on overall survival (OS) stratified by the receipt of preoperative biologic-agent remains largely unknown. As such, we sought to examine the interplay of biologic-agent administration and margin status among patients with CRLM who received pre-operative chemotherapy with or without biologic-agent. Methods: Patients who underwent curative-intent surgery for CRLM at the Cleveland Clinic between 2003-2013 and who had received preoperative chemotherapy were identified. Data regarding surgical margin status, preoperative biologic-agent administration, and overall survival (OS) were collected and assessed using multivariable analyses. Results: The study cohort consisted of 185 patients met inclusion criteria. Median patient age was 59 years (IQR,51-66 years); Of these, 104 (56.2%) received preoperative chemotherapy+biologic-agent, while 81(43.8%) received only preoperative chemotherapy. Median and 5-year OS in the entire cohort was 50.2 months and 44.1%, respectively. In the entire cohort, positive surgical margin status was associated with worse 5-year OS compared with R0 resection (47.6% vs. 25.2%; P=0.018). After stratifying by the receipt of preoperative biologic-agent, the prognostic value of surgical margin only persisted among patients who did not receive preoperative biological-agent (HR;3.47 95%CI 1.04-11.5, P=0.042). In contrast, surgical margin status was not associated with OS among patients treated with preoperative biological-agent (HR;0.96 95%CI 0.48-1.87, P=0.874). Conclusions: The impact of margin status varied according to the receipt of biological-agent. Specifically, an R1 margin was not associated with a detrimental survival among patients treated with biological-agent.

PT267

Staging ^{18} F-FDG PET/CT Influences the Melanoma Treatment Plan in Patients with (Micro)Satellites or In-Transit Metastases L.H.J. Holtkamp,[1]* A. Chakera,[1] S. Fung,[2] J. Stretch,[1] R. Saw,[1] K. Lee,[1] M. Gonzalez,[1] J. Thompson,[1] L. Emmett,[3] O.E. Nieweg.[1] *1. Melanoma Institute Australia, Sydney, NSW, Australia; 2. Mater Hospital, Sydney, NSW, Australia; 3. St Vincent's Hospital, Sydney, NSW, Australia.*

Background Whole body ^{18} F-FDG PET/CT and MRI of the brain are commonly used to stage patients with lymph node metastases from melanoma, but there is no common approach in other stage III patients. The aim of this prospective study was to establish the diagnostic value of PET/CT and brain MRI in patients with (micro)satellites or in transit metastases, and to assess the implications of these scans for subsequent management. Methods Between May 2014 and May 2015, twenty-five patients with a first presentation of (micro)satellites or in transit metastasis and without clinical evidence of palpable nodal or distant metastasis underwent PET/CT and brain MRI after a tentative treatment plan had been made. Sensitivity and specificity of PET/CT and brain MRI were determined by pathological confirmation, clinical follow up and imaging after six months. The study was conducted with ethics committee approval. Results Five PET/CT scans were true positive, 2 false positive, 6 false negative and 12 true negative. The sensitivity of PET/CT was 45%, specificity 86% and positive predictive value 71%. The false positive PET/CTs were a Schwannoma and a papillary thyroid carcinoma. None of the brain MRI scans was true positive, none false positive, 1 false negative and 22 true negative. In two patients the MRI outcome could not be determined. The PET/CT led to a change in the AJCC stage of 3 patients (12%). In 4 patients (16%) the initially planned treatment was modified, two of them had presented initially with microsatellites and two with multiple palpable in transit metastases. MRI did not result in any changes of stage or treatment plan. Conclusions Sensitivity, specificity and positive predictive value of PET/CT were 45%, 86% and 72%, respectively. MRI of the brain did not provide useful information. PET/CT changed the tentative treatment plan in 16% of melanoma patients who presented with (micro)satellites or in transit metastasis. Based on these results PET/CT appears a useful staging procedure and is recommended in melanoma patients with (micro)satellites or in transit metastases.

PT268

Harnessing the Personalized T-Cell Response Targeting Cancer Germline Antigens in Patients with Metastatic Cancer S. Ilyas,* A. Gros, E. Tran, A. Pasetto, R. Yossef, E.M. Groh, T.D. Prickett, J.J. Gartner, S.A. Feldman, P.F. Robbins, S.A. Rosenberg. *Surgery Branch, National Institutes of Health - NCI, Bethesda, MD.*

Cancer germline antigens (CGA) represent targets for immunotherapy as they can be shared between patient tumors and expression in normal tissues is limited or absent. Adoptive transfer of T cells genetically modified to express T cell receptors (TCRs) targeting CGAs, such as NYESO1, can mediate tumor regression. However, this approach is limited by the identification of immunogenic epitopes that are primarily presented by a few common HLAs, such as HLA-A*02:01. To overcome these limitations, we screened T cells derived from patients with metastatic melanoma and epithelial cancers for recognition of CGAs regardless of the HLA restriction element or the specific epitope presented. Various T cell subsets were sorted from peripheral blood and/or tumor from patients with metastatic cancers based on expression of activation or exhaustion markers, such as PD-1, which has been shown to enrich for tumor-reactive cells. These subsets were screened for T-cell reactivity against autologous dendritic cells electroporated with full-length RNA or pulsed with peptide pools encompassing a specific CGA. We evaluated T-cell responses against a panel of 12 CGAs described to be expressed in human melanoma and epithelial cancers. TCRs targeting CGAs were isolated, cloned into a retroviral vector and used to transduce peripheral blood lymphocytes (PBL). In 1 patient with melanoma we identified a polyclonal T-cell response targeting

NYESO1 in the context of 3 HLA alleles, A*02:01, B*13:02, and C*06:02, suggesting that NYESO1 was highly immunogenic in this patient. In addition, CXorf61-specific T cells restricted by HLA-A*30:01 and B*44:03 were identified in a patient with gastric cancer. Overall, endogenous NYESO1, MAGEA3, SSX2, or CXorf61 reactive T-cell responses were found in 5 of 6 patients with metastatic melanoma and 2 of 3 patients with epithelial cancers. Moreover, PBL genetically engineered to express the isolated TCRs conferred CGA-specificity. Naturally-occurring CGA reactive T cells were identified in the majority of the patients screened. These findings may broaden the therapeutic utility of adoptive cell therapies targeting cancer germline antigens.

PT269

PET/CT Surveillance Detects Asymptomatic Recurrences in Stage IIIB and IIIC Melanoma Patients: A Prospective Cohort Study M.F. Madu,[1]* P. Timmerman,[1] M.W. Wouters,[1] B. van der Hiel,[2] J.A. van der Hage,[1] A.C. van Akkooi.[1] *1. Surgical Oncology, Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands; 2. Nuclear Medicine, Netherlands Cancer Insitute - Antoni van Leeuwenhoek, Amsterdam, Netherlands.*

Introduction. AJCC stage IIIB and IIIC melanoma patients are at risk for disease relapse or progression. The advent of effective systemic therapies has made curative treatment of progressive disease a possibility. Since resection of oligometastatic disease can confer a survival benefit and immunotherapy is possibly most effective in a low tumor load setting, there is a likely benefit to early detection of progression. The aim of this pilot study was to evaluate a PET/CT surveillance schedule for resected stage IIIB and IIIC melanoma. Methods. From 1-2015, stage IIIB and IIIC melanoma patients at our institution underwent 6-monthly surveillance with PET/CT, together with 3-monthly S100B assessment. When symptoms or elevated S100B were detected, an additional PET/CT was performed. Descriptive statistics were used to evaluate outcomes for this surveillance schedule. Results. Twenty-five patients were included. Fourteen patients (56%) were suspected of relapse on PET/CT. Relapses were confirmed in 11 patients. Recurrences were mostly regional in stage IIIB patients (2 out of 3) and mostly distant in stage IIIC cases (5 out of 9). Three cases were false positive. There were no false negative cases. Six out of 11 recurrences detected by PET/CT were asymptomatic at that time, with a normal range S100B. Nine patients received curative treatment after diagnosis of relapse. Conclusions. Surveillance imaging with S100B in combination with PET/CT seems an effective strategy to detect asymptomatic recurrence in stage IIIB and IIIC melanoma patients in the first months after complete surgical resection.

PT270

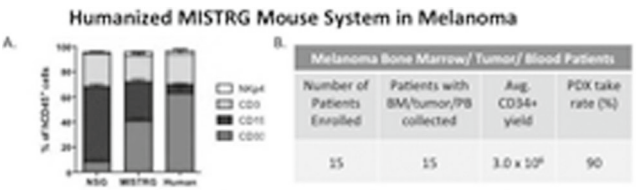
Conditional Survival of Melanoma in the Sentinel Lymph Node Era: Meaningful Prognostic Information for Patients and Physicians L. Kerivan,* M. Reintgen, E. Reintgen, S. Swaminathan, D.S. Reintgen. *Surgery, University of South Florida, Morsani School of Medicine, Tampa, FL.*

Conditional survival (CS) estimates are more meaningful for patients as they progress in their follow-up from a cancer diagnosis. Methods: A retrospective query of a prospective database was used to abstract patients diagnosed with invasive malignant melanoma during the years 1988-2016. Patients were stratified by Stage of Disease at diagnosis. Data was generated based on 5 year disease-free survival (DFS) and overall survival (OS) from the date of diagnosis, as well as 5 year DFS and OS if patients survive 1,2,3 and 4 years without recurrence or death (Conditional Survival). All deaths in the series were from metastatic melanoma. Results: There were a total of 7531 melanoma patients in the study. For all stages of disease as patients with melanoma were followed without recurrence or death, the prognosis improved. For stage I patients 5 -year DFS calculated from diagnosis increased from 61.7% to 93.2% if patients survive up to 4 years without recurrence. Similar trends were noted for Stage II -IV disease. 5-year OS from date of diagnosis for Stage I patients also increased from 88.8% to 98.6% if patients survived 4 years. 5-year OS at any period of time during the recurrence free follow-up period was similar for patients with Stage I (88.8%, 87.2%, 86.2%, 86.4%, 86.2%) and II (66.7%, 62%, 62.8%, 64.2%, 66.1%) disease but improved significantly for Stage III (50.7%, 50.2%, 56.5%, 59.8%, 71.4%) and IV patients (27.6%, 34.9%, 48.3%, 50.0%, 68.7%) as patients survived 1,2,3 and 4 years from diagnosis. For example, if Stage III patients survive 4 years, the 5-year OS increases from 50.7% at the time of diagnosis to 70.4% at the 4 year mark. The best prognostic group, those patients with Stage I melanoma who survive without recurrence for the first 4 years of follow-up continued to have an increased death rate compared to the normal population. Conclusion: Prognosis improves for melanoma patients if they survive during the follow-up period without recurrence. This data provides more meaningful recurrence and survival information for patients and their families.

PT271

Development of a Humanized Mouse Model of Melanoma to Evaluate Cancer Immunotherapeutics B. Krasnick,[1]* M.S. Strand,[1] Y. Bi,[1] E. Pittman,[1] T. Fleming,[1] P. Goedegebuure,[1] K. Paluka,[2] R. Flavell,[3] R. Fields.[1] *1. Surgery, Washington University School of Medicine, St. Louis, MO; 2. The Jackson Laboratory for Genomic Medicine, Farmington, CT; 3. Yale University School of Medicine, New Haven, CT.*

Introduction: Syngeneic murine models of cancer have proven to be invaluable in cancer research, but significant limitations are present due to their lack of ability to study human tumors. Patient derived xenografts (PDXs) have utilized human tumor implanted into immunodeficient nonobese diabetic/severe combined immunodeficient (NOD/SCID) mice. This lack of an immune system enables successful engraftment, but also creates a model with limited translational value. Utilizing the MISTRG mouse system, with knocked in human genes for M-CSF, IL-3, SIRPα, thrombopoietin and GMCSF, along with a reconstituted human immune system, we have been able to create a humanized mouse model that more accurately recapitulates the innate and adaptive aspects of the human immune system. Methods: We prospectively collect tumor, peripheral blood (PB), and bone marrow (BM) from all consenting patients undergoing resection of melanoma. The patient's tumor is implanted into NOD/SCID mice to generate a PDX. The BM stem cell progenitor $CD34^+$ cells are isolated. MISTRG mice are irradiated at 1-3 days old, at which time $CD34^+$ cells are injected into the liver. After 8 weeks, flow cytometry is utilized to characterize the percent $CD45^+$ human hematopoietic cells. These mice are then injected subcutaneously with the already generated matching PDX tumor. Results: We have collected tumor, PB, and BM from 15 patients, and successfully generated PDXs in 90% of cases. From all patients we have successfully expanded tumor-infiltrating lymphocytes ex-vivo. The BM from these patients on average yields 3 million $CD34^+$ cells. In a pilot study, we have been able to demonstrate successful engraftment of human cells at 8 weeks. The matching melanoma tumors were successfully implanted in both cases. Conclusion: A humanized MISTRG mouse model allows for recapitulation of the human tumor environment. This may allow for evaluation of cancer immunotherapeutics in a mouse system using human tumors, both for true precision medicine and further evaluation of immunotherapy and cancer vaccines—two promising areas of research with current limited applicability in immunodeficient murine PDX models.



Abbreviations: NSG, NOD/SCID gamma mice; MISTRG, knocked in human genes for M-CSF, IL-3, SIRPα, thrombopoietin and GMCSF mouse model; PB, peripheral blood; BM, bone marrow; Avg., average; PDX, patient derived xenograft

Figure. A. WBC composition of humanized MISTRG mice, demonstrating the presence of NK cells (NKp4+), lymphoid T (CD3+) and B (CD19+) cells, and myeloid cells (CD33+), as compared to reconstituted NSG mice and humans B. Overview of patients with harvested melanoma components for reconstituted humanized MISTRG mouse model

PT272

Use of Circulating Microvesicles, Exosomes, as a Biomarker to Track Response to Immunotherapy J. Cintolo-Gonzalez,[1]* S. Cohen,[1] W. Michaud,[1] D. Plana,[1] D. Panka,[2] R. Sullivan,[1] G.M. Boland.[1] *1. Surgery, Massachusetts General Hospital, Boston, MA; 2. Beth Israel Deaconess Medical Center, Boston, MA.*

Introduction: Immunotherapy targeting programmed cell death protein 1 (PD-1) leads to durable responses and improved progression free survival in

melanoma, but not all patients respond. Exosomes are extracellular microvesicles, which contain a variety of nucleic acids and proteins. Exosomes can be analyzed from archived serum/plasma samples to study tumor-based changes. We examined the feasibility and accuracy of exosomal mRNA analysis to track response to therapy with PD-1 inhibitors. Methods: Serial tumor and blood samples were collected under IRB approved protocols from melanoma patients receiving anti-PD-1 therapy. Plasma samples were obtained prior to initiation of therapy (pretreatment) and either 3 or 6 weeks after starting therapy (early on treatment). Exosomes were isolated from plasma using combined filtration and ultracentrifugation. RNA was extracted from exosomes using the exoRNA serum/plasma kit (Qiagen) and from tissue samples using the RNeasy mini kit (Qiagen) according to manufacturer instructions. Paired exosomal and tumor mRNA from patient samples and healthy controls underwent whole transcriptome sequencing using Affymetrix Whole Transcriptome Pico Array and analysis with the Affymetrix® Transcriptome Analysis Console (TAC) Software to perform principle component analysis (PCA) unsupervised clustering. Results: Patients with melanoma demonstrated a higher burden of exosomes compared with healthy controls (data not shown). Exosomal expression of the BRAF V600E mutation correlated with the mutational status of the parent tumor. Whole transcriptome analysis of patient-derived exosomes and paired tumors demonstrated 80% concordance of gene expression between RNA isolated from exosomes and tumor. (Figure 1A) Unsupervised clustering of exosomal RNA from pre-treatment samples demonstrated two distinct cohorts of patients, with an enrichment of responders/non-responders in the distinct cohorts. (Figure 1B) Conclusions: Exosomal mRNA reflects parental tumor mRNA, showing high concordance in gene expression. Notably, exosomal RNA signatures demonstrate evidence of clustering that may allow the stratification of responders from non-responders to anti-PD-1 therapy.

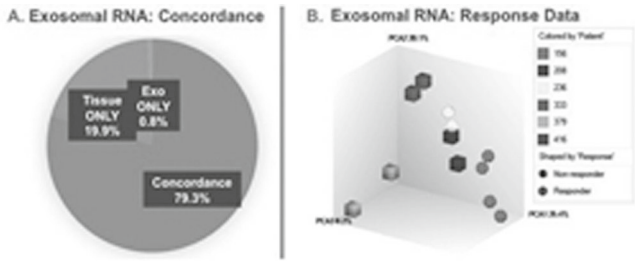
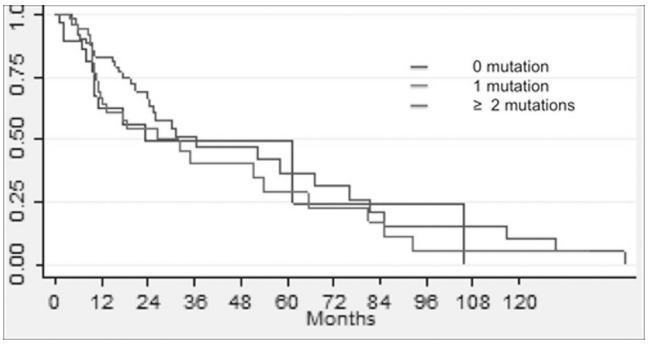


Figure 1 - (A) There is 80% concordance between tumor and exosomal RNA. (B) Clustering of exosomal RNA samples stratifies cohorts enriched for responders and non-responders.

PT273

Common Mutations Related to Recurrence in Melanoma Using Next-Generation Sequencing: A NCI-Designated Cancer Center's Experience E.P. Lamb,[1]* F. Zih,[1] M. Renzetti,[2] I. Soliman,[3] L.S. Anewenah,[4] H. Wu,[1] B. Luo,[1] E.A. Handorf,[1] S. Movva,[1] A. Olszanski,[1] M. Lango,[1] S.S. Reddy,[1] J.M. Farma.[1] *1. Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University School of Medicine, Dresher, PA; 3. Temple University, Philadelphia, PA; 4. Mercy Catholic Medical Center, Philadelphia, PA.*

Introduction: Melanoma is the deadliest type of skin cancer and its incidence has been rapidly increasing. This study investigates next-generation sequencing (NGS) and association with recurrence in melanoma patients at a NCI-designated cancer center. Methods: After obtaining IRB approval, patients with a diagnosis of melanoma underwent molecular profiling using institutional NGS platform, which evaluates for 50 commonly mutated cancer genes. Clinicopathologic characteristics, mutations, and recurrence were evaluated. Survival analysis was utilized to evaluate the association between number of mutations and recurrence. Results: We evaluated 158 melanoma patients with NGS (63% male). Median age was 65 years (range 24-93). 70 (44%) patients had ulceration, and the median number of mitoses was 5 (range 0-47). The pathologic stage included 10 patients with stage I, 53 with stage II, 68 with stage III, and 16 with stage IV disease. 13% received adjuvant radiation therapy and 24% received adjuvant systemic therapy. 19% had no mutations, 46% had 1, 19% had 2, 10% had 3, and 6% had 4+. The most common mutations overall were BRAF (n=45), NRAS (n=44), TP53 (n=26), and CDKN2A (n=19). 74 patients (47%) had a recurrence. Of these 74 patients with recurrence, 18% had no mutations, 44% had 1, 19% had 2, 12% had 3, 7% had 4+. The most common mutations in patients with recurrence were NRAS (n=24), TP53 (n=19), BRAF (n=16), and CDKN2A (n=7). Median length of follow up for this cohort was 1.4 years (range 0-18.5). At time of last follow-up, 45% had no evidence of disease, 23% were alive with disease, and 27% had died of disease. There was no assoication with increasing number of mutations and time to recurrence (Figure 1). Conclusion: The most commonly mutated genes found overall were BRAF, NRAS, and TP53, with NRAS being the most common in patients with recurrence. Increased number of mutations was not associated with recurrence. NGS use has increased in the clinical setting as an adjunct to guide therapy. However, it remains to be seen whether data from NGS prolongs overall patient survival.

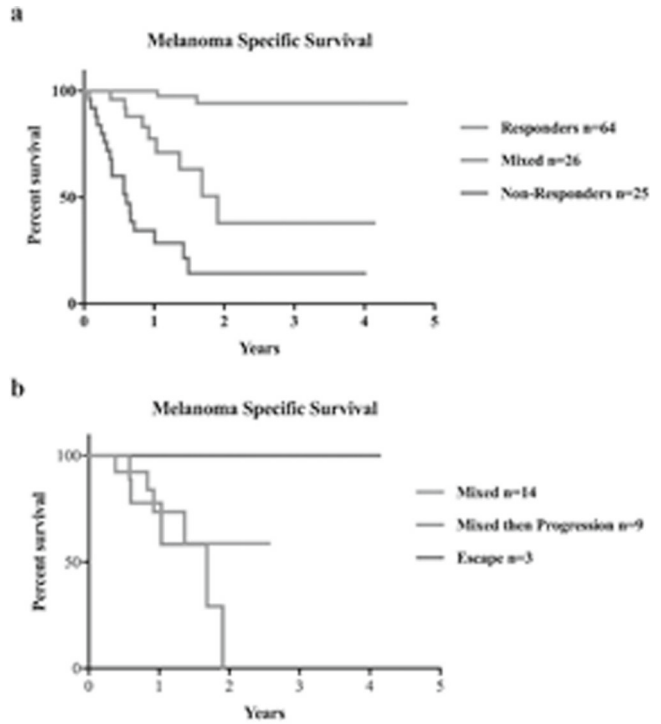


Time to Recurrence Based on Number of Mutations

PT274

Mixed Responder Cohort of Metastatic Melanoma Patients Treated with Anti Programmed Cell Death-1 S. Cohen,* J. Cintolo-Gonzalez, D. Plana, R. Sullivan, G.M. Boland. *Massachusetts General Hospital, Boston, MA.*

INTRODUCTION: Patients with advanced melanoma have historically had a dismal prognosis. However, the current immunotherapeutic agents are associated with long-term, durable clinical responses in a subset of patients. We describe 3 distinct cohorts of patients treated with aPD-1 therapy and associated clinical outcomes. METHODS: We reviewed prospectively collected data from 115 patients with metastatic melanoma treated at our institution. Mixed responders were defined by either: 1) clinical documentation of a mixed response or 2) radiographic evidence of tumor shrinkage in a subset of tumors and stability/progression in others. RESULTS: The clinical outcomes for 115 patients with advanced melanoma who underwent treatment with aPD-1 immunotherapy were reviewed. Of this cohort 58% were clear aPD-1 responders, 23% were mixed responders, and 22% were non-responders. Melanoma-specific survival data demonstrates a statistically-significant survival difference between the responders and non-responders at median follow up of 7.3 months ($p<0.0001$, Log-rank test), with 100% survival for responders and only 47% for non-responders (Figure 1). Mixed responders demonstrated a statistically-significant intermediate survival difference ($p<0.0001$, Log-rank test) (Figure 1a). We then subdivided patients with mixed response patterns based on their clinical course: 1) those who showed an ongoing mixed-type response to aPD-1 therapy; 2) those who demonstrated an initial mixed response but whose disease ultimately progressed on therapy; 3) and those whose metastatic disease demonstrated an almost complete response to aPD-1 immunotherapy but developed 'escape' lesions amenable to surgical intervention or radiation therapy (Figure 1b). CONCLUSIONS: aPD-1 immunotherapy is effective in advanced melanoma, offering durable disease remission. We have defined a subgroup of patients with a mixed response to aPD-1. Prospectively, our goal is to examine the mixed responders subgroup, which captures a heterogeneous population of tumors, and identify characteristics of those with more or less favorable biology in order to inform clinical decision-making regarding surgical management of metastatic disease.

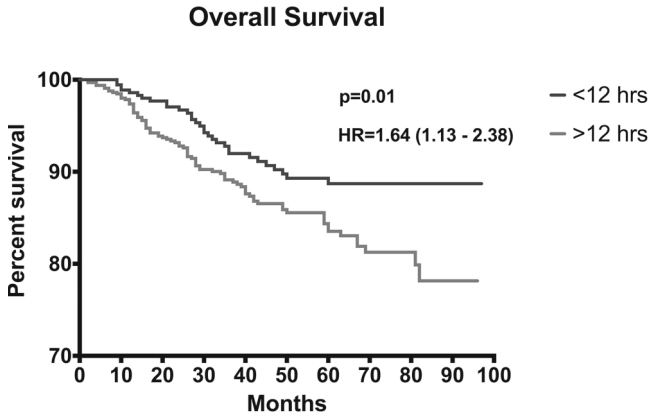


Melanoma Specific Survival in 115 Patients Treated with PD-1 Inhibitors

PT275

Survival Outcomes and Interval Between Lymphoscintigraphy and Sentinel Node Biopsy in Cutaneous Melanoma: Findings of a Large Prospective Cohort Study F. O'Leary,* C.J. Beadsmoore, D. Pawaroo, J. Skrypniuk, M. Heaton, M. Moncrieff. *Plastic Surgery, Norfolk and Norwich University Hospital, Bury St Edmunds, United Kingdom.*

Hypothesis: Sentinel lymph node biopsy (SLNB) in cutaneous melanoma (CM) is performed to identify patient at risk of regional and distant relapse. We hypothesized that timing of lymphoscintigraphy may influence the accuracy of SLNB and subsequent patient outcomes. Methods: We reviewed all prospective data on patients undergoing SNLB for CM at a large university cancer center between 2008-2015. SLNs were identified using a standardised dual-localisation technique of pre-operative lymphoscintigraphy using 20-40 MBq Tc99-labelled nanocolloid with early and delayed imaging in addition to intra-operative Patent Blue dye. Alongside demographic and tumour data, we recorded time of lymphoscintigraphy and time of surgery. Outcome data, including site of recurrence and survival, was collected. Kaplan-Meier survival analysis assessed disease-specific (DSS) and overall survival (OS), stratified by timing of lymphoscintigraphy. Cox multivariate regression analysis assessed independent risk factors for survival. Results: We identified 1015 patients. Median follow-up was 45 months (IQR 26-68 months). Univariate analysis showed a 6.8% absolute DSS (HR 1.6 [1.03-2.48], p= 0.04) benefit and a 10.7% absolute OS (HR 1.64 [1.13-2.38], p=0.01) benefit for patients whose SLNB was performed within 12 hrs of lymphoscintigraphy (n= 363) compared to those performed later than 12 hours (n=652). Multivariate analysis identified timing of lymphoscintigraphy as an independent predictor of OS (p=0.007) and DSS (p=0.016) when competing with age, sex, Breslow thickness and SLN status. No difference in nodal relapse rates (5.2% v 4.6%; p=0.67) was seen. Both groups were matched for age, sex, Breslow thickness and SLN status. Conclusion: We believe our data has significant implications for SLNB services. It suggests that delaying SLNB beyond 12 hours after lymphoscintigraphy using a Tc99-labelled nanocolloid has a significant and large negative survival impact for patients and should be avoided. We hypothesise that temporal tracer migration is the underlying cause and we advocate further trials investigating alternative, 'stable' tracer agents.

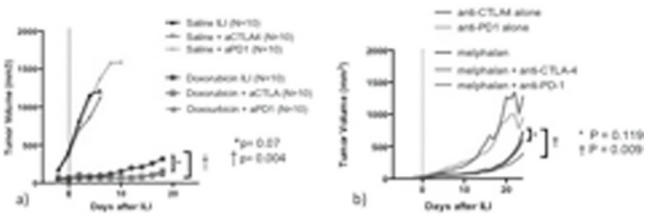


Kaplan Meier curve showing overall survival between early (<12 hours) and late (>12 hours) groups

PT276

Combination of Regional Therapy with Systemic Immunotherapy in a Murine Melanoma Model J. Perone,* T. Tamesa, M. Tsutsui, R. Alvarado, P. Dolber, I. Pinchuk, K. Olino, D. Tyler. *Surgery, University of Texas Medical Branch- Galveston, Galveston, TX.*

Introduction: While systemic immunotherapy strategies have resulted in marked improvement in melanoma treatment options for patients with metastatic disease, the role of regional therapeutics in potentially priming or augmenting this response has yet to be determined. The goal of this study was to determine if regional chemotherapy treatments could augment the effectiveness of systemic immunotherapy by generating immunogenic cell death. Methods: B16 F10.9-OVA melanoma was injected intradermally into C57BL/6 female mice to create a solitary leg tumor. Mice received treatment with systemic aCTLA4 alone, aPD-1 alone, or both or received unilateral isolated limb infusion (ILI) with the maximally tolerated dose either of vehicle, melphalan, or doxorubicin on day 0, with or without systemic aCTLA4, aPD-1, or both on days -2, 0, and 2 (100μg i.p.). Tumor volumes were measured daily. Results: Systemic immunotherapy in the form of anti-CTLA4 or anti-PD1 when used alone led to no significant change in melanoma tumor growth compared to saline control (figure 1a). Regional ILI alone with either doxorubicin or melphalan led to marked tumor responses in the treated leg. The addition of anti-PD1 but not anti-CTLA4 to regional chemotherapy led to a statistically significant improvement in the response of the regionally treated tumor, p= 0.004 and p=0.009 doxorubicin and melphalan respectively (figure 1a and 1b). Bioplex analysis of immunologic pathways in tumor samples suggested a role of innate immune response as evidenced by changes in the following cytokines: VEGF, GMCSF, and MIPs 1α, MIP 1β and MIP 2. Conclusion: The addition of systemic checkpoint blockade therapy with regional chemotherapy using melphalan or doxorubicin ILI markedly augmented regional tumor responses. Preliminary data suggests that immunologically based pathways may be important in this process.



PT277

Phenotype Switching is Regulated by Inflammation in Melanoma

M. Lim,* J. Wang, H.P. Redmond. *Cork University Hospital, Cork, Ireland.*

Background: In melanoma the clinical effect of an increased neutrophil to lymphocyte ratio indicates a worse prognosis, but data on the in vitro effect of neutrophils is conflicting. The process of phenotype switching has been described in melanoma, whereby melanoma cells may gain or lose proliferative or invasive properties depending on stimuli from their microenviroment. The purpose of our study was to show that phenotype switching is regulated by neutrophils in melanoma. Methods: Primary and metastatic WM3248, WM164, A375, and SkMel28 melanoma cell lines were studied. Conditioned media (CM) was prepared by inoculating 10^6 melanoma cells, 10^6 neutrophils, or 10^6 melanoma cells & neutrophils at a 1:1 ratio, in 15ml of culture media for 24hrs, and then collecting the filtrate through a 0.2μm membrane. 1μg/mL of lipopolysaccharide (LPS) was used to stimulate neutrophil activation. The CM was then used to culture melanoma cells for 24, 48, and 72hrs each, at starting concentrations to achieve 80% confluency at each time-point, and proliferation was then assessed using the MTT assay. Experiments were conducted in triplicate and repeated twice. Differences between groups were compared using ANOVA and a p value of <0.05 was considered statistically significant. Results: Melanoma cells cultured with CM treated with neutrophils result in reduced proliferation in the WM3248, WM164, and A375 cell lines compared with CM treated with melanoma cells alone ($p<0.0001$). This was independent of neutrophil-melanoma co-culture and activation with LPS. This effect was not seen in the SkMel28 cell line, but CM treated with melanoma cells and LPS resulted in increased proliferation for this cell line ($p<0.001$). Conclusion: Neutrophils result in a phenotype switch towards reduced proliferation in these primary malignant and nodal metastatic melanoma cell lines, but not in the visceral metastatic cell line. This effect was achieved in the absence of direct contact between the neutrophils and melanoma cells. The secretory neutrophil may play a role in melanoma cells switching towards either an invasive or dormant phenotype. Further study is required to assess this and the underlying mechanisms therein.

PT278

Prognostic Factors in Cutaneous Head and Neck Melanoma

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Introduction: Head and neck (H&N) melanoma accounts for 15-30% of primary melanomas. The objective of this study is to identify and assess novel prognostic features associated with cutaneous melanomas of the head and neck. Methods: Retrospective review of patients undergoing sentinel lymph node biopsy for cutaneous melanoma of the H&N (1998-2016). Using Cox proportional hazards model, variables associated with disease free survival (DFS) and overall survival (OS) on univariate analysis with a $p<0.1$ were analyzed on multivariate analysis. Results: Among 256 patients identified, median age was 57 years (range 14-91) years, 196 (77%) were male, and median tumor depth was 1.6 mm (range 0.25-12.0). The majority of melanomas (65%) were first noticed by patients although 9% were diagnosed by a hairdresser. Cryotherapy was performed on the melanoma site prior to diagnosis in 9% of patients. Transection at the base of the diagnostic biopsy occurred in 96 (38%) patients, yet 74 (77%) had no residual melanoma on the wide local excision (WLE). In total, residual melanoma was found on WLE in 108 (42.2%) patients. A positive SLN was identified in 40 (16%) patients. At a median follow-up time of 2.3 years, 40 (16%) patients had a loco-regional recurrence and 43 (17%) had distant disease. Gender, diagnostician, prior cryotherapy, type of melanoma, mitosis, and a transected biopsy were not associated with DFS or OS. On multivariate analysis, factors associated with both a worse DFS and OS included increasing age and tumor depth, scalp melanoma, ulceration, and a positive SLN. Although residual melanoma on the wide local excision was associated with a poorer DFS, it was not found to be significant for OS (Table 1). Conclusion: Increasing age and tumor depth, scalp melanoma, ulceration, and a positive SLN are poor prognostic features in H&N melanoma. Three quarters of patients with a positive deep margin on diagnostic biopsy had no residual melanoma at WLE. Independent of other prognostic variables, residual melanoma was associated with a worse DFS.

Multivariate hazard ratios using Cox proportional hazard models of variables associated with overall survival (OS) and disease free survival (DFS) with a p-value <0.10 on univariate analysis.

Variable	Overall Survival Multivariate HR (95% CI)	p-value	Disease-Free Survival Multivariate HR (95% CI)	p-value
Age	1.05 (1.02-1.08)	0.000	1.04 (1.01-1.06)	0.003
Location				
Face	1.0 (reference)	0.025	1.0 (reference)	0.145
Ear	1.22 (0.37-4.03)		0.80 (0.26-2.52)	
Scalp	2.58 (1.27-4.23)		2.07 (1.02-4.19)	
Neck	4.28 (1.11-16.43)		1.62 (0.34-7.70)	
Ulceration	3.72 (1.93-7.28)	0.000	2.69 (1.39-5.18)	0.003
Residual Tumor	1.00 (0.53-1.89)	0.999	2.19 (1.13-4.24)	0.021
Depth, mm	1.24 (1.08-1.43)	0.002	1.14 (1.01-1.31)	0.046
Positive SLN	2.16 (1.05-4.42)	0.036	2.62 (1.23-5.57)	0.013

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Outcomes from Sentinel Lymph Node Biopsy in Melanoma of the Ear and Nose

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Background: In comparison to melanoma in other anatomical regions, sentinel lymph node biopsy (SLNB) for head and neck melanoma is complicated by anatomically variable lymphatic drainage. In particular, predicting the lymphatic drainage of the ear and nose has proven challenging given their position at the anastamoses of multiple lymphatic drainage areas. This study describes the location of sentinel lymph nodes (SLN) from melanoma of the ear and nose, the incidence of positive SLNB, and the incidence of melanoma recurrence following SLNB in these patients. Methods: A retrospective review was performed from a single-institution database with patients treated between 2001 and 2015 inclusive. Patients with primary melanoma of the nose or external ear who underwent SLNB were selected. Patient demographics, primary tumour details, sentinel lymph node level and histological findings, and recurrence data were determined. Results: Of the 32 selected patients, 27 had primary tumours of the external ear and five had primary tumours of the nose. The median number of SLN was two (range 1-4). Six patients (18.8%) had SLN identified in more than one lymph node level. Of patients with ear primaries, 51.8% of SLN were identified in cervical level II and 37% within the parotid. Patients with nose primaries had 40% of SLN identified in each of cervical levels I and II, and facial nodes. Six patients (18.8%) had a positive SLN identified, all had primary tumours of the ear. After a median follow up of 55 months, four patients developed ipsilateral nodal recurrence (15.4% of all negative SLNB). The median number of SLN in the false negative group was two compared to 1.5 SLN in the true positive group. Three of the four patients with false negative SLNB had nodal recurrence in a different nodal station than the initial SLNB. All three of the patients with ear primaries and false negative SLNB had nodal recurrence in the parotid or pre-auricular lymph nodes. Conclusion: The location of the SLNB in melanoma of the ear and nose is varied and unpredictable. The parotid gland is a common site for nodal failure after a negative SLNB for melanoma of the ear and should be carefully monitored for recurrence.

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Melanoma Margins Trial: Early Effects of Narrow Excision Margins for Melanoma on Quality of Life, a Feasibility Study

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Introduction: A Phase III randomized controlled trial of 1cm vs 2cm excision margin of the primary lesion for adult patients with primary invasive cutaneous melanoma (pT2-4) is currently recruiting with a primary aim of detecting if there is any difference in local recurrence and/or melanoma-specific survival rates. It is hypothesized that a reduction in margins will also improve quality of life (QoL) in patients. We present an early analysis of QoL and complication rates in patients at one recruiting centre over the first 6-months of the trial from January 2015 to August 2016. Methods: All patients recruited to MelMarT from our unit after January 2015 with at least 6-months follow-up were included. Patient demographics, randomisation arm and patient-filled

questionnaires were analysed. Questionnaires included FACT-M, EQ-5D-5L, Follow-up Cost Questionnaire and 30-day complication rates. All scores were compared between groups at baseline, 3-months and 6-months. Results: A total of 55 patients were included; 28 in the 2cm margins and 27 in the 1cm margins arm. There was an equal male to female distribution in both (M:F, 15:13 2cm, 13:14 1cm). FACT-M scores in both groups were comparable at all points. There was a significantly higher 30-day complication rate in the 2cm group (42.9% versus 25.9%, p=0.02). Health related quality of life (HRQoL) were analysed; baseline EQ5D score was >0.9 for both groups. There was a near significant trend for a worse HRQoL at 3 months in the 2cm versus 1cm group (p=0.08). Mean HRQoL is lower in the 2cm group at 6 months but not significantly so. Total days lost in workforce, outpatient clinic visits made and days lost of usual activities was greater in the 2cm group compared to the 1cm group but this did not reach statistical significance. Conclusions: This feasibility study based on the data from a single centre provides some evidence that there may be negative effects on HRQoL from having a 2cm wide excision margin compared to 1cm for melanoma. The data also suggests this effect may be transient and resolves by 6 months. Future analysis from the full dataset will help to quantify the effect of this.

PT281

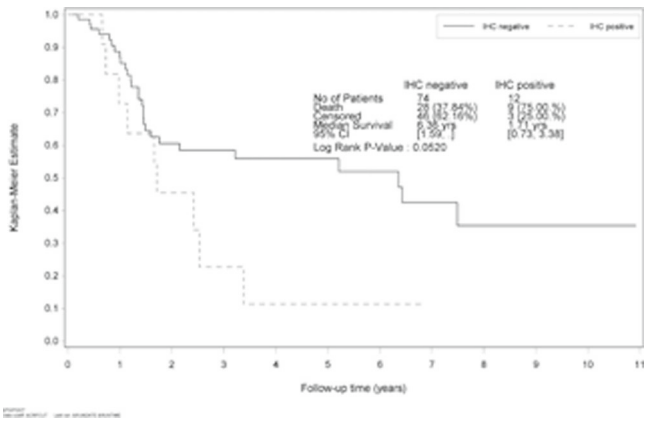
Effects of Histopathologic Margin Measurements on Recurrence for Invasive Melanomas R.J. Vidri Alonso-Rochi,[1]* A.M. Blakely,[2] G. Baird,[2] T.J. Miner,[2] M. Vezeridis.[2] *1. St. Mary's Regional Medical Center, Lewiston, ME; 2. Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI.*

Introduction Multiple prospective randomized trials have aimed to evaluate the optimal margin of excision for invasive melanoma, all of which were based on surgical excision margin rather than histopathologic margin (HPM). Perceived inadequate HPM has been used as justification for re-excision to reduce recurrence rates. However, literature regarding reported HPM and disease recurrence is lacking. Methods Retrospective review of a prospectively maintained database of all invasive melanoma treated surgically at a tertiary care center. Excision margins were 1 cm or 2 cm. Statistical analysis was by Cox proportional hazards model. Results Of 819 cases analyzed, 699 (85.3%) contained HPM measurements. Median tumor thickness was 3.4 mm (SD 7.4). Melanocytic atypia was seen in 210 specimens (25.6%), ulceration was present in 140 lesions (17%), and 452 tumors (55.2%) had mitotic rate ≥1. Median follow-up was 27.4 months. Disease recurrence was identified in 61 patients (7.4%), classified as local (n=15), regional (n=21), or distant (n=25). HPM smaller than excision margin was reported in 516 specimens (73.8%); 6 margins (0.9%) were positive. Overall recurrence was not associated with smaller HPM for either 1 cm (p=0.47) or 2 cm (p=0.1) excision margin cohorts. Local recurrence was not associated with smaller HPM in 1 cm excision margins (p=0.26); smaller HPM in 2 cm excision margins were associated with higher risk of local recurrence (HR: 0.88, p=0.016). Increased risk of local recurrence was associated with melanoma thickness for 1 cm (p<0.005) and 2 cm groups (p<0.005). However, no association was found between tumor thickness and overall recurrence (both p>0.1). Ulceration was associated with increased overall recurrence by 5 and 2.6 times when 1 and 2 cm margins were used, respectively (p=0.018 and p=0.001). Conclusions This study revealed that smaller HPM measurements increase the risk of local recurrence for intermediate thickness and thick melanomas. Treatment guidelines are based on excision margins, but HPM may serve as a surrogate marker of quality melanoma care. A larger, randomized trial could better determine if definitive recurrence patterns exist based on HPM measurements.

PT282

The Prognostic Implication of BRAF V600E Mutation in Patients with Stage IIIb In-Transit Metastatic Melanoma R. Read,* R. Rawson, J. Madore, S. Lo, R. Scolyer, J. Thompson. *Melanoma Institute Australia, Sydney, NSW, Australia.*

Purpose To determine the incidence, prognostic significance and clinicopathologic correlates of the BRAF V600E mutation in patients with in-transit melanoma (ITM) metastases as a first site of recurrence. Methods 11,614 patients with single primary cutaneous melanomas were treated at Melanoma Institute Australia between January 1994 and December 2009. Of these, 505 developed ITM. ITM was the first recurrence in 190 patients. Sufficient archival paraffin-embedded ITM tissue samples were available for 86 of the patients who had ITM as their first site of recurrence. A tissue array was constructed using one mm cores punched from the 86 tissue samples and embedded in paraffin blocks. Immunohistochemistry used the BRAF V600E specific VE1 antibody (Long 2013).[1] Results The BRAF V600E mutation was present in 12 of 86 ITM (14%). There was a trend toward BRAFV600E mutations occurring in younger patients (mean age 64.2 years versus 70.8 years, p=0.066). There was no difference in the time from primary diagnosis to ITM diagnosis (24.8 months in BRAF V600E mutated versus 32.5 months in non-BRAF V600E mutated patients, p=0.351). Patients with BRAF V600E-mutated ITM had a 5YS of 20% while those without the BRAF V600E mutation had a 5YS of 64% (p=0.052). Discussion This study demonstrates a very poor prognosis in patients with BRAF V600E-mutated ITM. However, only 14% of ITM patients had a BRAF V600E mutation, making it a relatively uncommon in comparison with other advanced stage melanoma patients where BRAF mutations occur in approximately 40%, of which about 80% are BRAFV600E mutations.[2,3] This highlights the need for effective adjuvant and systemic therapies in this group of patients. 1. Long GV et al. Immunohistochemistry is highly sensitive and specific for detection of BRAF V600E mutation in melanoma. 2013. Am J Surg Path. 37:61-5. 2. Chapman PB et al. Improved survival with Vemurafenib in melanoma with BRAF V600E mutation. 2011. NEJM 364:2507-16. 3. Long GV et al. Prognostic and clinicopathologic associations of oncogenic BRAF in metastatic melanoma. 2011. JCO 29:1239-46.



Overall survival (years) from time of ITM diagnosis stratified by BRAF V600E IHC

PT283

Triangular Intermuscular Space Sentinel Nodes in Patients with Melanoma: Management and Relation to the Axilla T. Schoenfeldt,[1]* A. Chakera,[2] S. Lo,[1] K.T. Drzewiecki,[4] R.F. Uren,[3] J. Thompson,[1] O.E. Nieweg.[1] *1. Melanoma Institute Australia, Copenhagen, Denmark; 2. Department of Plastic surgery, University Hospital Herlev, Herlev, Denmark; 3. Royal Prince Alfred Hospital, Sydney, Sydney, NSW, Australia; 4. Department of Plastic surgery, University Hospital Copenhagenagen, Copenhagen, Denmark.*

Background: The triangular intermuscular space (TIS), defined by the teres major and minor muscles and the long head of triceps, is a known site of interval sentinel nodes (SNs) in melanoma patients. The efferent lymphatic from a TIS node passes anteriorly into the posterior axilla alongside circumflex scapular vessels. Management of TIS SNs is controversial, particularly when they are involved. The aim of this study is to analyze our management of such patients and their outcome. Methods: In this retrospective study melanoma patients with a SN in the TIS seen on preoperative lymphoscintigrams between 1992 and 2015 were retrieved from a single institution prospective database. Median follow-up time was 47 months. Results: Lymphoscintigraphy visualized TIS SNs in 261 patients, of whom 16 had bilateral TIS SNs. The primary tumors were located on the upper back in 256 patients (98.1%), on the arm in 4 (1.5%) and in the neck in 1 (0.4%). Seventy per cent of the patients were male. TIS SNs were surgically pursued in 156 patients (60%) and retrieved in 143 of them (92%), In 4 patients bilateral TIS SNs were retrieved. A TIS SN was tumor-positive in 15 patients (10.5%). Eight of these 15 patients underwent a concurrent ipsilateral axillary SN biopsy that revealed metastasis in 3. Two of these 3 patients underwent axillary lymph node dissection (ALND). The patient who did not undergo ALND later recurred in the axilla. The other 5 patients with a tumour-positive TIS SN and a negative axilla SN did not undergo

ALND and one of them later recurred in the axilla. Six of the 7 patients with a positive TIS SN and no concurrent axillary SN underwent ALND, of which one revealed more disease. None of these 7 patients recurred in their axilla. Conclusion: TIS SNs are most often seen in patients with melanoma on the upper back. They can usually be retrieved. Their pursuit is recommended for staging, as they are tumor-positive in 10.5% of the cases. As the ipsilateral axilla is the next nodal tier and can be involved, we recommend ALND in case of an involved TIS SN, even in the absence of an axillary SN or if an axillary SN is negative.

PT284

Profile of Mood States (POMS) Scoring in Early Stage Melanoma: Effects on Outcome T. Fischer,[1]* D. Nelson,[1] S. Gaitonde,[1] B. Bandera,[1] M.S. Jones,[1] M. Sim,[2] M. Faries.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. UCLA, Los Angeles, CA.*

Introduction: Profile of Mood States (POMS) 2 is a validated psychological test that has had limited but intriguing use in oncology; some suggesting a relationship of POMS scoring to outcome. We hypothesized that mood states would have an effect on outcome in patients with melanoma and evaluated the testing in a large, prospective international clinical trial. Methods: Subjects enrolled in the first Multicenter Selective Lymphadenectomy Trial were evaluated with POMS 2 testing pre-operatively, at 6 months and annually during follow up. In this analysis, we considered baseline scores in relation to clinical and outcome variables. Results: Among 2001 enrolled patients, 1947 patients were evaluable for this analysis. In this cohort, 1168 were randomized to sentinel lymph node (SLN) and 223 (19.1%) had SLN metastases. Mean total POMS scores were 13.6 with no difference between trial arms. Lower baseline total POMS score was associated with male sex ($p<0.001$), less ulceration ($p=0.0039$) and older age (54 vs 50 years old, $p<0.001$). Total POMS score was also associated with disease-free (DFS) and melanoma-specific survival (MSS). This effect seemed to be derived from the effect of the vigor component of the score. On multivariate analysis, higher vigor was associated with improved DFS and MSS (HR 0.97, 95% CI 0.96-0.98; HR 0.95, 95% CI 0.93-0.96). After dichotomizing patients as either high or low vigor, high vigor patients were more male predominant ($p=0.003$), with less ulceration ($p=0.002$), older age (53 vs 51 years old, $p<0.001$) and lower Breslow thickness (2.29 vs 2.69 mm, $p<0.001$). Conclusions: When including evaluation of baseline mood states collected from MSLT-I, increased vigor is associated with improved DFS and MSS. While the biological mechanism of this effect is not clear, it offers and intriguing target for interventional modification in future prospective studies.

Melanoma-Specific Survival

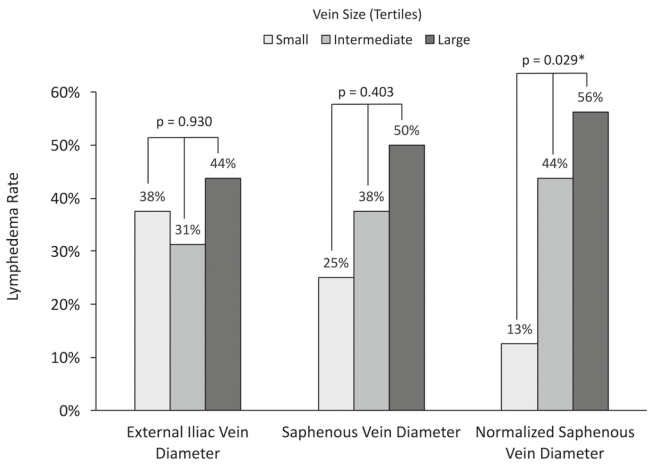
Cox PH Model	HR	95% CI		p-value
Vigor	0.947	0.933	0.961	<0001
Age	1.026	1.017	1.034	<0001
Male sex	1.377	1.085	1.748	0.0085
Breslow thickness	1.112	1.082	1.144	<0001
Ulceration	1.765	1.409	2.211	<0001
SLN positive	1.903	1.391	1.391	<0001
Site (ref: Extremity)				
Scalp	2.16	1.177	3.963	0.0129
Trunk	1.504	1.164	1.944	0.0018

PT285

Saphenous Vein Size Predicts Risk of Lymphedema Following Inguinal Lymph Node Dissection for Melanoma J.S. Lee,[1]* B.K. Chang,[1] A. Durham,[2] T. Johnson,[2] S.C. Wang,[1] M.S. Cohen.[1] *1. University of Michigan Department of Surgery, Ann Arbor, MI; 2. University of Michigan Department of Dermatology, Ann Arbor, MI.*

INTRODUCTION: Secondary lymphedema (SLE) is a common and morbid complication for melanoma patients undergoing inguinal lymph node dissection (ILND). Preservation of the saphenous vein (SV) has been associated with reduced risk of SLE, but venous insufficiency has not been well-studied as a potential preoperative risk factor for lymphedema, and could be assessed objectively using morphomics and cross-sectional imaging. We hypothesize that enlarged proximal SV diameter, suggesting venous insufficiency, is a direct predictor of increased risk of SLE following ILND. METHODS: We retrospectively reviewed preoperative CT scans (n=48) from a prospectively collected institutional database of melanoma patients undergoing ILND from 2005 – 2015. Using these scans, we measured the external iliac vein (EIV) diameter and SV diameter at the saphenofemoral junction bilaterally and calculated mean diameters. SV diameter was then normalized to EIV diameter to account for variation in patient size. Patients were then stratified into tertiles based on vein size. The rate of SLE between groups was compared using Fisher's exact test (significance = $p<0.05$). SLE was defined as referral to lymphedema clinic after surgery. RESULTS: For the cohort (n=48), mean age was 57 ± 2 years with 56% males and 44% females. Mean BMI was 29.2 ± 0.9 kg/m^2. Mean proximal SV diameter was 9.6 ± 0.3 mm and mean EIV diameter was 13.7 ± 0.3 mm. The overall rate of SLE for this cohort was 38%. Figure 1 shows the rate of SLE with patients stratified into tertiles of vein size. Normalized SV diameter was strongly associated with increased risk of SLE. Patients in the largest tertile of normalized SV diameter had a significantly higher risk of SLE compared to those in the smaller tertiles (56% vs. 44% vs. 13%, $p=0.029$). CONCLUSIONS: This is the first study to identify that enlarged proximal SV diameter is strongly associated with increased risk of SLE after ILND. This may reflect an underlying relationship between preoperative venous insufficiency and the risk of SLE. Evaluating this quantitative risk factor preoperatively may assist with patient risk stratification and operative decision making.

Figure 1. Lymphedema Risk Stratified by Tertiles of Vein Size



PT286

Combined Experience of Two Tertiary Referral Centers with MelanomaDx GEP Testing M. Renzetti,[1]* J.M. Farma,[1] E.A. Handorf,[1] I. Soliman,[1] M. Orloff,[2] A. Christopher,[2] S.S. Reddy,[1] H. Wu,[1] A. Olszanski,[1] S. Movva,[1] M. Lango,[1] H. Liu,[1] A. Berger.[2] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Thomas Jefferson University Hospital, Philadelphia, PA.*

INTRODUCTION: DecisionDx-Melanoma Gene Expression Profile (GEP) is a prognostic test for melanoma patients. It calculates a probability value (PV) for recurrence within 5 years of diagnosis through Class 1 (PV 0-0.49) or 2 (PV 0.5-1) stratification. Low risk Class 1 patients have a 97% rate of 5 years without metastasis. High risk Class 2 patients drop as low as 31%. Here we examine the initial combined experience of two tertiary referral centers use of this GEP in predicting clinical outcomes. METHODS: Patients with primary stage I, II, or III MM were included. Primary tumor tissue samples were sent for GEP. Clinical data was collected. RESULTS: We collected specimens from 95 patients with stage I (n=25), II (n=68), and III (n=6) MM. Median age at diagnosis was 62 (range 21-87), 50.5% were male (n=56). Median follow-up was 11 months (range 1-65). At last follow-up, 83 patients had no evidence of disease (NED), 7 were alive with disease (AWD), and 4 died of disease (DOD). 43.2% were Class 1 (n=41), and 56.8% Class 2 (n=54). In Class 1 patients, most common Stage was IIA (range IA-IIIB), and median PV was 0.36 (range 0-0.49). Median Breslow's thickness was 2mm (range 0.35-23), 22% were ulcerated (n=9), and 90.2% had mitosis >1/mm^2 (n=37). 39 patients (95.2%) had sentinel lymph node biopsy (SLNB), 4.9% were positive (n=2). In Class 2 patients, most common Stage was IIB (range IB-IIIC), and median PV was 0.65 (range 0.50-1.00). Median Breslow's thickness was 2.63 mm (range 1.1-19), 59.3% were ulcerated (n=32), and

96.3% had mitosis >1/mm^2 (n=52). 52 patients (96.3%) had SLNB, 13.5% were positive (n=7). 4.9% Class 1 patients recurred (n=2), 2.4% recurred with distant metastasis (n=1). 24.1% Class 2 patients recurred (n=13), 18.5% of patients recurred with distant metastasis (n=10). Median time to recurrence was 9 months (range 1-53), and PFS trends were found (P=0.18) (Figure 1). CONCLUSIONS: In our collaboration, we found Class 2 patients had higher rates of ulceration, high mitotic activity, and positive SLNB. They also had higher rates of first time recurrence, and recurrence with distance metastasis. Further studies will correlate Class subgroups with recurrence rate.

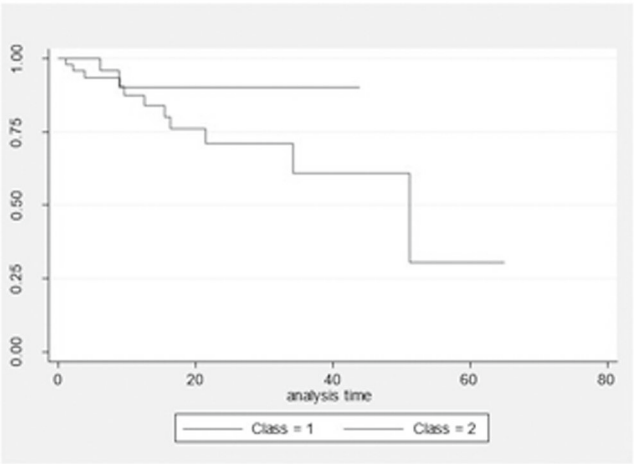


Figure 1: Progression Free Survival in Class 1 patients vs. Class 2 patients. Class 1 patients had higher rates of survival without recurrence (P=0.18).

PT287

Combining TIL and CARs in the Management of Metastatic Melanoma J.K. Mills,* M.A. Henderson, P. Petrone, J.A. Westwood, P.K. Darcy, M.H. Kershaw, D.E. Gyorki. *Peter MacCallum Cancer Centre and Victorian Comprehensive Cancer Centre (VCCC), Melbourne, VIC, Australia.*

Adoptive Cell Therapy (ACT) is a highly personalised form of systemic therapy for patients with cancer. For advanced melanoma, the most common form of ACT involves tumour infiltrating lymphocytes (TIL) extracted from metastatic tumour deposits, expanded in vitro away from the immunosuppressive tumour microenvironment and re-infused into a pre-conditioned patient. Other methods include genetically engineering peripheral lymphocytes to express antigen-specific receptors capable of inducing a T cell response (TCR engineering) with chimeric antigen receptors (CARs). This study combines these methods to create TIL transduced with anti-Her2 CAR to optimise ACT and enhance anti-tumour response in melanoma. Methods We generated a biobank of melanoma specimens and extracted TIL and generated autologous tumour lines from 33 patients. Tumour lines #10, #11 and #15 were examined by flow cytometry and found to express Her2. Cultured TILs were transduced with anti-Her2 CAR. We examined TIL-tumour pairs for in vitro activity measuring cytokine production and cytotoxic capacity. An in vivo analysis was performed using a melanoma xenograft model with NSG mice treated with ACT and monitored for circulating T cells, tumour growth and survival. Results Cultured TIL were transduced with anti-Her2 CAR with expression up to 92% following antibiotic selection. Transduced TIL demonstrated function in vitro against matched melanoma tumour cells with production of IFNγ through both TCR and CAR. Transduced TIL demonstrated significantly higher production of IFNγ and greater killing capacity than non-transduced TIL against patient matched melanoma cell lines. Our pilot in vivo study yielded promising early results, with tumours in NSG mice injected with anti-Her2 CAR TIL demonstrating the slowest rate of tumour growth, including tumour regression, compared to matched non-transduced TIL and matched peripheral T cell controls. Conclusion These results suggest transduction of TIL with anti-Her2 targeted CAR increases the anti-tumour efficacy of TIL against human melanoma. Further work is required to identify whether TIL engineered with tumour-specific CAR will increase the efficacy of ACT in treating patients with metastatic melanoma.

PT288

Incidence, Predictors and Significance of Pelvic Sentinel Lymph Nodes in Inguinal Sentinel Lymph Node Biopsy for Melanoma D.S. Swords,* R.H.I. Andtbacka, T.L. Bowles, J.R. Hyngstrom. *University of Utah, Department of Surgery, Salt Lake City, UT.*

Introduction: Drainage to pelvic (iliac/obturator) sentinel lymph nodes (SLNs) is common for trunk, lower extremity and perineal melanomas, but management is variable. We hypothesized that pelvic SLNs provide valuable prognostic information. Methods: Our melanoma registry was queried from 1/06-6/16 for inguinal SLNBs. Exclusions: age < 18, clinically metastatic nodes, SLNB for recurrence and patients (pts) without superficial inguinal SLNs. Data were analyzed with descriptive statistics and logistic regression for factors associated with pelvic SLNs. Results: 421 inguinal SLNBs were performed in 409 pts. The radiologist correctly identified pelvic SLNs on scintigraphy before surgery in 7% of pts. At surgery, pelvic SLNs were identified and removed in 71 inguinal SLNBs (17%). In pts with a pelvic SLN, 86% had ≥ 1 blue superficial inguinal SLN but only 35% had ≥ 1 blue pelvic SLN (P<0.001). In 80% of pts, superficial inguinal SLNs were more radioactive than pelvic SLNs. By univariate analysis there were no differences in patients with/without pelvic SLNs in age, race, BMI, primary melanoma location, T stage, or other pathologic factors. Pts with pelvic SLNs were more often female (76% vs 63%, P=0.04) and had ≥ 1 metastatic superficial inguinal SLN (37% vs 22%, P=0.01). On multivariate analysis, female sex (OR 1.9, 95% CI 1.1,3.5) and inguinal SLN metastasis (OR 2.1, 95% CI 1.2,3.7) were independently associated with presence of pelvic SLNs. Only 1 pt (1.4%) had a metastatic pelvic SLN; this pt also had a metastatic superficial inguinal SLN. Among 70 pts with metastatic superficial inguinal SLNs who underwent superficial groin dissection only, there were no differences in superficial inguinal/pelvic or any recurrence and melanoma-specific or overall survival for those with/without pelvic SLNs (P>0.35 for all, Log-rank). Conclusion: Pelvic SLNs were found in 17% of pts with trunk, lower extremity and perineal melanoma and associated with female sex and superficial inguinal SLN metastases. The very low rate of pelvic SLN metastases and similar recurrence/survival compared to patients without pelvic SLNs challenge the value of removing pelvic SLNs.

PT289

Factors Influencing Choice of Completion Lymph Node Dissection After a Positive Sentinel Lymph Node in Patients with Melanoma: A Large Single Institution Experience K. Isaacs,[1]* S. Pasquali,[2] A. Spillane,[1] J. Thompson.[1] *1. Melanoma Institute of Australia, North Sydney, NSW, Australia; 2. University of Padova, Padova, Italy.*

Most guidelines recommend completion lymph node dissection (CLND) for melanoma patients with a positive sentinel lymph node (SLN); however rates of CLND vary widely. The value of CLND is under investigation in the Multicentre Selective Lymphadenectomy Trial 2 (MSLT2) and the DeCOG study. We sought to establish the rates of CLND at Melanoma Institute of Australia (MIA), and to explore reasons why patients did not proceed to CLND. Data were obtained from a prospectively maintained database. We included patients with a positive SLN between Oct 2004-Feb 2014. We assessed features including patient demographics, primary tumor characteristics, SLN characteristics and treating surgeon, and investigated their influence on treatment with CLND. We also investigated if these features influenced screening and randomization to MSLT2. Of 599 SLN-positive patients, 62% had CLND. Patients with interval SLNs and multiple SLN fields were less likely to undergo CLND. No other features were significantly associated with CLND. The majority of patients not undergoing CLND did so due to personal choice, rather than doctor recommendation. Males living closer to MIA, with thinner, non-ulcerated primary tumors and a lower SLN tumour burden were significantly more likely to be screened for MSLT2. Of 401 screened patients, 215 were randomized. Significant differences existed for both screening and randomization rates between the 6 MIA surgeons who enrolled >10 patients to MSLT2, despite no significant differences in the clinico-pathological features of patients they treated. Among patients screened for MSLT2, the overall rate of randomization per surgeon ranged between 18-85%. Almost two thirds of SLN-positive patients received a CLND. The strongest predictor for no CLND was a positive interval node or multiple nodal fields. Patient choice was a significant factor for no CLND. The strongest predictor of screening for MSLT2 and the likelihood of being randomized in the trial was the treating surgeon.

PT290

Implementation of the 7th Edition AJCC Staging System: Effects on Staging and Survival for pT1 Melanoma, a Dutch Population-Based Study C.M. Oude Ophuis,[1]* M.W.J. Louwman,[2] D.J. Grünhagen,[1] K. Verhoef,[1] A.C. van Akkooi.[3] *1. Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2. Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, Netherlands; 3. Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands.*

INTRODUCTION: In the 7th edition of the AJCC staging system the mitotic rate criterion replaced Clark level to increase correct classification of high risk thin melanoma patients (pT1B). Additionally, sentinel node biopsy (SNB) was recommended for nodal staging for pT1B melanomas. Aim: to evaluate the effects on pT1 substaging and clinical implications in the national pT1 melanoma population. METHODS: All pT1 melanomas diagnosed in the Netherlands between 2003 – 2014 were selected from the national cancer registry. Patients were stratified by cohort: according to AJCC edition: 1) 2003–2009 (6th) and 2), 2010–2014 (7th). Relative survival was calculated to estimate melanoma specific survival. RESULTS: A total of 29.546 pT1 melanoma patients were included. The pT1b proportion increased from 10.1% in cohort 1, to 21.5% in cohort 2. The proportion of performed SNBs per cohort increased: for pT1b melanomas alone from 4.5% to 13.0%. SNB positivity rate decreased from 10.5% to 8.8% for the entire pT1 population, and for pT1b melanomas from 11.3% to 8.6%. At 5 year, the relative survival rate was similar for pT1a and pT1b in both cohorts, namely pT1a 100% vs pT1b 97% (cohort 1), and pT1a 100% vs. pT1b 98% (cohort 2). CONCLUSIONS: The 7th edition of the AJCC staging system has caused an increased number of patients to undergo SNB, without an increase in SNB positivity rate. Survival between pT1 subgroups remains similar. The mitotic rate criterion for pT1b classification and the recommendation to perform SNB for pT1b melanomas should be reconsidered.

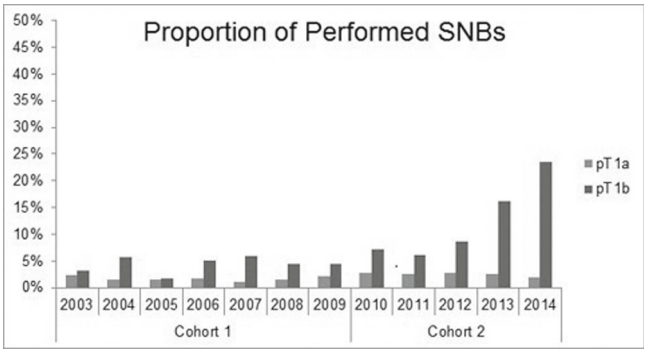


Figure 1. Proportion of Performed Sentinel Node Biopsies per Year.

PT291

Knockdown of ABCB5 Transporter Sensitizes CD133$^+$ Melanoma Subpopulation to RAS-RAF Pathway Inhibitors-Based Therapy M. Hassan,[1]* P. Friedlander,[1] A. Eshaq,[4] R. Wahl,[2] J.B. Hamner,[1] Y. Youssef,[3] M. Megahed,[2] M. Killackey,[1] E. Kandil.[1] *1. Tulane University School of Medicine, New Orleans, LA; 2. University Hospital of Aachen, Aachen, Germany; 3. University Hospital of Strasbourg, Strasbourg, France; 4. Alfaisel University, Rihyda, Saudi Arabia.*

Background: Despite the improved treatment options for melanoma patients, prognosis of patients with advanced malignant melanoma remains poor. Neoplastic clones are maintained by a small fraction of cells with stem cell properties. The focus of this study was to determine whether the resistance of CD133$^+$ melanoma subpopulation to available chemotherapeutics is attributed to the elevated expression of the stem cell marker, ATP-binding cassette sub-family B member 5 (ABCB5) that may be responsible for drug efflux and subsequent chemo-resistance of CD133$^+$ melanoma subpopulation. Material and Methods: Immunogenetic separation of CD133$^+$ cells from established melanoma cell lines BLM/NRAS-mutated and A375/BRAF-mutated, colony formation assay, Scratching assay, Cell viability assay, Flow cytometry analysis, Western Blot analysis. Results: The CD133$^+$ melanoma subpopulations isolated from established NRAS-mutated and BRAF-mutated melanoma cell lines have been confirmed for their ability to self-renew and to migrate. Data of the cell viability assay revealed that the CD133$^+$ subpopulations derived from either NRAS-mutated and BRAF-mutated cells conferring resistance to trametinib and dabrafenib, respectively, when compared to CD133$^-$ subpopulations. While the knockdown of the stem cell marker ABCB5 sensitized CD133$^+$cells to trametinib as well as to dabrafenib-induced cell death, as evidenced by MTT assay and Western blot analysis of PARP. Trametinib and dabrafenib-induced cell death was associated with the inhibition of the basal phosphorylation of extracellular regulating kinase 1 and 2 (ERK1 and2) and the expression of mitogen activated protein kinase phosphatase-1 (MKP-1) expression together with the activation c-jun-N-terminal kinase (JNK) and p38 pathways. Conclusion: Knockdown of ABCB5 by its specific siRNA is essential to overcome the resistance of CD133$^+$ melanoma subpopulation to NRAS/BRAF pathway-based therapy.

PT292

Utilization of Radiation Therapy for Regional Nodal Positivity in Cutaneous Melanoma of the Head and Neck: A Review of the NCDB P.D. Lorimer,* B.M. Motz, K.K. Walsh, Y. Han, J.C. Salo, R.L. White, J. Hill. *Surgical Oncology, Levine Cancer Institute, Charlotte, NC.*

Introduction Cutaneous melanoma of the head and neck (MHN) presents unique challenges as a single lesion may spread to multiple regional nodal basins. Current guidelines espouse utilization of adjuvant therapy such as interferon, biologic agents and/or radiation therapy (RT) in patients with positive nodes and high-risk features. Rates of utilization of RT for regional nodal positivity in MHN are poorly described. Methods The National Cancer Data Base (NCDB) was queried for adult records with invasive node positive MHN (ICD-O-3 codes C440-C444) who underwent nodal dissection (2004-2012). Patients with distant metastases, unknown primary tumors and/or incomplete pathologic staging were excluded. Statistical analyses include Chi-square, univariate and multivariable regression with stepwise selection (significance level of .1 for inclusion) on the likelihood of receipt of RT. Results 2,500 patients were identified; 75.8% were male and 97.6% White. Median age was 59 years. The majority of patients had thick tumors; (71.6% with a T3 or T4 lesion). Overall, 14.0% of patients underwent RT. Of pN1 patients, 7.9% underwent RT, compared to 14.4% of patients with pN2 and 30.0%. On univariate analysis, men underwent RT more often (11.7% v. 2.0%). Patients undergoing RT had a higher median number of positive lymph nodes (3 vs. 1) and a higher median number of nodes examined (31 vs. 20, $p<0.05$). On multivariable analysis (Table), patients with fewer positive nodes were less likely to undergo RT. Patients who had more nodes examined were more likely to undergo RT. Patients treated in the hospitals in the lowest volume quartile were more likely to be treated with RT. Age, sex, race, distance to treating facility, ulceration, tumor thickness, type of facility, insurance status and income did not significantly influence receipt of RT. Conclusions Adjuvant RT for patients with MHN who have regional nodal disease who have had lymph node dissection appears underutilized in the NCDB. This does not seem to be due to limits in access to care, or demographic disparities. Increased utilization of RT in high-risk patients with MHN may improve patient outcomes.

Multivariable analysis of covariate influence on likelihood of receipt of radiation therapy

Covariate Examined	Odds Ratio	95% Confidence Interval
Pathologic N		
pN1	0.23	[0.17, 0.31]
pN2	0.42	[0.31, 0.57]
pN3	referent	
Number of Nodes Examined	1.01	[1.01, 1.02]
Hospital Volume (quartiles)		
Q1 (lowest)	1.63	[1.12, 2.39]
Q2	1.49	[0.99, 2.23]
Q3	1.47	[1.06, 2.03]
Q4 (highest)	referent	

PT293

Clinical and Pathologic Profiles of BRAF Genotypes N. Goel,* M. Renzetti, I. Soliman, S.S. Reddy, S. Movva, H. Wu, B. Luo, H. Liu, M. Lango, A. Olszanski, J.M. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: BRAF mutations are associated with approximately 66% of melanomas. Even though the V600E mutation is the most common oncogenic driver in melanoma, this mutation only represents a subset of genotypes. This study utilizes next generation sequencing (NGS) to evaluate patients with all BRAF genotypes. Methods: Patients with primary or recurrent MM of all stages were identified. Using NGS tissue samples were analyzed for BRAF mutations. Clinical and pathologic data, overall survival (OS), and disease-free survival (DFS) were collected. Results: Specimens from 162 patients with MM were collected. Of these, 50 (31%) had BRAF mutations. The majority were 34 (68%) which had V600E mutations, 9 (18%) had V600K mutations, 4 (8%) had V600R mutations, and 3 (6%) had G466V mutations. The median age was the highest for V600K at 67 and the lowest for V600E at 56. The median Breslow depths(mm) were 2.13, 2.5, 1.9, and 5 for V600E, V600K, V600R, and G466V, respectively. The majority of patients at presentation were stage 2 across all genotypes, except V600R where the majority were stage 3. 13 (38%) V600E patients recurred, 4 (44%) V600K recurred, 1 (25%) V600R recurred and no G466V patients recurred. 100% of V600K and V600R patients had metastatic recurrence compared to 69% of V600E patients. 4 (11%) V600E patients died of MM, 2 (22%) V600K died of MM, 2 (50%) V600R died of MM, and 1 (33%) G466V died of MM. Median OS for V600E was not reached. Median OS was 18.6 months for V600K, 11.7 months for V600R, and 8.8 months for G466V. The median DFS for V600E was 14.6 months, 17.6 months for V600K, 11.3 months for V600R, and 5.8 months for G466V. Conclusions: Analysis of our BRAF genotypes suggests that patients with V600K mutations tend to be older at presentation, have the highest recurrence rate at 44%, with all of these recurrences being metastatic. However, only 50% of V600K patients died of their disease. This could be attributed to presentation at an older age and death from other comorbidities. On the other hand, V600E patients presented at an earlier age and more commonly died of MM (66%). Further studies will examine these genotypes to evaluate trends that may lead to more effective individualized treatment plans.

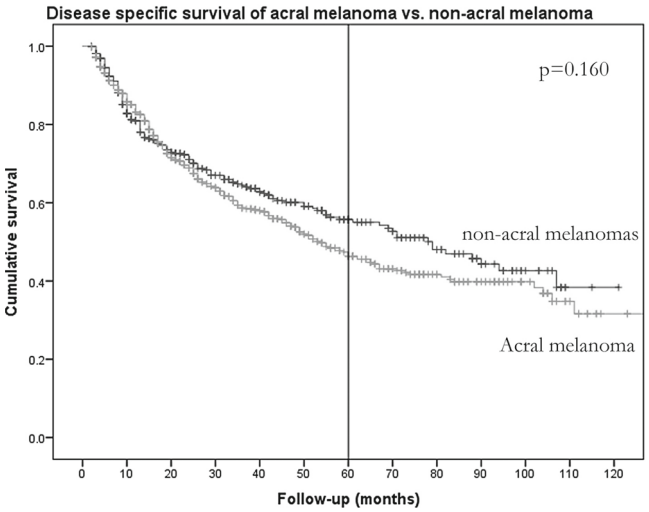
Clinical and Pathologic BRAF Genotype Data

BRAF Genotype	V600E (n=34)	V600K (n=9)	V600R (n=4)	G466V (n=3)
Median Age	56	67	62	66
Male	22 (65%)	6 (67%)	2 (50%)	1 (33%)
Race				
White	34 (100%)	8 (89%)	4 (100%)	3 (100%)
Other	0 (0%)	1 (11%)	0 (0%)	0 (0%)
Median Breslow (mm)	2.13	2.5	1.9	5
Clinical Stage				
1	6 (18%)	1 (11%)	0 (0%)	0 (0%)
2	16 (47%)	4 (44%)	1 (25%)	2 (67%)
3	5 (15%)	2 (22%)	1 (25%)	0 (0%)
4	4 (12%)	2 (22%)	2 (50%)	1 (33%)
Lymphovascular Invasion	6 (18%)	2 (22%)	0 (0%)	2 (67%)
Mitosis >1	27 (79%)	8 (89%)	3 (75%)	2 (67%)
Ulceration	13 (38%)	4 (44%)	2 (50%)	3 (100%)
Primary Site				
Head and Neck	7 (21%)	2 (22%)	1 (25%)	1 (33%)
Extremities	11 (32%)	2 (22%)	1 (25%)	0 (0%)
Trunk	11 (32%)	5 (56%)	1 (25%)	1 (33%)
Unknown/Other	1 (3%)	0 (0%)	1 (25%)	1 (33%)
Metastatic	4 (12%)	0 (0%)	0 (0%)	0 (0%)
Type				
Superficial Spreading	11 (32%)	4 (44%)	1 (25%)	0 (0%)
Nodular	14 (41%)	2 (22%)	1 (25%)	1 (33%)
Metastatic	4 (12%)	0 (0%)	2 (50%)	1 (33%)
Nevoid	0 (0%)	1 (11%)	0 (0%)	0 (0%)
Other	5 (15%)	2 (22%)	1 (25%)	1 (33%)
Recurrence	13 (38%)	4 (44%)	1 (25%)	0 (0%)
Local	3 (23%)	0 (0%)	0 (0%)	0 (0%)
Metastatic	9 (69%)	4 (100%)	1 (100%)	0 (0%)

PT294

Acral Lentiginous Melanoma has a Worse Prognosis? Survival Analysis of 715 Cases R. Salcedo Hernandez, L.S. Lino-Silva, C. Zepeda Najar,* L. García-Pérez. *Surgical Oncology, Instituto Nacional de Cancerología de México, Mexico city, Mexico.*

Background. Acral lentiginous melanoma (ALM) is an aggressive variant of melanoma; however, there are population differences in their incidence, prevalence and prognosis. We analyzed clinicopathologic features and survival of ALM cases in Hispanics, a population with high ALM prevalence. Material and methods. We analyzed 715 ALM from a National Referral Cancer Centre and we used 429 of non-ALM cases to perform a survival analysis comparison. Results. From ALM, 62.8% were female with median age of 58 years. The mean Breslow thickness was 3 5.6 mm + 7.16 SD. During a mean follow-up period of 34.02 months, ALM showed an estimated 5-years disease specific survival (DSS) for stage I, II and III of 53.3%, 52.7% and 40.8%, respectively and for non-ALM were 66%, 60.8% and 48.4%, respectively (p=0.168). Overall one-, three and five-year DSS for ALM were of 85.1%, 59.4% and 46.3 %, respectively, for non-ALM were 81.3%, 64.8% and 55.7 %, respectively (p=0.168). In the multivariate analysis the Factors associated with decreased DSS were high Breslow thickness (HR 1.565, 95% CI 1.322-1.854, p<0.001), recurrence (HR 1.658, 95% CI 1.256-2.188, p<0.001), ulceration (HR 1.550, 95% CI 1.120-2.144, p<0.001), male sex (HR 1.426, 95% CI 1.082-1.880, p=0.012) and advanced stage (HR 1.321, 95% CI 1.069-1.798, p=0.009). Conclusions. The 1-, 3- and 5-year DSS of ALM was not statistically different to non-ALM patients. Additionally to known adverse prognostic factors, male sex was associated with worse survival.



PT295

Impact of Time to Definitive Surgery When Residual Melanoma is Present Following Initial Biopsy A. Nadler,* M. Renzetti, I. Soliman, A. Olszanski, S. Movva, M. Lango, H. Wu, J.M. Farma, S.S. Reddy. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

INTRODUCTION: The impact of time from initial biopsy to definitive excision, or surgical interval (SI), for melanoma when residual melanoma (RM) is present in the final specimen is unknown. This study was undertaken to assess whether SI as it relates to RM affects prognosis. METHODS: A retrospective review from 2005 to 2016 was performed. The median SI was calculated. An SI of 30 days was used to divide groups (≤ 30 days for shorter SI vs. > 30 days for longer SI). Extreme outliers with an SI > 180 days were excluded. Survival was estimated with Kaplan Meier methods and compared with the log-rank test. Cox proportional hazards regression was used to adjust for covariates. RESULTS: 448 patients with non-metastatic cutaneous melanoma were included. The median age was 63 and 56% were male (n=250). All patients underwent radical excision of the primary lesion and 62.5% (n=280) underwent sentinel lymph node biopsy. The median SI was 33.5 days (range 0-87). On final pathology, 43.8% (n=196) had RM present. Thirteen percent (n=56) had positive lymph nodes. Median disease-free survival (DFS) was 94 months (CI 74-114) and median overall survival (OS) was 151 months (CI 95-207). There was no difference in DFS or OS for SI or RM alone. Those with

a longer SI in combination with RM had a significantly lower 5-year DFS at 57% compared to those with a shorter SI and no RM at 75% (p=0.033). There was also a significant difference in 5-year OS between the two extremes of SI and RM status (75% vs. 90%, respectively, p=0.043). On multivariate analysis, adjusting for age, gender, primary site, biopsy type, depth, mitoses, ulceration, and lymph node status, DFS and OS were no longer significant (p=0.430 and 0.191, respectively). CONCLUSION: When accounting for known prognostic factors, a longer SI and the presence of RM do not appear to affect outcomes for melanoma. Time pressures should not take priority over an appropriate pre-operative work up.

PF296

Disparities in the Utilization of Immunotherapy in Patients with Stage III Cutaneous Melanoma: A National Perspective

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Introduction: Immunotherapy combined with surgery has been shown to be associated with better survival in patients with advanced melanoma. In this study, we aim to examine the utilization pattern of immunotherapy in relation to population characteristics and the associated overall survival benefit. Methods: Retrospective cohort study utilizing the National Cancer Data Base, 2004 – 2012. The study population included adult (≥18 years) patients with stage III cutaneous melanoma who underwent surgery. Results: A total of 6,165 patients were identified with melanoma, median follow-up time was 32.0 months (interquartile range: 18.4 – 55.3). Immunotherapy was used in 1,854 (30.1%) subjects. Immunotherapy was associated with an overall survival benefit [HR: 0.66, 95%CI: (0.56, 0.77), p<0.001]. Younger patients and those with no comorbidities were more likely to receive immunotherapy (p<0.05 each). There was no racial disparity in the utilization of immunotherapy (p=0.07), however patients with Medicaid (29.9%) and Medicare (13.8%), as compared to those with private insurance (39.9%), were less likely to receive immunotherapy (p<0.01 each). Similarly, for patients who live in communities with low levels of education [OR: 0.59, 95%CI: (0.45, 0.76), p<0.001]. Conclusions: Immunotherapy demonstrates survival advantage in patients with advanced melanoma who underwent surgery. There are demographic and economic disparities in the utilization of immunotherapy at the national level.

PF297

Temporal Trends in Immunotherapy for Metastatic Melanoma

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Background: Development of novel immunotherapies has dramatically changed the therapeutic landscape for metastatic melanoma. Ipilimumab, the first agent with overall survival benefit in a randomized controlled trial, was FDA approved in 2011 and incorporated into national guidelines in 2012. However, the extent to which it has been integrated into clinical practice remains unknown. Methods: Patients diagnosed with stage III-IV melanoma in 2004-2013 were identified from the National Cancer Data Base. We used log-linear Joinpoint regression analysis to evaluate temporal trends in immunotherapy and chemotherapy (including targeted therapies such as BRAF inhibitors) use in stage IV as compared to stage III patients used as control for time trends. Multivariable logistic regression was used to determine patient and system-level factors associated with receipt of immunotherapy in 2011-2013. Results: For stage III (n=28937), chemotherapy use decreased from 2004-2013 while immunotherapy was unchanged until 2007, then decreased (APC -4.3%, p=0.0002). For stage IV (n=13422), rates of surgery were unchanged. Receipt of chemotherapy and immunotherapy was unchanged until 2009, then chemotherapy significantly decreased (APC -8.1%, p=0.004) while immunotherapy increased (APC 28.5%, p=0.0009). There was over a 2.5 fold difference in immunotherapy use between facilities with the lowest (13.1%) and highest (33.8%) stage III-IV melanoma patient volumes. Younger age, private insurance, less comorbidity, year of diagnosis, and treatment at a high volume center were associated with immunotherapy use. Conclusions: Immunotherapy use for patients with stage IV melanoma has increased; however, overall uptake remains low. This may reflect regionalization of care based on toxicity concerns, greater familiarity and access to new agents at specialized centers, or ambiguity surrounding optimal patient selection and sequencing of immunotherapy versus targeted agents. Efforts to clarify optimal treatment algorithms may enable oncologists to identify patients most likely to benefit from immunotherapy and could inform referral and treatment decisions for newer immunotherapies including anti-PD1 and combined immune checkpoint blockade.

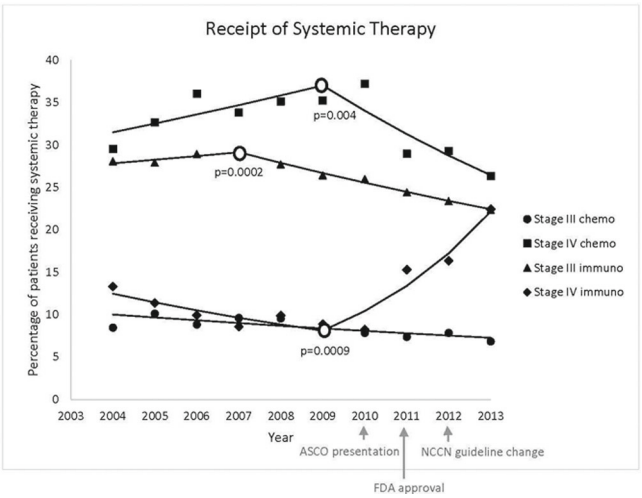

Figure: Joinpoint regression analysis for receipt of immunotherapy and chemotherapy for patients with stage III-IV melanoma. Open circle indicates that a change in slope has occurred and the associated p-value indicates statistical significance associated with this change.

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Oncologic Outcome of Videoscopic Groin Dissection for Lymph Nodes Metastasis from Melanoma

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Background Groin dissection is the recommended treatment in patients with melanoma metastases in the groin. The videoscopic ilio-inguinal lymphadenectomy showed a lower wound-related morbidity than the open technique. However, oncologic outcome data are still lacking. Aim of the study is to review the oncologic outcome of videoscopic groin dissection in a single institution caseload. Methods Data were prospectively gathered on patients with inguinal melanoma metastasis that underwent videoscopic inguinoiliac lymphadenectomy (VIL) from 2011 to 2016. Clinical data including age, race, sex, tumor histology, node counts, number of metastatic nodes, and size of the largest metastatic node were noted. Disease-free survival and overall survival were monitored during institutional follow-up schedule. The study was approved by the local ethics committee. Results We analysed 36 videoscopic groin dissections conducted on 35 patients (a patient underwent bilateral VIL). Median age was 54 years (IR, Interquartile Range, 38-63),. Female/male ratio was 23/12. Melanoma primary site was on the lower limb, trunk, anal canal and unknown in 21, 11, 1 and 2 cases, respectively. Indication for surgery was positive inguinal sentinel biopsy and cytological confirmed clinical disease in 29 and 7 cases, respectively. Median lymph node retrieval count was 19 (IR, 13-24).. After a median follow-up of 21,5 months (IR,9-42), locoregional recurrence (lymphatic basin) was observed in 2 cases (6%), both of them associated with systemic progression. Conclusions VIL for melanoma lymph node metastases is associated with a favourable oncologic outcome. In particular, lymph node yield and locoregional recurrence rate obtained with videoscopic dissection are similar to those reported with the open technique. Prospective and multicenter trials are needed to confirm these results in a larger cohort of patients.

PF299

Chemokines as Modulators of Mechanical Barrier Molecule Gene Expression in Melanoma

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Introduction: Immune cell infiltration into the tumor microenvironment (TME) is associated with improved overall survival in melanoma and other

cancers. We have recently found that decreased immune signatures in tumor and worse overall survival are associated with overexpression of a set of genes – filaggrin (FLG), dystonin (DST), and TACSTD2 (Trop-2), which mediate mechanical barrier function via cell-cell adhesion molecules. We hypothesize that barrier molecule gene expression can be modulated by chemokines and cytokines in the TME. Methods: Human melanoma DM93 cells cultured with various chemokines and cytokines were harvested at 24 hours. Total RNA was isolated with TRIZOL, complementary DNA was generated and qRT-PCR analysis was performed using forward and reverse primers for FLG, DST, and Trop-2. Samples were normalized to control DM93 expression of FLG, DST, and Trop-2 and beta-actin housekeeping protein, and were run in triplicate. Statistical analysis was performed using MedCalc. Results: CXCL10 increased expression of DST by 162-fold, of FLG by 128-fold, and of Trop-2 by 59-fold compared to untreated control group in DM93 human melanoma cells (Figure 1). CCL5 and CXCL9 induced 10- to 20-fold increases in FLG, Trop-2, and DST expression. Additionally, IL-4 increased Trop-2 1200-fold, and DST and FLG expression increased by 6- to 8-fold, respectively. IL-15 increased Trop-2 13-fold, and IL-21 increased FLG and DST 5-fold (Figure 1). Conclusions: CCL5, CXCL9, and CXCL10 are known to mediate T cell recruitment into the TME. Thus, findings of the present study suggest a novel and unexpected regulatory mechanism that limits chemokine effects in tumor tissues, as these chemokines induce overexpression of FLG, DST, and Trop-2 in human melanoma cells, which may thus fortify cancer-associated immune evasion. On the other hand, striking upregulation of Trop-2 by the Th2 cytokine IL-4 suggests that therapeutic enhancement of the Th1/Th2 cytokine balance in the TME may decrease tumor-induced immunologic barriers and support tumor control.

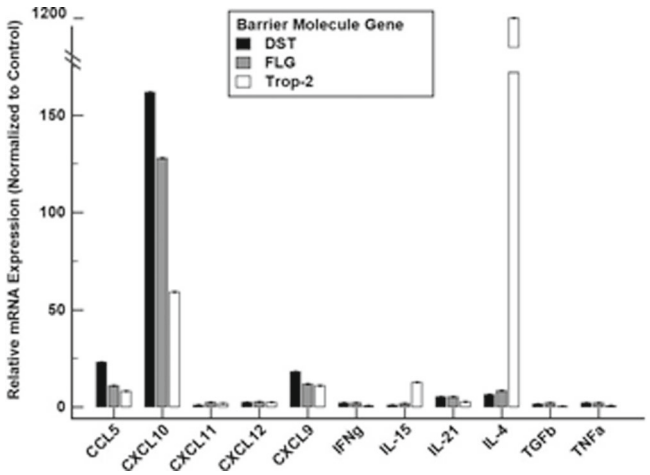

Figure 1: Relative mRNA Expression of Barrier Molecule Genes normalized to control DM93 human melanoma cells after treatment with various chemokines and cytokines.

PF300

Improved Survival in Melanoma Patients Following Resection of Solitary Gastrointestinal (GI) Tract Metastases A. Berger, G. Barmettler,* J. Kairys, M. Mastrangelo, K. Feeney, T. Sato. *Surgery, Thomas Jefferson University, Philadelphia, PA.*

Introduction: Patients with metastatic melanoma often develop GI tract metastases. When symptomatic, resection is often performed in the palliative setting. However, survival tends to be dismal. We hypothesized that in this current era of improving systemic therapy, patients with solitary GI metastases would have improved survival. Methods: A retrospective IRB approved chart review was completed on 40 patients with melanoma who underwent resection of alimentary tract metastases for melanoma between 1990 and 2015. We reviewed electronic and paper records for information regarding both melanoma primary and recurrent disease including whether the GI tract metastasis was symptomatic and/or isolated. Results: The average age of patients was age 53 at time of GI tract metastasis diagnosis. Thirty two had cutaneous primary melanoma sites, 3 had uveal primary sites, 4 unknown primary locations and 1 had a mucosal primary melanoma. Breslow thickness was 2.94 mm on average for primary melanomas with known location. Presentation was asymptomatic in 25%, with metastases found on surveillance imaging, pain in 33%, GI bleeding in 25%, anemia in 18%, and obstructive symptoms in 15%. Patients who had solitary alimentary tract metastases at the time of surgery (n=8) had a significantly higher median survival as compared to the median survival of patients with multiple distant metastases (n=28) at time of resection (33.2 months vs 7.4 months, P=0.003), with 5 of these patients having greater than 30 month survival. Conclusion: Patients with solitary GI metastases from melanoma who underwent surgery had significantly longer survival compared to those with widespread metastases. The role of surveillance imaging in melanoma cannot be understated as 25% of the patients undergoing resection of melanoma small bowel metastases were found on PET or CT with asymptomatic presentation. With longer survival times seen in cases with isolated metastases, resection should be the first-line treatment in those patients. As the treatment of metastatic melanoma has advanced with newer check-point inhibitors and targeted agents, there may be an increasing incidence of such cases.

PF301

Melanoma Patterns of Care in Ontario: A Call for Strategic Alignment of Multidisciplinary Care N.J. Look Hong,[1]* S.Y. Cheng,[2] N. Baxter,[3] F. Wright.[1] *1. Surgical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 3. St. Michael's Hospital, Toronto, ON, Canada.*

INTRODUCTION: Variability in the diagnosis and management of melanoma has prompted concerns about equitable, accessible, and timely treatment. The goal of this project is to identify population-based patterns of melanoma diagnosis and management in Ontario, Canada. METHODS: Patients with invasive, cutaneous melanoma were identified retrospectively from the Ontario Cancer Registry (2003–2012) and deterministically linked with administrative databases to identify incidence, disease characteristics, multimodal treatment within a year of diagnosis, and overall survival (OS). Treatment was categorized as inadequate or adequate based on standard multidisciplinary algorithms. Multivariable logistic regression was used to model factors associated with treatment adequacy. RESULTS: 21,876 patients with invasive melanoma were identified with annual age-sex standardized incidence rates of 11.7–14.3 for females and 13.4-15.9 for males (/100,000). Most melanomas occurred between ages 50-69 (median 62) and on extremities (43.9%). At median follow up of 5 years, OS was superior in females compared to males (80.9% vs. 69.1%, p<0.001). With significant geographic variation, 84.2% of patients received surgery as primary therapy, and 30.4% were staged with sentinel lymph node biopsy. Interferon therapy was more common in males (6.7%vs.4.8%, p<0.001), possibly reflecting worse disease at presentation. 2,891 (13.2%) patients received inadequate treatment, with worse survival than those with adequate treatment (76.1% vs. 64.3%, p<0.001). Adequacy was associated with age <49 (OR 1.38, 95% confidence interval (CI) 1.08-1.76), and consultation with dermatology (OR 1.62, CI 1.46-1.78), plastic surgery (OR 1.74, CI 1.59-1.92), or general surgery (OR 3.17, CI 2.87-3.50). CONCLUSIONS: Significant variations exist in melanoma management in Ontario. One in 8 patients are inadequately treated with associated worse survival. Provincial strategies to improve care may include physician/public education initiatives and creation of referral networks to promote guideline-congruent care.

PF302

Management of Thin Melanomas in the Community Hospital Setting C.R. Christ,* L.N. Weigand, M. Hellan, J. Ouellette, R.M. Tuttle. *Department of Surgery, Division of Surgical Oncology, Wright State University, Centerville, OH.*

Introduction: While the likelihood of identifying nodal metastasis in thin melanomas (<0.75 mm) is low, there is a lack of clarity for the use of sentinel lymph node biopsy (SLNB) in this population. The National Comprehensive Cancer Network (NCCN) guidelines state SLNB can be considered if there is uncertainty about the adequacy of microstaging allowing for differing interpretations. Here, we examine the use and outcomes of SLNBs for thin melanomas in a community hospital setting. Methods: Retrospective review of tumor registry data for thin melanomas (</=0.75 mm) treated at two community hospitals from 2010 to 2015. Results: 167 patients were treated for melanomas </=0.75 mm. Median age at diagnosis was 57 (Range 22-89). Means of diagnosis were: shave (52%), punch biopsy (6%), excisional biopsy (7%), multiple methods (1%), and unknown (34%). Biopsy margins were positive in 25% of patients and unknown in 53%. Median Breslow depth was 0.5 mm (range 0.11-0.75). 37 patients had mitotic index >/=1. Ulceration was present

in 6% of samples. 27% of patients were considered to have T1b lesions, and 27% of patients had attempted SLNB. 46 patients had residual melanoma on wide local excision (WLE). Breslow depth was found to be >0.75 mm on 9 patients on final pathology. There were zero positive sentinel lymph nodes identified in this patient subset. One patient developed a local recurrence and was found to have positive nodal disease on subsequent SLNB. Conclusions: Despite the presence of high risk features (mitotic index >/=1 or ulceration), the likelihood of identifying positive SLNs in patients with thin melanomas is exceedingly low questioning the benefit of this procedure for this patient population. Additional guidance added to national recommendations may improve the management of these patients.

PF303

Prognostic Significance of Microsatellitosis Melanoma

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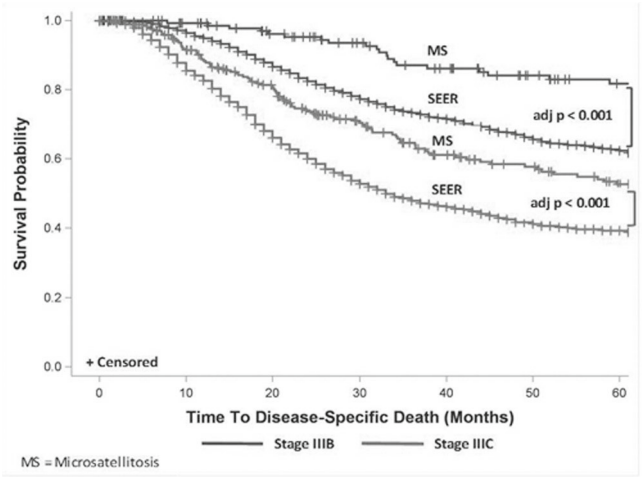
Introduction: Microsatellitosis (MS) in melanoma has been considered a marker of unfavorable tumor biology and has led to the staging of such patients with IIIB/C disease. To date, studies investigating MS have been limited by small sample sizes and incomplete nodal microstaging, making it difficult to discern its prognostic significance. We sought to better characterize outcomes and prognostic factors in a large cohort of patients with MS and compare these to a contemporary cohort of similarly staged patients from the Surveillance, Epidemiology and End Results (SEER) Program. Methods: Retrospective review of a multi-institutional and Sentinel Lymph Node (SLN) Working Group database identified 414 patients with MS who underwent SLN biopsy. Clinicopathologic characteristics in MS patients were associated with survival by univariate and multivariate analyses. Survival of MS patients was compared with stage IIIB/C patients from the SEER Program (2004-2012) using the log rank test. Results: Median age of the MS group was 64.9 years and 39.6% were female. Median thickness was 3 mm, 40.6% of cases were ulcerated and the SLN positivity rate was 46.7%. Factors significantly associated with decreased disease-specific survival (DSS) in MS patients in the multivariate analysis were increasing thickness (HR=1.05, p=0.017), presence of ulceration (HR=1.63, p=0.008), male gender (HR=1.58, p=0.018) and number of metastatic nodes (HR=1.12, p<0.001). 5-year DSS for MS patients with and without nodal metastases was 48.8% (40.2-57.4% 95%CI) and 76.9% (70.2-83.6% 95%CI) respectively (p<0.0001). DSS of both stage IIIB and IIIC patients with MS was significantly better (p<0.0001) than similarly staged IIIB (81.8% versus 62.3%) and IIIC (52.6% versus 39.2%) SEER patients (Figure). Conclusion: There is significant heterogeneity in outcomes among MS patients; SLN metastasis is observed at a high rate in this group and the presence of nodal metastasis is associated with significantly decreased survival. By contrast, survival in MS patients without other adverse tumor features (nodal metastases or ulceration) is considerably more favorable than the stage of these patients would otherwise suggest extrapolating from contemporary SEER data.



PF304

Melanoma Risk Prediction in Elderly Melanoma Patients with a 31-Gene Expression Profile Test

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Background: The elderly account for a substantial proportion of melanoma patients (pts), and melanoma mortality is rapidly increasing in this age group. Age >70 years is a poor prognostic factor and is significantly associated with other high-risk features including increased Breslow thickness (BT), ulceration, and regression. Conversely, there is a decline in the incidence of sentinel lymph node (SLN) positivity with increasing age, suggesting that SLN biopsy is less effective in the elderly population and/or they experience primarily hematogenous metastasis. As such, molecular prognostication using primary tumor tissue may be useful to improve metastatic and mortality risk estimates. Methods: The predictive performance of a previously validated 31-gene expression profile (31-GEP) test was evaluated in 521 patients, of whom 163 were ≥70 years-old ("elderly" cohort). Distant metastasis free (DMFS) and melanoma specific (MSS) survival were assessed using Kaplan-Meier and Cox regression analysis. Results: Compared to pts younger than 70 years of age, the elderly cohort predictably had a greater median BT (2.1 vs.1.4mm, p=0.063), more T3/T4 tumors (p=0.001) and more ulceration (p=0.043). The 5-year DMFS was 70% and and MSS was 86%. Median follow-up time for the elderly cohort was 4.2 years. The 31-GEP was able to stratify elderly cohort into risk groups (67 Class 1 and 96 Class 2 pts). Class 1 pts had a DMFS rate of 92% compared to 53% for Class 2 (Table), while MSS rates of 98% and 75% were observed for Class 1 and Class 2 groups, respectively. Univariate analysis of BT, mitotic rate, ulceration, SLN status and GEP class showed that all were significant predictors of distant metastasis risk (p<0.05). Combining those factors in a multivariate model, SLN status and GEP were the only significant predictors of risk (HR=2.8 and 9.6, p-values=0.01 and 0.03). Conclusions: In summary, the 31-gene expression profile test may provide additional prognostic value, and subsequently contribute to determining risk-appropriate management, in the elderly group of patients who often have high-risk pathology but benefit less from standard prognostic tools.

Table. Risk estimates according to molecular class in patients ≥70 years-old

Endpoint	Entire Cohort (n=163)	Class 1(n=67)	Class 2 (n=96)	p-value
Distant-metastasis free survival	70%	92%	53%	<0.0001
Melanoma-specific survival	86%	98%	75%	=0.0003

PF305

Tumor Biology of the Primary Melanoma is the Main Determinant in Predicting Those Unlikely to Benefit from Completion Lymphadenectomy (CLND) L. Cherkassky,* D. Comissiong, M. Vezeridis, T.J. Miner. *Surgery, Brown University, Providence, RI.*

Introduction: Whether melanoma patients with positive sentinel lymph node biopsy (SLNB) should proceed to CLND is controversial. Our objective was to assess the factors most strongly associated with non-sentinel lymph node metastases (NSLNM) and to identify a patient subset with extremely low likelihood of having additional metastases on CLND. Methods: This study is a retrospective analysis of a prospectively collected database containing all operative melanoma patients at Rhode Island Hospital. All patients enrolled between June 2005 and March 2015 with a positive SLNB were included for analysis. Patient, primary tumor and sentinel lymph node biopsy details were assessed for their association with NSLNM using Chi-square univariate analysis and multivariate logistic regression analysis. Results: 303 patients underwent SLNB, of which 77 were positive. The majority (65 of 77, 84%) of patients with positive SLNB underwent CLND, only 16 (74% negative CLND rate) of which had NSLNM. 14 additional lymphadenectomies for patients with clinically positive nodes all found positive nodes on lymphadenectomy. Univariate analysis demonstrated significant associations between NSLNM and depth of invasion (OR 1.45 [95% CI 0.24, 2.72]; p=0.047), mitotic count (OR 1.56 [95% CI 0.27, 3.11]; p=0.016), and angiolymphatic invasion (OR 1.77 [95% CI 0.52, 3.08], p=0.0057). A risk score that stratifies patients (0 to 6) according to these 3 variables of primary tumor aggressiveness remained independently associated with NSLNM. Only 2 of 24 patients (8%) with the lowest risk scores (2 or 3) displayed NSLNM, whereas patients with a score higher than 3 were 35% positive. Histologic features of SLNB, and radioactivity threshold for selecting SLNs, did not associate with NSLNM. Conclusion: Primary tumor aggressiveness, rather than patient or SLN characteristics, independently associates with risk for NSLNM. While we identify a patient subset at low risk for NSLNM that can be used to help counsel patients deciding to pursue CLND, further trials are necessary to determine who can safely forego CLND after a positive SLNB.

PF306

Risk Factors for Recurrence After Axillary or Inguinal Lymph Node Dissection for Melanoma B. Sunkara,* S. Diljak, R. Kramer, R. Strobel, D. Mercante, J. Jehnsen, J. Friedman, A. Durham, T. Johnson, M.S. Cohen. *Surgery, University of Michigan, Ann Arbor, MI.*

Objective: Although rates of recurrence and survival after lymph node dissection for melanoma have been well reported, the identification of risk factors correlating with this recurrence have not been well described to date. We hypothesize that from our large cohort, several risk factors will be identified that significantly increase the rate of melanoma recurrence after axillary (ALND) or inguinal lymph node dissection(ILND). Methods: We retrospective reviewed 375 patients from 2005-2015 from a prospectively collected institutional database of patients having ALND or ILND. Recurrence included local recurrence as well as distant metastasis. Patients having bilateral or multiple LNDs or follow-up less than 180 days were excluded. Recurrence rates in relation to each risk factor were statistically analyzed for significance($p<0.05$). Results: Of the 375 patients reviewed: 185 patients(49.3%) developed a recurrence[47(12.5%) local vs. 138(36.8%) distant]. Patients were less likely to have a recurrence if (a) they had a sentinel lymph node biopsy (SLNB) vs. presenting with clinically positive regional node(s) at diagnosis(45% vs 65%;p=0.03) or (b) had micrometastasis on SNLB vs. macroscopic disease on SLNB (39% vs 58%; p=0.004). Conversely, higher recurrence rates were observed in (a) patients positive nodes found on completion dissection vs. none found (64% vs 43%;p=0.001; however the number of additional nodes positive did not correlate with increased recurrence rates), or (b) 30-day readmission to the hospital (66% with recurrence if readmitted vs 45% with recurrence if not readmitted;p= 0.004), or (c) older patients at time of dissection (mean age of recurrent group: 58.1 vs 54.6 in group without recurrence; p=0.02). Conclusion: Following ALND or ILND, we identified from our large melanoma cohort several important risk factors correlating with higher recurrence rates, such as (1) older age at time of surgery, (2) 30-day hospital readmission after surgery, (3) macroscopically positive SLNB, and (4) positive nodes on completion lymphadenectomy. These important risks should be included in prognostic discussions with patients having ALND and ILND for metastatic melanoma.

PF307

Impact of Genetic Expression Profile on Decision-Making in Clinically Node Negative Melanoma Patients After Surgical Staging D. Schuitevoerder,* M. Heath, K. Massimino, J. Fortino, S. Leachman, J.T. Vetto. *Oregon Health & Science University, Portland, OR.*

Introduction: The surgeon's role in the follow-up of pathologic stage I and II melanoma patients has traditionally been minimal, with referral back to Dermatology. Melanoma genetic expression profile (GEP) testing can assist in predicting metastasis and formulating appropriate follow up. The objectives of this study were to determine the impact of GEP results on the management of clinically node negative cutaneous melanoma patients staged with sentinel node biopsy (SNB). Methods: Retrospective review of IRB-approved prospectively gathered data from a university multi-disciplinary melanoma program, consisting of patients seen from September 2015 - August 2016. Results: A total of 119 clinically node negative melanoma patients underwent GEP testing, of which 91 underwent SNB. Of these 38 (42%) were stage I, 42 (46%) were stage II, 10 (11%) were stage III, and 1 was stage IV. GEP testing showed 53 (58%) class 1 (Low risk) and 38 (42%) GEP class 2 (High risk). Of the patients with low risk GEP, 30 followed up with dermatology alone, 13 with surgery, 7 with surgery and recommendations for adjuvant trial, and 3 were followed by surgery and medical oncology. Of the 38 GEP class 2 patients, none followed up with dermatology alone, 13 followed up with surgery, 21 with surgery and recommendations for adjuvant trial, and 4 with surgery and medical oncology. On Fisher's exact test this follow up pattern was significantly different between high and low risk groups ($p < 0.001$). Among stage 1 patients, GEP class 1 were more likely to follow up with dermatology alone compared to GEP class 2 patients (82 vs. 0%, $p < 0.001$). In stage II patients, more class 1 patients following up with dermatology alone and more class 2 patients following up with surgery and recommendations for adjuvant trial ($p <0.05$). Conversely there was no difference in follow up for stage III patients based on the GEP results ($p = 0.76$). Conclusion: This study suggests that GEP results significantly impacts the management of stage IA - IIC melanoma patients after staging with SLB. Within this stage grouping, high risk GEP results (class 2) led to more aggressive follow up and management.

PF308

Application of Gene Expression Profiling in the Management of Cutaneous Melanoma X. Huang,* W.P. Hewgley, W. Guerrero, M. Fleming. *Surgical Oncology, The University of Tennessee Health Science Center, Memphis, TN.*

Introduction: The management of cutaneous melanoma (CM) is guided by metastatic risk since localized disease treated with wide local excision (WLE) carries an excellent prognosis. High-risk pathologic features determine whether patients require sentinel lymph node biopsy (SLNB) in addition to WLE. The use of gene expression profiling (GEP) as prognostic indicator has yet to be established despite achieving success in management of uveal melanoma. Methods: This is a prospective study of 139 patients with invasive CM at a single academic tertiary-care center. Primary tumor specimens were submitted for GEP categorizing the risk of the tumor as Class I (low) or Class II (high). The GEP classification was then compared to the pathologic features and clinical outcome. Results: Of 128 successful assays, GEP identified 24 Class II patients (18.75%) and 104 Class I patients (81.25%). Failed assays included 8 with inadequate cellularity (5.8%) and 3 with unsuccessful gene amplification (2.2%). Breslow thickness, ulceration, and mitotic rate were correlated with GEP risk classification on multivariate analysis ($P < 0.05$ for all), but they fail to explain 53.7% of the variation in GEP risk classification. Patients with Class II GEP were significantly more likely to have a positive SLNB on univariate analysis (OR 19.2, 95% CI 5.0-87.4), compared to pathologic features such as Breslow thickness (OR 3.2 per mm2, 95% CI 1.7-7.0), ulceration (OR 4.9, 95% CI 1.4-18.1), and mitotic rate (OR 1.3 per mitosis/hpf, 95% CI 1.1-1.6). Insurance companies initially denied payment for GEP in 65.5% of cases; written justification from the physician was required for coverage. Conclusion: CM's pathologic features correlate well with the results of GEP. However, high-risk GEP classification increases the odds of positive SLNB much more than traditional high-risk pathologic features. Obtaining GEP prior to definitive surgical planning may be beneficial, especially when SLNB is not indicated by pathologic features. In addition, patients with negative SLNB but high-risk GEP may be undertreated by current standard of care. Long-term follow up of these patients may require frequent exams and regular imaging.

PF309

Positive Sentinel Node in the Groin Area: Extent of Completion Lymphadenectomy and Prognosis for Melanoma Patients

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INTRODUCTION: The therapeutic effect of completion lymphadenectomy (CLND) after a positive sentinel node (SN) is still being investigated. Historical data may give valuable insight in whether the extent of a groin CLND, i.e. superficial groin dissection (SGD) or combined superficial and deep groin dissection (CGD) including pelvic nodes, is important for survival. The aim of the present study is to investigate if the extent of groin CLND after a positive inguinal SN is associated with disease free survival (DFS), distant metastasis free survival (DMFS), and melanoma specific survival (MSS). METHODS: Data of all SN positive patients who underwent a groin CLND at four tertiary melanoma referral centers were retrieved retrospectively. Inclusion was based on complete CLND details and absence of positive SNs outside the groin area. Patients were categorized as SGD or CGD. Baseline, patient and tumor characteristics were collected for descriptive statistics, survival analyses and Cox proportional hazards regression analyses. RESULTS: A total of 255 patients were included, of which 125 (49%) were men. Median age was 51 years [interquartile range (IQR) 39-62 years], median follow-up was 51 months [IQR 26-99 months]. Median Breslow thickness was 2.90mm [IQR 1.80-4.55mm], and 108 (42%) patients had ulcerated primaries. 137 (54%) patients underwent SGD, 118 (46%) a CGD. A high SN tumor burden (>1.0mm) was present in 30 (22%) SGD patients and in 46 (39%) CGD patients (p=0.003). SGD positivity rate was 11%, CGD positivity rate was 28% (p=0.001). Site of first recurrence was similar for SGD and CGD. 5-year MSS, DFS, and DMFS were similar between SGD and CGD. In MSS Cox-proportional hazards model CLND type was not significant, even after adjustment for known risk factors. CONCLUSIONS: CGD was significantly more often positive compared to SGD, but recurrence rate was similar. No relationship was found between extent of groin dissection and survival, indicating that SGD may be a safe first approach as CLND.

PF310

Outcomes Following Failed Sentinel Lymph Node Biopsy Due to Non-localizing Lymphoscintigraphy

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Introduction: In rare instances pre-operative lymphoscintigraphy fails to localize a sentinel lymph node in the draining nodal basin of a primary melanoma. We routinely proceed with excision of the primary without sentinel lymph node biopsy (SLNB), but outcomes following this strategy are largely unknown. Methods: Patients undergoing pre-operative lymphoscintigraphy followed by excision of a primary melanoma without SLNB between 2000 and 2015 were identified. Results: Lymphoscintigraphy failed to localize a sentinel lymph node in 15 patients. All patients underwent excision of their melanoma without SLNB, and search for sentinel lymph node intraoperatively was unsuccessful when performed. Median age was 64 (range 30-85). The primary melanoma was located on the trunk in 11 cases and on the extremity in four cases. Mean Breslow thickness was 2.3 (±1.8) mm; four were less than 1.0mm. Ulceration was present in three patients, and 12 patients had 1 mitosis per mm^2. The presence of mitoses served as the justification for lymphoscintigraphy in three patients with thin melanoma. No patients received adjuvant therapy. At a median follow up of 36.6 months (range 1-127 months), four patients experienced recurrence. Two patients had lymph node recurrence in the expected regional basin at 8.1 and 8.2 months. Both underwent therapeutic lymph node dissection upon detection of recurrence, and both have no evidence of disease (NED) at last follow up. One patient developed a single lung metastasis at 76.3 months, and she is NED after metastasectomy. One patient developed diffuse metastases at 13.2 months and died of disease. The remaining 11 patients have not developed regional or distant metastases despite failing to perform SLNB. Conclusion: When lymphoscintigraphy fails to localize a sentinel lymph node, proceeding with wide excision without SLNB, rather than attempting to repeat lymphoscintigraphy, is a reasonable approach. Not performing a SLNB following a non-localizing lymphoscintigraphy appears to have no adverse effect on outcomes. Additional studies may identify risk factors for regional recurrences in the absence of a localizing sentinel lymph node.

PF311

Early Detection of Disease Progression in AJCC Stage III Melanoma Patients Using Serum S-100B

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Introduction: In the current era of new and promising systemic treatment options for Stage IV melanoma patients, early detection of disease progression in Stage III melanoma patients is essential. The aim of this study was to identify disease progression in asymptomatic Stage III melanoma patients during follow-up using serum S-100B as biomarker. Methods: All Stage III melanoma patients in follow-up at the University Medical Center Groningen, were prospectively registered between February 2015 and September 2016. Follow-up was performed according to national guidelines. In addition, S-100B serum samples were collected during every outpatient clinic visit. In case of an elevated S-100B level (reference cut-off 0.10 μg/L), a S-100B increase of more than 40% within the reference cut-off, or in case of clinical symptoms, a FDG-PET scan was performed. Results: A total of 112 patients were included. Median age was 57 (range 49-68) years, 57 (51%) were female. Median follow-up time from the diagnosis of Stage III melanoma was 3.2 (range 1.8-5.1) years. Forty FDG-PET scans were performed, indications were the presence of symptoms in 50% (n = 20), an elevated serum S-100B in 28% (n = 11) and both symptoms and S-100B elevation in 8% (n = 3) (table 1). Local or distant disease progression was detected through FDG-PET scan in 25 patients, of which almost half (48%, n = 12) were performed based on serum S-100B elevation. Conclusion: These preliminary results suggest S-100B to be a useful biomarker for early detection of disease progression during follow-up in Stage III melanoma patients. Future studies will have to evaluate whether early detection is associated with lower tumor load, resulting in more surgically resectable tumors, or improved survival after systemic treatment.

Indications for, and outcome of FDG-PET scans (n = 40)

Indication	PET positive	PET negative
↑ S-100B	9 (36.0%)	2 (13.3%)
↑ S-100B and symptoms	3 (12.0%)	-
Symptoms only	13 (52.0%)	7 (46.7%)
Other	-	6 (40.0%)
Total	25	15

PF312

Clinical Patterns and Management of Primary Mucosal Melanoma

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Background. Primary mucosal melanomas (MM) are rare neoplasms that arise from melanocytes located in mucosal membranes lining the respiratory, gastrointestinal and urogenital tract. Delayed diagnosis and aggressive disease biology contribute to a poorer prognosis compared to their cutaneous counterparts. There is paucity in our understanding of the disease and the optimal management has yet to be established. We aim to describe the clinical patterns of MM treated in a large tertiary centre, over a period of 22 years, and investigate the differences between MMs in the head and neck versus those in other anatomical sites. Methods. A retrospective review of all patients diagnosed with MM from January 1993 to December 2015 in a single institution was conducted. Patient demographics and clinicopathological factors were collected and analyzed. MM in different sites were compared and overall survival (OS), disease-free survival (DFS) and time to locoregional recurrence (LRR) were calculated. Results. 50 patients were treated during the study period. Distribution of head and neck, gastrointestinal, urogenital and respiratory tract sites was 38% (n=19), 32% (n=16), 26% (n=13), and 4% (n=2) respectively. The median age was 63 years old (range 23-88), and 32 patients (64%) were female. The majority of patients (n=21, 42%) had localized disease, while 18 (36%) had nodal spread and 8 (16%) had distant metastasis at diagnosis. Surgical resection was the primary treatment and was performed with curative intent in 34 patients (68%), while 2 (4%) had palliative surgery for symptom control. Of the remaining patients who did not undergo

surgery, 6 had palliative chemotherapy and/or radiotherapy. The median DFS was 13 months (range 2-180), although there was a significantly longer LRR in the head and neck compared to other sites (p=0.01). Median OS for patients who had curative surgery was 42 months versus 9 months in patients who did not have surgery (p<0.0001). Conclusion. MM of the head and neck is diagnosed at an earlier stage and associated with a longer time to LRR. Surgical resection is the mainstay of treatment and is associated with improved OS.

PF313

Proteasome Inhibitor-Induced Sensitization of Melanoma-Initiating Cells to Fotemustine Depends on the Stabilization of the Tumor Suppressor Protein p53 M. Hassan,[1]* P. Friedlander,[1] F. Murad,[1] R. Wahl,[2] J.B. Hamner,[1] Y. Haikel,[3] M. Megahed,[2] M. Killackey,[1] E. Kandil.[1] *1. Tulane University School of Medicine, New Orleans, LA; 2. University Hospital of Aachen, Aachen, Germany; 3. University of strasbourg, Strasbourg, France.*

Background: Treatment failure in melanoma patients results mainly from the development of tumor heterogeneity as a consequence of the formation of genetically divergent subpopulations, including melanoma-initiating cells (MICs) with stem cell properties of self-renewal and differentiation. The anti-cancer agent fotemustine is a nitrosurea that has provenefficacy in metastatic melanoma and particularly on cerebral metastases. While bortezomib is a highly selective, reversible inhibitor of the 26S proteasome which has been approved for the treatment multiple myeloma. The aim of the present study is to investigate whether the inhibition of the ubiquitin- proteasome system can overcome the chemo-resistance of MICs to fotemustine. Material and Methods: Immune histochemistry (IHC) of melanoma specimens derived from primary (n=10) and metastatic (n=10) melanoma patients, Immunogenetic separation of $CD133^+$ cells, colony formation assay, Scratching assay, Cell viability assay, Flow cytometry analysis, Western Blot analysis. Results: The functional analysis of the melanoma subpopulation, $CD133^+$ cells (derived from melanoma specimens) demonstrated the self-renewal potency of $CD133^+$ cells as evidenced by colony formation assay. $CD133^+$ cells was characterized by the expression of the stem cell markers CD20, CD133, CD166 and CD271. $CD133^+$ cells confer resistance to fotemustine. While the combination of fotemustine with bortezomib was able to overcome the chemo-resistance of $CD133^+$ cells to fotemustine. Bortezomib-induced sensitivity of $CD133^+$ cells is attributed to bortezomib-induced stability of p53 protein that is essential for the modulation of fotemustine-induced apoptosis of $CD133^+$ cells. Conclusion: Our data provide evidence that the inhibition of the ubiquitin-proteasome system pathway is essential to improve the outcome of melanoma treatment with fotemustine.

PF314

Age-Dependent Variability in the Prognostic Utility of Node Evaluation in Patients with Melanoma M. Neuwirth,* A. Sinnamon, R. Roses, R.R. Kelz, D.L. Fraker, G. Karakousis. *Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction: Sentinel lymph node (SLN) biopsy is a well-established prognostic tool for patients with early stage melanoma, offered routinely to patients primarily based on primary tumor characteristics. While decision for lymph node evaluation is predominantly based on likelihood of SLN positivity, variability in its prognostic utility across tumor thickness and age has been less well studied. Methods: The American College of Surgeons National Cancer Database (NCDB) for melanoma was queried between the years 2004-2013 for patients with clinical stage I or II disease undergoing lymph node evaluation and found to have N0 or N1 disease. Cox proportional hazards models were then applied to determine relative hazard ratios of a positive lymph node across increasing age groups as well as primary tumor thicknesses. Results: Among patients with melanoma >0.5mm, 80,290 were identified who underwent nodal examination with either negative nodal status (N0) or a single positive node (N1). Fifty-eight percent of these patients were male, while median age was 60 (IQR 48, 71), median thickness was 1.4 mm (IQR 0.98, 2.5), and rate of nodal positivity was 9.1%. In serial multivariable proportional hazard model analysis, nodal positivity remained prognostically significant, however the associated hazard ratio decreased in value from 2.67 at age 25 to 1.57 at age 85 or older (p<.001), as shown in Figure 1. In contrast, the hazard ratio of nodal positivity across tumor thicknesses did not decrease significantly from 1.87 at 0.5mm to 1.76 at 10.0mm and thicker (p=0.70). Conclusion: The prognostic significance of lymph node status appears to diminish with increasing age while maintaining a fairly uniform significance across primary tumor thicknesses. These findings support prior recommendations for sentinel lymph node biopsy in patients even with thick melanoma. The variability in prognostic significance of lymph node status across age groups carries important implications when counseling and deciding for SLN biopsy in elderly patients.

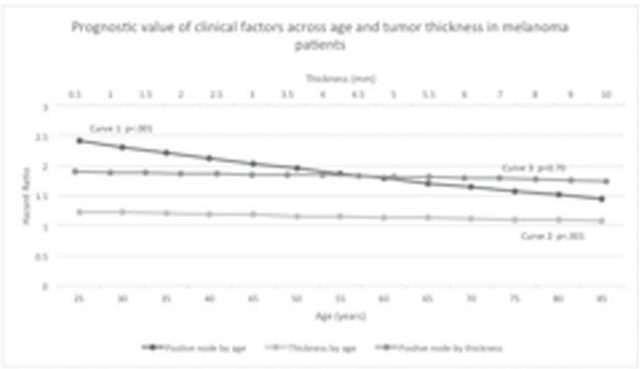


Figure 1. Changes in prognostic value (represented by cox regression hazard ratio) of lymph node status across increasing age groups and tumor thickness (curves 1 and 3). Change in prognostic value of tumor thickness across age (curve 2). Significant p-values (p<.05) represent a significant rate of change along the slope of the curve.

PF315

Preoperative PET/CT and Clinical Decision Making in Patients with Thick (T4 and Stage 3) Melanomas N. Goel,* M. Renzetti, I. Soliman, S.S. Reddy, S. Movva, H. Wu, B. Luo, H. Liu, M. Lango, M. Yu, A. Olszanski, J.M. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Although studies have shown a low yield for identification of regional or distant metastases by preoperative PET/CT for thin and intermediate thickness melanoma, the utility of preoperative PET/CT in patients with thick melanomas remains unknown. The objective of this study was to determine the clinical impact of PET/CT for initial staging in patients with thick T4 melanomas or Stage 3 disease. Methods: Retrospective cohort study of 178 patients with T4 and stage 3 melanomas. Inclusion criteria were initial presentation with T4 or stage 3 melanoma, no clinical evidence of metastatic disease, and an initial PET/CT. Results: 78 patients with an average tumor thickness of 5.13mm(range 0.37-25) were identified. 27 were stage 2 and 51 were stage 3. PET/CT identified 11 patients with regional metastatic disease. On final pathology, 10 of these 11 patients had regional metastatic disease. Our study shows a sensitivity and specificity for PET/CT with regional metastatic disease of 14% and 88%, respectively. In the literature, the sensitivity and specificity varies from 8%-100% and 84%-100%. In terms of distant metastasis, PET/CT identified 1 patient with pulmonary metastasis, however the CT chest was negative. One patient with anal melanoma had an intraoperative finding of liver metastasis not identified on preoperative PET/CT. For distant metastatic disease, the sensitivity and specificity of our study is 0% and 99%, respectively. In the literature, the sensitivity and specificity for distant metastatic disease ranges from 78%-100% and 22-87%. 9 patients also had incidental colon, thyroid, parotid, and cerebellar pathology. One required a hemicolectomy for a cecal mass with high grade dysplasia. The others had benign pathology. Conclusion: The melanoma related treatment plan was altered in 3 (4%) patients. Two patients went straight to completion lymph node dissection and 1 patient underwent systemic therapy. Additionally, 9 patients had incidental findings that required further workup. Our study suggests that patients with thick melanomas can benefit from a preoperative PET/CT, although the majority of patients will not have any findings to alter management.

Demographics and Preoperative PET/CT Imaging Results.

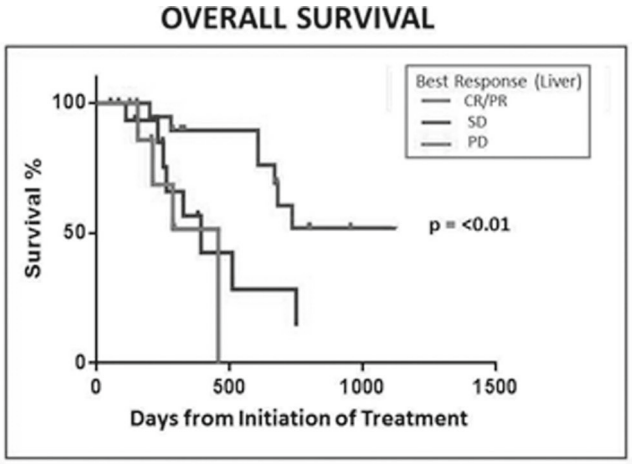
Patient Characteristics	
Patients	78
Male	45
Age (mean, range)	69
Race	
White	76
Black	1
Asian	1
Tumor Characteristics	
Mean Tumor Thickness (mm)	5.13 (range 0.37-25)
Lymphovascular Invasion	54
Mitosis	75
Ulceration	72
Location	
Trunk	29
Extremities	40
Head and Neck	5
Genital	1
Other	3
Imaging	
Positive Preoperative PET/CT for:	
Confirmed Regional Metastatic Disease	10
No Regional Metastatic Disease	1
Confirmed Distant Metastatic Disease	0
No Distant Metastatic Disease	1
Negative Preoperative PET/CT for:	
Confirmed Regional Metastatic Disease	59
No Regional Metastatic Disease	8
Confirmed Distant Metastatic Disease	1
No Distant Metastatic Disease	76

Sensitivity and specificity for PET/CT with regional metastatic disease is 14% and 88%, respectively.
Sensitivity and specificity for PET/CT with distant metastatic disease is 0% and 99%, respectively

PF316

Percutaneous Hepatic Perfusion (PHP) for Unresectable Metastatic Ocular Melanoma to the Liver: A Multi-Institutional Report of Outcomes A. Gangi,[1]* I. Karydis,[2] K. Thomas,[1] S. Sileno,[3] D. Hardman,[3] J. Choi,[1] M. Wheater,[2] B. Stedman,[2] C.H. Ottensmeier,[2] J.S. Zager.[1] *1. Surgical Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of Southampton, Southamptom, United Kingdom; 3. University of South Florida, Tampa, FL.*

Background: Patients with metastatic ocular melanoma (OM) have poor prognosis and limited therapeutic options. Percutaneous hepatic perfusion (PHP), a regional cancer therapy, allows for hepatic isolation and hemofiltration of high dose chemotherapy via a percutaneous approach. PHP has shown improved progression free survival (PFS) and outcomes in selected OM patients with hepatic metastases. Historically, survival rates for metastatic OM are reported as less than 12 months. Methods: Multi-institutional databases were reviewed. All patients with primary OM with liver metastasis treated with PHP between 2008 and 2016 were included in this retrospective analysis. Chart review was performed to evaluate response, PFS, hepatic PFS (hPFS), and overall survival (OS). Results: 49 patients underwent 115 melphalan based PHPs (median = 2, range =1-6). 57% of patients were female with a median age of 57.9 years (range, 27.9-77.1). 85% of patients had no extrahepatic disease at time of treatment and 33% had previous systemic therapy. Hepatic response to PHP was evaluable in 46 patients (94%). Of these, 45.7% showed complete or partial response (CR/PR), 37.0% had stable disease (SD), and 17.4% had progressive disease (PD). Projected median OS was 657 days. Median hPFS and PFS were 267 and 222 days, respectively. In those patients who had CR/PR, OS was 1207 days compared to 394 for SD/PD patients. Conclusions: The development of effective treatment strategies to provide durable control of hepatic metastases from OM remains a challenge. PHP provides an additional option for treatment of hepatic metastases from OM with high disease control rates. In this small series, responders had a median survival of over 3 years which is three times greater than historical data of patients with hepatic metastases from OM. In appropriately selected patients, PHP may provide long term control of unresectable metastatic OM confined to the liver.



PF317

Predicting Lymph Node Positivity in Melanoma Patients E.E. Abbott,[1] K. Shaffer,[1] A. Bayci,[1] Z. Hothem,[1] B. Thibodeau,[2] S. Ahmed,[2] A. Uzieblo,[1]* G. Wilson,[2] R. Keidan.[1] *1. General Surgery, William Beaumont Hospital, Royal Oak, MI; 2. Beaumont BioBank, Royal Oak, MI.*

Introduction The five-year survival of melanoma patients is dramatically decreased for those with regional disease (62.6%) compared to those with localized tumors (98.1%). Sentinel lymph node biopsy (SLNB) as a staging tool carries risk of operative morbidity and increases cost. While SLNB is only performed for lesions felt to be high-risk for nodal or distant metastasis, only 15% of patients undergoing SLNB will have positive lymph nodes. We aimed to find variations in gene expression in primary melanoma lesions and nodal tissue of patients with confirmed positive or negative lymph nodes in order to avoid unnecessary SLNB. Methods Formalin-fixed paraffin-embedded samples of skin lesions of SLN-positive (n=1) and SLN-negative (n=2) patients as well as nodal samples [SLN-positive (n=5) and SLN-negative (n=2)] were examined. Laser capture microdissection was used to isolate pathologist-identified tumor cells. DNA was isolated and used to prepare libraries for next generation sequencing using the TruSeq Amplicon - Cancer Panel on the Illumina NextSeq 500. Software was used for alignment and variant calling based upon mutation percentage, total coverage, and balance ratio of forward and reverse reads. Further biological interpretation was performed using variant analysis software. Results Analysis focused on genomic variation in 48 cancer-related genes. Fourteen genes were found to have variants in >70% of the positive node samples while not being present in any samples with negative nodes. These included EGFR and PDGFR. Variants in ERBB4 were present in all of the positive node samples but were not seen in any of the negative node samples. Genes such as ATM, PIK3CA, and TP53 were found to have variants in the positive node samples. These variants were not found in any of the negative node samples. Conclusion While this is a pilot study, we are currently increasing our sample size to develop a more robust predictor of positivity. There are several gene variants seen in melanoma lesions with positive nodes that are not expressed in lesions with negative nodes. These may become useful in determining a genetic signature to predict lymph node positivity in melanoma patients.

Name	# if SLN (+)	# of SLN (-)
ERBB4	6	0
ATM	5	0
EGFR	5	0
ERBB2	5	0
FGFR2	5	0
FLT3	5	0
GNA11	5	0
GNAQ	5	0
KDR	5	0
PDGFRA	5	0
PIK3CA	5	0
RET	5	0
SMO	5	0
TP53	5	0

Table 1. Genes that contain variants that occur in >80% SLN (+) cases and 0 controls.

PF318

Survival and Factors Associated with False Negative (FN) Sentinel Lymph Node Biopsy (SLNB) for Melanoma C. Lamb, J. Kairys, M. Mastrangelo, N. Dabbish, K. Feeney, B. Leiby, T. Sato, A. Berger.* *Surgery, Thomas Jefferson University, Philadelphia, PA.*

Introduction: SLNB has become the de facto standard of care for patients with melanoma greater than 1mm thick and is one of the most important prognostic factors. The rate of FN-SLNB has been reported from 2-10% in the literature. We hypothesized that melanoma-specific factors contribute to the incidence of FN-SLNB and report our institutional experience with over 1000 SLNBs. Methods: We performed an IRB-approved retrospective chart review and identified 1049 patients from January 1995 to June 2015 who underwent SLNB with complete information. FN-SLNBs were defined as those who had a recurrence in the lymph node basin in which they had previously undergone SLNB or to a known lymphoscintigraphy drainage basin for that primary site. The FN-SLNB rate was defined as FN/(FN+ true positive (TP)). Univariate logistic regression was carried out to determine factors contributing to a FN-SLNB followed by a multivariate analysis using backwards selection. Univariate survival analysis was performed using Cox regression. Results: There were 33 patients (3% of entire population) with FN-SLNB and 162 with TP-SLNB for a FN-SLNB rate of 16.9%. The true negative (TN) comprised 854 patients. Factors predictive of FN-SLNB on univariate analysis included the following: head and neck (HN) primary site (OR=3.3, p<0.001), T stage (p<0.001), ulceration (OR=4.9, p<0.001), and tumor thickness (OR=1.2, p<0.001). On multivariate analysis, thickness (OR=1.2, p<0.001) and HN primary (OR=2.8, p=0.008) remained significant. When analyzing survival (graph), there is no significant difference in overall survival between FN and TP-SLNB patients (p=0.25). Five-year survivals by group are as follows: TN=90%, FN=81% and TP=60% with a significant difference between TP and TN (HR=3.8, p<0.0001) and between FN and TN (HR=2.4, p=0.04). Conclusion: SLNB status is an important factor in melanoma staging. FN-SLNB appears to be more frequent in patients with thicker primaries and a head and neck primary. These should undergo further imaging including nodal ultrasound. Further follow-up is needed to determine whether there is a difference in survival between FN and TP.

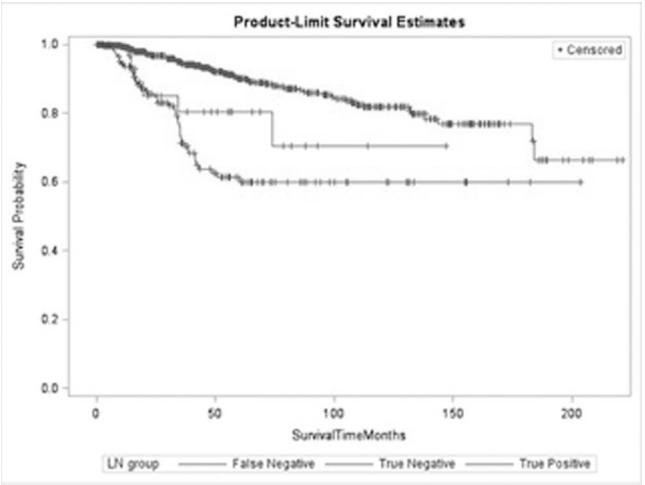


Figure 1. Kaplan Meier plot for survival, with lymph node group strata

PF319

Utility of Gene Expression Profiling in Determining Necessity of Sentinel Node Biopsy in Melanoma J.K. Keller,* T. Schwartz, J.M. Lizalek, E.C. Hsueh. *Surgery, Saint Louis University, St. Louis, MO.*

Introduction: Current National Comprehensive Cancer Network (NCCN) guidelines recommend patients with >1mm thick cutaneous melanoma and select patients with ≤1mm thick melanoma undergo sentinel node biopsy (SNB) for further staging purposes. Recently, gene expression profiling (GEP) with DecisionDx-Melanoma test (Castle Biosciences, Inc) has shown promise in predicting an individual patient's future risk of developing distant metastatic disease. It is unknown, however, if GEP testing can predict sentinel lymph node positivity. We sought to determine if there is a correlation between GEP testing and SNB results in a prospective cohort of patients with AJCC T1 and T2 primary cutaneous melanoma. Methods: From November 2013 to June 2016, 175 patients (ages 18-88) with T1 or T2 primary cutaneous melanoma undergoing SNB were prospectively enrolled. GEP testing was performed at the time of surgery. GEP testing results were reported as class 1 (low risk), class 2 (high risk), or insufficient sample (INS). Patient demographics, SNB results, GEP results, and clinical outcome parameters were collected. Statistical analysis was performed using Chi-square analysis. Results Of the 175 patients in our sample, 12 could not undergo GEP testing due to INS. The final sample size was 163. There were 72 and 91 patients with T1 and T2 disease, respectively. High-risk class 2 GEP results were noted in 3% (n=2) of T1 and 14% (n=13) of T2 patients. The SNB was positive in 7% (n=5) of T1 and 10% (n=9) of T2 patients. Within the class 2 cohort, 0 of 2 T1 and 3 of 13 (23%) T2 patients had a positive SNB. GEP class was not a statistically significant predictor for SNB positivity for either the T1 or T2 cohort (p= 0.695, and 0.085, respectively). Conclusion Despite the promise of GEP testing for predicting the risk of distant recurrence in primary melanoma, these results cannot predict SNB positivity. GEP testing should not be used as a substitute for SNB in staging of cutaneous melanoma patients.

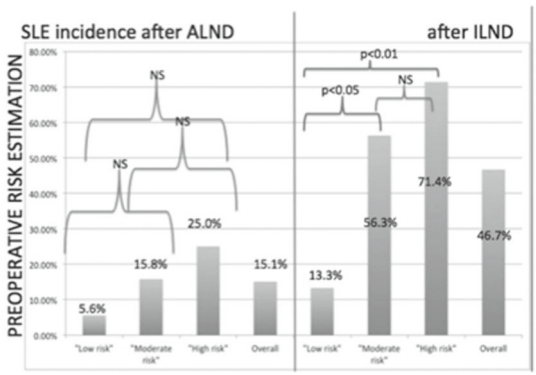
PF320

Preoperative Risk Factors Alone Accurately Predict Risk of Lymphedema in Melanoma Patients A. Kelsall, T. Novice,* B. Sunkara, B.K. Chang, C. Ky, J. Noda, K. Ogu, R. Hoogmoed, J. Loh, H. Cheriyan, M. Martin, A. Durham, T. Johnson, M.S. Cohen. *Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Secondary lymphedema(SLE) is a significant complication following axillary(ALND) or inguinal lymphadenectomy(ILND) in melanoma patients. While many risk factors contribute to SLE, no statistical tool for predicting lymphedema risk is currently in use. Utilizing the largest institutional prospective melanoma database, we hypothesize that SLE risk can be predicted using preop and postop risk factors and that preop factors dominate in this comparison. Methods: A retrospective review of our prospectively collected melanoma database identified 526 patients(304 ALND,222 ILND)

undergoing surgery from June 2005-June 2015(model cohort). Next a test cohort was collected(N=98;53 ALND,45 ILND) of patients having ALND or ILND between November 2015 and June 2016. Patients having bilateral LND, iliac dissections, or preop chemotherapy were excluded. Patient characteristics were collected from the electronic medical record. Stepwise logistic regression modeled the impact of preop risk factors on developing SLE in the model cohort. These models were then used to calculate risk scores for patients in the test cohort and procedure-specific tercile thresholds were used to assign patients to "low","moderate", and "high" risk categories that were evaluated for accuracy by clinically observed SLE rates. Results: Of 526 patients in our model cohort, neither creatinine levels nor incidence of chronic kidney disease significantly predicted SLE following ALND or ILND. These levels did not meet inclusion criteria in the stepwise model. Conversely, smoking, peripheral vascular disease, and cancer stage all met criteria for inclusion in the risk assessment model. In the test cohort, a significantly different incidence of SLE risk was noted only in the ILND and not ALND groups when comparing "low" and "high" risk patient terciles ($p<0.01$ for SLE risk: Figure 1). Conclusion: Our findings demonstrate preop factors alone reasonably predict SLE rates following ALND or ILND and a low risk score in ILND patients significantly lowers SLE rates (comparable to ALND rates). Accurate preop risk-assessment may better inform surgeon-patient discussions and guide expectations or postop management.

Figure 1: Lymphedema incidence in test cohort patients assigned to "low", "moderate" or "high" risk strata using preoperative risk estimation model, with paired proportions test results comparing statistical significance of lymphedema incidence in respective group to "low risk" group.



PF321

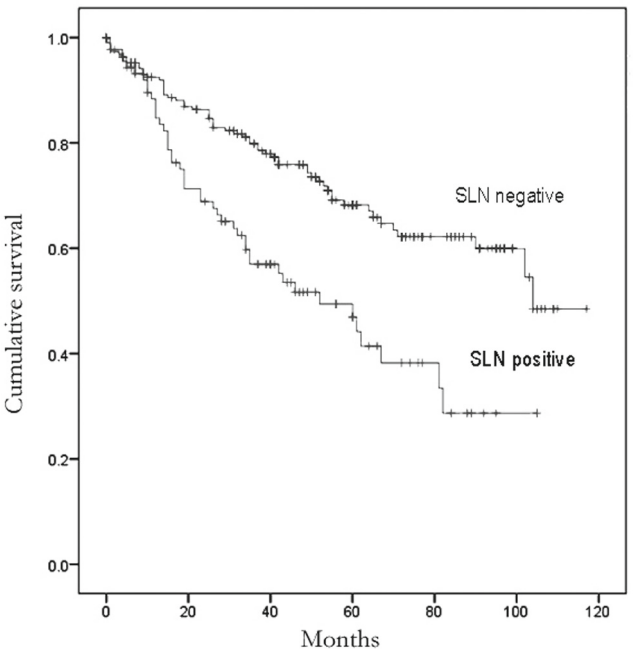
Surgical Outcomes After Axillary Lymphadenectomy for Melanoma L.M. Postlewait,* A. Seamens, G. Carlson, N. Le, M. Rizzo, M. Russell, M. Lowe, K. Delman. *Surgery, Emory University, Atlanta, GA.*

Introduction: Limited data exist characterizing complications after axillary lymphadenectomy for melanoma. In light of high rates of complications reported after lymphadenectomy for breast cancer and data suggesting a limited benefit to completion lymphadenectomy, we characterized morbidity to facilitate clinical decision making. Methods: We reviewed a prospectively maintained database of primary cutaneous melanoma for patients who underwent axillary lymphadenectomy at a single center between 2003 and 2015. Patients were stratified by potential risk factors for complications. Results: A total of 239 patients underwent 254 axillary lymphadenectomies. We assessed the following risk factors for surgical complications: age greater than 55 years (n=133; 52%), BMI of 30 kg/m^2 or more (n=90; 40%), diabetes (n=40; 16%), smoking (n=81; 32%), location of primary tumor on the extremity (n=71; 28%), therapeutic lymphadenectomy (n=105; 41%), and adjuvant radiation (n=33; 13%). Wound complications included 38 (15%) seromas, 3 (1%) dehiscences, and 10 (4%) hematomas. There were 5 (2%) reoperations for hematoma. The 30-day readmission rate was 6% (n=14). Lymphedema occurred in only 13 (5%) patients. Wound dehiscence occurred only in smokers (4% vs 0%; p=0.03) and was associated with adjuvant radiation (6% vs 0.5%; p=0.04). Twenty-eight (11%) patients developed frozen-shoulder, which was related to smoking (18% vs 8%; p=0.02). Lymphedema was more likely in patients after therapeutic dissection (9% vs 3%; p=0.04). Other risk factors were not associated with increased complications. Conclusions: This analysis supports historical data that axillary dissection for melanoma is a low risk procedure. Although morbidity of lymphadenectomy is often cited as a reason to alter surgical approach or even forego intervention, this may be less of a concern for axillary lymphadenectomy.

PF322

Exhaustive Pathologic Work-Up in Sentinel Lymph Node Biopsy for Melanoma: Is It Necessary? R. Salcedo Hernandez, L.S. Lino-Silva, C. Zepeda Najar,* L. García-Pérez. *Surgical Oncology, Instituto Nacional de Cancerología de México, Mexico city, Mexico.*

Objective: Determine if a less-exhaustive pathologic work-up to detect melanoma metastasis is clinically useful and do not affects patient prognosis. Background. The success and evolution of the sentinel lymph node (SLN) depends on histological techniques. Several exhaustive protocolos of SLN analysis are published but are time and cost consuming, with light increases in the rates of metastasis detection. Methods. From 281 patients with SLN biopsy, each SLN was sectioned every 2 mm and from each paraffin block 2 - 3 histological sections were evaluated. The patients were dichotomized: the first group (n= 185) with extensive SLN examination (eSLNe), and the second (n=96) without extensive SLN examination (wSLNe). Results: The average SLN resected was two (range 1 – 7), evaluating one in 50.9%. The SLN metastasis detection rate was 28.5%, while eSLNe increased by 3.2%. During follow-up, 4 / 26 cases (17.4%) in the wSLNe group showed recurrence in the SLN basin. Factors associated with decreased survival in univariant analysis were: recurrence, Breslow, advanced clinical stage, ulceration and SLN metastasis. eSLNe did not affect disease-specific survival. Multivariate analysis showed recurrence (HR 23,475, 95% CI 1903-4559, $p<0.001$) and Breslow >3.5 mm (HR 15,222, 95% CI 1448-3059, $p<0.001$), as independent risk factors for decreased survival. Conclusion. Our routine for SLN examination permitted an adequate rate of SLN metastasis detection, and the eSLNe increased the rate of detection in 3.2% but did not affect the survival. We did not find any benefit from performing the eSLNe in patients with Breslow < 3.5 mm.



PF323

Improved 10-Year Disease-free Survival in Intermediate Thick Melanoma Patients at a Single Institution After Introduction of Sentinel Lymph Node Biopsy: Initial Analysis L.D. Rothermel,[1]* A. Visioni,[2] D. Super,[1] B.D. Li,[1] N. Joseph,[1] S.M. Sharpe,[1] J. Brell,[1] A. Funovits,[1] B.J. Averbook.[1] *1. MetroHealth Medical Center, University Heights, OH; 2. Roswel Park Cancer Institute, Buffalo, NY.*

Intro: Using a longstanding database for melanoma, we sought outcome corroboration with results of the MSLT-1 trial. AJCC 7th ed primary melanoma

staging criteria was retrospectively applied to intermediate thick melanomas to compare patients before and after the introduction of sentinel lymph node biopsy (SLNB). Methods: 2296 consecutive patients prospectively registered (Nov 1970-Feb 2015) and 662 patients with primary cutaneous intermediate thick melanomas were retrospectively evaluated. Patient and tumor characteristics as well as time to recurrence were evaluated in melanomas between 1.01-4mm thicknesses, stratified by the initial use of SLNB in Nov 1996 (Pre-SLNB n=278; Post-SLNB n=384). Patients with thinner or thicker tumors, metastatic disease, or multiple primaries were excluded. Follow-up period for these patients was 10 years. T-tests and Chi Square analyses were used to compare isolated variables. Kaplan-Meier curves were constructed for disease free survival (DFS) and compared by log-rank test. Results: 10 year DFS was significantly improved for patients with intermediate thick melanomas post-SLNB vs pre-SLNB (89.3% vs 75.9%; p<0.001). There was no difference in mean thickness or ulceration between these groups. In a Kaplan-Meier analysis, the mean disease free interval was longer in the post-SLNB versus the pre-SLNB period (8.86 vs 8.15 years; p=0.004). Variables significantly associated with DFS rates at 10 years include tumor thickness (11% for 1.01-2mm vs 22% for 2.01-4mm; p<0.001), gender (females 13% vs males 25%; p=0.02) and ulceration status (absent 15% vs present 31%; p<0.01). Mean age in the pre-SLNB and post-SLNB periods was significantly different (pre=52.2 years vs post=61.2 years; p<0.001). Conclusion: Introduction of sentinel lymph node biopsy to the management of intermediate thick melanomas was strongly associated with improved 10-year DFS in our patients, and was independent of tumor thickness or ulceration status. The potential causes associated with these differences, other prognostic factors, and overall survival will be evaluated in a multivariable analysis.

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Factors Associated with Adjuvant Radiotherapy for Stage III Melanoma: A National Study of 15361 Patients L. Pontius,* S.M. Thomas, R.P. Scheri, S. Roman, J. Sosa. *School of Medicine, Duke University, Durham, NC.*

Introduction: The use of adjuvant regional radiotherapy in stage III melanoma is controversial. Current guidelines recommend consideration of radiotherapy for patients at high risk for regional recurrence (clinical N1-3 and ≥2 axillary/cervical or ≥3 inguinal pathologically positive nodes). Given this recommendation, this study sought to examine use of radiotherapy in stage III melanoma. Methods: The National Cancer Database (2004-2013) was queried for all patients with stage III melanoma without in-transit metastases. Patients were divided based on treatment with/out external beam radiation (EBRT). Demographic, clinical, and pathologic features at time of diagnosis were determined. Multivariable analysis was performed to identify covariates associated with receipt of EBRT. Results: 15361 patients met inclusion criteria; 1115 (7.3%) were at high risk for recurrence. Overall 6.0% received EBRT, while 21.7% of high risk patients received EBRT. During the study period, the rate of EBRT increased from 3.8% to 7.6% overall, and 18.9% to 29.1% for high risk patients. Patients who received EBRT were older (61 vs 58 years, p<0.01), more likely to be male (72.4% vs 61.8%, p<0.01), have more comorbidities (4.6% vs 2.5%, p<0.01), thicker primary tumor (3.8 vs 2.3 mm, p<0.01), head/neck location (42.6% vs 13.1%, p<0.01), more positive nodes (2 vs 1, p<0.01), receive treatment at an academic center (49.5% vs 42.9%, p=0.04), and be considered high risk for recurrence (26.2% vs 6.0%, p<0.01). After adjustment, receipt of EBRT was associated with tumors >4mm (OR=1.65), head/neck location (OR=4.20), number of positive lymph nodes (OR=1.13), treatment at an academic center (OR=1.42), and those at high risk for recurrence (OR=2.40) (all p<0.01). Conclusion: Although usage of EBRT has increased over time, only a minority of high risk stage III melanoma patients receive EBRT. Selective treatment of high-risk patients likely reflects current guidelines recommending consideration of EBRT weighing the benefit/toxicity of treatment. Additional studies are recommended to identify the patients who derive optimal benefit from EBRT in order to develop more definitive guidelines.

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Comparison of SPECT/CT and 2-D Planar Lymphoscintigraphy for Sentinel Lymph Node Biopsy in Melanoma of the Head and Neck D. Prettel,[3] J. Collins,[4] C. Schammel,[1] D.P. Schammel,[1] E. Farnesworth,[5] S.D. Trocha.[2]* *1. Academic Department of Pathology, Pathology Associates, Greenville, SC; 2. Greenville Health System Department of Surgery, Greenville, SC; 3. Emory University, Atlanta, GA; 4. Medical University of South Carolina, Charleston, SC; 5. Greenville Health System Department of Radiology, Greenville, SC.*

New cases of melanoma of the head and neck (H/N) are expected to reach 14,600 in 2016 with a 5-year survival of 17%. While sentinel lymph node biopsy (SLNB) is essential determination of prognosis of melanoma overall, the utility of this procedure for H/N lesions has been limited due to the complexity of drainage and difficulty in accurate detection. Imaging has typically relied on planar lymphoscintigraphy (PL); however, SPECT-CT has recently been used to identify SLNs, reducing the masking effect of PL and increasing SLN yield ultimately reducing local relapse (LR) and prolonging disease-free survival (DFS). Our goal was to evaluate localization and excision accuracy of SLNs between PL and SPECT-CT/PL and the effects on LR and DFS at a regional medical center. We completed a retrospective review of all H/N melanomas diagnosed, pre-operatively imaged with PL or SPECT-CT/PL and treated between 1/1/2005-1/1/2015 at our institution. Standard demographic, clinicopathologic, imaging and treatment variables were collected. T-tests and ANOVA were used to analyze the data. Results: Of the 87 patients identified, 23 had LN mapping by PL and 64 by SPECT-CT/PL. The Breslow depth and mitotic figures were significantly different between the cohorts (p=.02 and 0.01, respectively). For SLN retrieved, SPECT-CT>PL for overall SLN (2.9 vs 2.55, p=.47), positive SLN (0.3 vs. 0.17, p=.40), and the ratio of positive SLN over total per SLNB (.11 vs. 0.06, p=.46). For false negatives, SPECT-CT< PL (0% and 10%, respectively; p<.001). Additionally, the SLN ID/retrieved ratio of low and high BMI (<30, 0.1; >30, 0.13) were lower for SPECT-CT than PL (0.15 and 0.02, respectively) Conclusion: SPECT-CT/PL is the superior imaging modality for SLNB in H/N melanoma as SPECT-CT/PL identifies more SLN per patient, results in fewer LR per negative SLNB, and is not as affected by BMI in terms of SLN ID/retrieved when compared to PL only. To our knowledge, this study is the most comprehensive review evaluating the efficacy of PL and SPECT-CT in identification of SLN and the evaluation of LR.

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Using a Novel Interluekin-15 Construct (ALT-803) to Enhance Natural Killer Cell Activity Against Cetuximab-Treated Head and Neck Cancer Cells A. Ash,* E. McMichael, N. Courtney, A. Stiff, L. Atwal, W.E. Carson III. *Cancer immunology, Ohio State University Wexner Medical Center, Dayton, OH.*

Squamous cell carcinoma of the head and neck (SCCHN) is the 6th most common cancer worldwide. Overexpression of the epidermal growth factor receptor (EGFR) is observed in greater than 90% of SCCHN tumors. Cetuximab is an antibody that binds to EGFR, has a direct effect on EGFR-positive cancer cells, and can activate immune cells that bear receptors for the Fc (constant region) of immunoglobulin G such as natural killer (NK) cells. Interleukin (IL)15 is critical for the development, proliferation and activation of effector NK cells. Herein we report the anti-cancer effects of a novel interleukin 15 (IL15) compound (ALT803; Altor Bioscience Corp) that consists of genetically modified IL15 plus the IL15 receptor alpha protein (IL15Rα) fused to the Fc portion of IgG1. We hypothesized that ALT803 treatment of NK cells would enhance their response to cetuximab-coated EGFR positive SCCHN cells. NK cells from normal healthy donors and SCCHN patients were treated overnight with ALT 803 (10 ng/ml) and tested for their ability to lyse cetuximab-coated tumor cells in a standard 4 hour 51Cr release assay at effector:target ratios up to 50:1. NK cell killing of cetuximab coated HPV-positive and HPV negative cell lines was significantly higher following NK cell ALT803 activation (>75% lysis at the 50:1 E:T ratio), as compared to untreated controls (<10%) and was superior to that of native IL15 (54% lysis). In response to cetuximab-coated pancreatic tumor cells, ALT 803 treated NK cells secreted significantly higher levels of IFN-gamma than untreated control cells (70 % increase). NK cells showed significantly increased levels of phosphorylated STAT5 following exposure to ALT803 indicating strong induction of signaling pathways. In vitro, ALT803 activation of NK cells led to significant lysis of cells that had been pre-treated with cisplatin and cetuximab, providing a rationale for the addition of ALT803 to current care

treatments. Our present data suggests that cetuximab treatment in combination with ALT803 in patients with EGFR positive head and neck cancers results in NK cell activation and may have important anti-tumor activity.

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Head and Neck Dermatofibrosarcoma Protuberans Treated with Mohs Surgery in a Head and Neck Department A. Gonzalez,[2]* D. Etchichury,[1] M. Rivero,[2] M. Pistone Creydt.[2] *1. Cutaneous Oncology Unit, Alexander Fleming Institute, CABA, Argentina; 2. Instituto Angel H. Roffo, Buenos Aires, Argentina.*

Background Dermatofibrosarcoma protuberans(DFSP) is a rare, low-grade soft tissue sarcoma. Locally invasive, it usually extends beyond clinical margins but rarely metastasizes. Only 5-15% are located in the head and neck(HN). Mohs surgery(MS) is a tissue sparing technique with 100% margin control that has shown low recurrence rates. Objective Report the outcome of patients(pts) with HN-DFSP treated with MS. Patients-Methods We included 34 consecutive pts with HN-DFSP treated with MS over the last 15 years(6/00–6/15). Women: 20/34(58.8%), mean age: 40 years(18-68). Previous surgery: 16/34(47%). Site: forehead/temple 10, scalp 6, face 5, supraclavicular area 5, anterior neck 4, posterior neck 4. Mean size: 5.5cm (0.6-16). Technique: resections were performed under local anesthesia. Mean first layer margin: 1.7cm, it varied between 1-2cm according to site, size and previous treatment. First 12 patients underwent standard MS fresh tissue technique. Since 2006 we preferred permanent-tissue slow MS(22 cases). Inmunohistochemistry staining was used only in 1 case where dense inflammatory tissue (due to 5 previous surgeries) posed a difficulty to differentiate inflammation from tumor. Results In 15 cases more than one layer was necessary to obtain free margins. Tumor involved: deep margin(9), lateral margin(4) and both(2). Structures involved: fat(7), muscle(5), and periosteum(5). Mean number layers: 1.6(1-6). Follow-up: 100%. Median follow up: 60.3 months(12-188). Only 1 patient(2.9%) (16cm forehead DFSP with 8 previous surgeries) developed a local recurrence 26 months after MS. Conclusions This series includes 34 HN-DFSP with unfavorable prognostic factors: mean size 5.5cm, 47% previously treated. We observed only 1 recurrence in an extremely high risk tumor, for a recurrence rate of 2.9%, with a mean follow up of 60.3 months. This recurrence rate agrees with published literature for MS and compares favorably to the results of WLE. Reports of HN-DFSP are scarce. We believe MS should be the standard treatment for HN-DFSP because it is tissue sparing, while still complete tumor resection is performed.

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Should We Resect Pancreatic Metastases in Renal Cell Carcinoma? Yes A. Lewis,* Z. Jutric, P.H.G. Ituarte, S. Warner, L. Melstrom, G. Singh. *Department of Surgery, City of Hope, Duarte, CA.*

Introduction: While renal cell carcinoma (RCC) metastases to the pancreas are rare, incidence is increasing. The role of pancreatectomy is not clearly defined. Previous studies are limited to small single institutional series. This population-based study evaluates the role of pancreatectomy in patients with RCC. Methods: The California Cancer Registry was queried for patients with Renal Cell Carcinoma (RCC) with or without pancreatectomy. Patients with a history of any primary pancreatic tumors were excluded. Patients were evaluated based upon demographics, pancreatectomy, chemotherapy use, and concomitant extra-pancreatic metastases. Overall survival (OS) from the time of recurrence with GI-METs was estimated using Kaplan-Meier method and log-rank test. Results: GI-metastases including pancreas were identified in 429 patients with RCC; 46 underwent pancreatectomy. Concomitant extra-pancreatic metastases were identified in 359 patients (most often liver, bone, brain). In patients reviewed with or without pancreatectomy, extra-pancreatic metastases occurred in 69% and 92%, respectively ($p < 0.001$). Median number of extra-pancreatic sites were 1.6 in patients with pancreatectomy and 2.6 sites without pancreatectomy($p = 0.016$). Time to metastasis, demographics, comorbidities, and chemotherapy use were similar between groups. Median time from diagnosis of RCC to metastasis was 11 months. Five-year OS was 57% in patients with and 13% without pancreatectomy (Figure 1). On multivariate analysis while controlling for extra-pancreatic disease and comorbidity, pancreatectomy (HR 0.32, $p < 0.001$) was associated with improved OS. Conclusion: RCC GI-METs including the pancreas are extremely rare. A prolonged survival is appreciated in patients who undergo pancreatectomy for RCC metastases.

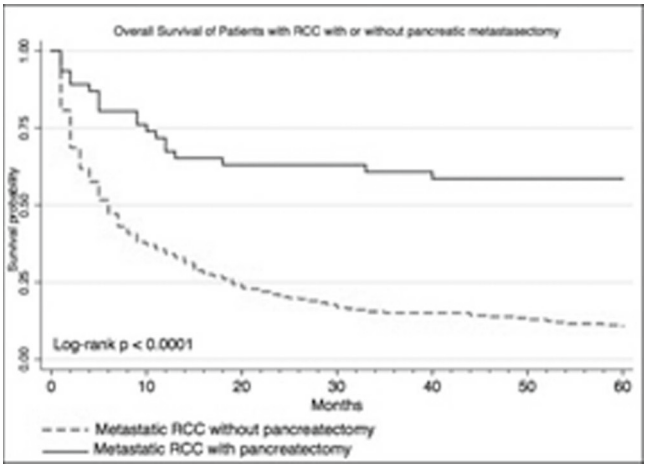

Figure 1. Overall Survival of Patients with GI-METs from the time of diagnosis of GI-METs with or without pancreatectomy

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A Feasibility Study of Returning Clinically Actionable Somatic Genomic Alterations Identified in a Research Laboratory N. Paez Arango,[1]* L. Brusco,[1] K. Shaw,[1] K. Chen,[1] A. Eterovic,[1] V. Holla,[1] A. Johnson,[1] B. Litzenburger,[1] Y.B. Khotskaya,[1] N. Sanchez,[1] A. Bailey,[1] X. Zheng,[1] C. Horombe,[1] S. Kopetz,[1] C. Farhangfar,[2] M. Routbort,[1] R. Broaddus,[1] E. Bernstam,[3] J. Mendelsohn,[1] G. Mills,[1] F. Meric-Bernstam.[1] *1. The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Levine Cancer Institute, Carolinas Healthcare System, Charlotte, NC; 3. The University of Texas Health Science Center, Houston, TX.*

Introduction: Clinical tests have to be performed in a Clinical Laboratory Improvement Amendments (CLIA) certified environment in order to be used for clinical decision-making, for this reason patients do not directly benefit from them. Through a prospective protocol, we sought to determine the feasibility of performing broad genomic testing in the research laboratory for discovery and the utility of giving physicians access to research data with the option of validation in the CLIA environment Methods: 1200 patients with advanced cancer underwent characterization of their tumors on an 11, 46 or 50 gene hotspot CLIA assay, as well as hybridization capture-based sequencing of 201 genes in the research laboratory. 80 genes were considered potentially actionable therapeutically. Results: 527 patients (44%) had at least one somatic mutation detected in an actionable gene using hotspot testing. With the 201 gene panel, we identified 945 patients (79%) that had at least one alteration in a potentially actionable gene that was undetected with the more limited CLIA panel testing. Sixty-four genomic alterations identified on the research panel were subsequently tested using an orthogonal CLIA assay. Of 16 mutations tested in the CLIA environment, 12(75%) were confirmed; the mutations that were confirmed had a higher mutation allelic frequency (31.5% vs 8.7%; P=0.006). All mutations with 10% MAF or higher on research testing were confirmed in the CLIA environment. Twenty five (52%) of 48 copy number alterations were confirmed: amplifications that were confirmed had a higher estimated copy number (18 vs 5). Nine (26.5%) of 34 patients with confirmed results received genotype-matched therapy, including a breast cancer patient thought to have HER2 negative tumor based on clinical testing that was confirmed to have HER2 amplification. Seven of the patients were enrolled onto genotype-matched targeted therapy trials. Conclusion: Expanded cancer gene sequencing identifies a greater number of genomic alterations in actionable genes. CLIA validation for research results can provide alternative targets for personalized cancer therapy.

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Quality Comes with the (Anatomic) Territory: Evaluating the Impact of Surgeon Operative Mix Volume on Patient Outcomes After Pancreaticoduodenectomy K. Hachey,* A. Rosen, S. Rao, G. Doherty, T. Sachs. *Department of Surgery at Boston University School of Medicine/Boston Medical Center, Watertown, MA.*

Introduction: Recent support for centralization of complex operations, such as pancreaticoduodenectomy (PD), are based on surgeon specific volume-outcome relationships. We evaluated whether volume of anatomically-related operations (operative mix), other than PD, would have similar associations with postoperative outcomes after PD. Methods: We queried the Nationwide Inpatient Sample (2004-2009) for surgeons performing PD. Operative Mix (OM) was defined as the year-specific number of other pancreatic, hepatic, biliary and gastric operations performed by individual surgeons. Adjusted regression models included surgeon and hospital PD volume and other hospital and patient specific factors. Results: Among 1,754 surgeons, 64.4% performed 1 PD/yr, 24.0% 2-5 PDs/yr, and 11.6% >5 PDs/yr. Low PD (<5 PD/yr) volume surgeons with high OM (>20 cases/yr) had similar mortality when compared to both high PD (6-16 cases/yr)/high OM surgeons (4.4% vs. 3.4%;p=.44 Figure), and highest PD (>16 cases/yr)/high OM surgeons (4.4% vs. 2.7%;p=.16). All groups demonstrated lower mortality than low PD surgeons with low OM (9.2%, all p<0.02). Subgroup analysis of low PD/high OM surgeons (2-5 PD/yr) demonstrated no statistical difference in mortality (4.8% vs. 3.0%;p=.15), length of stay (12 vs. 11 days;p=.10) or complication rates (32.5% vs. 27.6%;p=.13) as compared to high PD/high OM surgeons. Increasing OM was associated with lower prolonged hospitalization (adjusted OR 0.86;p=0.01) and decreased mortality (unadjusted OR 0.64;p<0.001). Conclusions: Surgeon PD volume is an important predictor of outcomes after pancreaticoduodenectomy, however, low operative mix volume identifies a group of surgeons with the worst outcomes and may be a valuable metric.

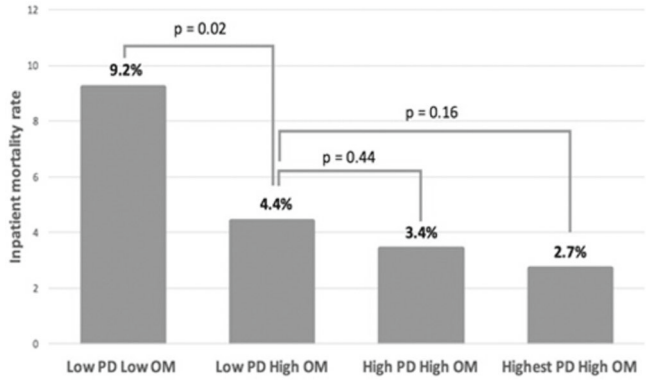

Figure. Inpatient mortality after pancreaticoduodenectomy (PD) by surgeon PD volume and operative mix (OM) volume. Low PD: ≤5 PDs/year; High PD: 6-16 PDs/year; Highest PD: >16 PDs/year; Low OM: ≤20 cases/year; High OM: >20 cases/year.

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Board Certification and Academic Rigor in Surgical Oncology M.S. Jones,[1]* T.D. Fischer,[1] S. Gaitonde,[1] B. Bandera,[1] D. Lee,[2] m. Goldfarb,[1] M. Faries.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. TriHealth Surgical Institute, Cincinnati, OH.*

Introduction: Complex General Surgical Oncology (CGSO) board certification was approved by the American Board of Medical Specialties (ABMS) in March of 2011. The first qualifying exam was given in 2014. Current CGSO fellows and programs are adapting to this new examination, however the educational benefit of this process has yet to be determined. The goal of this study was to examine differences in attitudes and formalized educational activities as programs entered the post-certification era. Methods: Following IRB approval, separate electronic surveys concerning board preparedness and educational activities were sent to 60 current fellows and 72 board eligible graduates and analyzed. Descriptive analyses and comparisons of graduates and current fellows were performed. Results: Of 132 potential respondents, there was an overall 55% response rate; 55% of current fellows and 54% of graduates completed the survey. With regard to formalized curricula for board preparation, over half of the current fellows (57.6%) reported formalized CGSO qualifying exam preparation as part of their training. This was in contrast to 25.6% of graduates who reported such preparation. These differences were significant for curricular programs targeting both the qualifying examination (p=0.006) and the certifying examination (p=0.002). Moreover, there was a significant increase in the number of current fellows following a year round reading schedule (p=0.043) as compared to graduates. The majority of current fellows (57.6%) thought that the knowledge gained during the CGSO board preparation process would be "very important" to their overall career success. Conclusions: ACGME certification and the introduction of board exams in surgical oncology appear to be associated with more formalized curricula and year round self study. Future research will be needed to determine the impact of these changes on fellows' fund of knowledge and/or board performance.

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Palliative Surgery for Disseminated Malignancy: Validation of UCDCCC Nomogram S. Lek,[1]* C. Chia,[2] M. Teo.[2] *1. SingHealth, Singapore, Singapore; 2. Division of Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

The necessity and appropriateness of palliative surgery in patients with disseminated malignancies is often questionable especially when predictive factors and surgical outcomes to guide therapeutic decisions are not well established. Adverse outcomes and factors independently associated with 30-day mortality in patients with peritoneal metastases and had palliative surgery for intestinal obstruction (IO) was studied. We also sought to validate the use of UC Davis Comprehensive Cancer Centre (UCDCCC) nomogram to predict 30-day mortality risks for patients with disseminated malignancy undergoing surgical intervention in our population. Patients with peritoneal metastases and underwent surgery for IO from January 2000 to May 2016 were included. Patient demographics, comorbidities and pre- and post- operative variables previously identified were examined. Continuous and categorical variables were analysed using independent t-test and Fisher's exact test respectively. Stepwise logistic regression was performed. Validation of the nomogram was analysed using concordance index and Hosmer-Lemeshow test. 208 palliative operations for IO were studied. Overall median survival was 101.5 days. Low ECOG status (p=0.008) and high pre-operative albumin levels (p<0.0001) were significantly associated with lower 30-day mortality. Primary malignancy site (p=0.063), ascites (p=0.072) and higher pre-operative hematocrit (p=0.076) suggested a potential prognostic role in predicting 30-day mortality. Subset analysis of primary malignancy site showed limited correlation due to small sample size. On multivariate analysis, low ECOG status and high pre-operative albumin levels remained statistically significant. Post-operative respiratory (p<0.0001), cardiac (p<0.0001), urologic (p=0.023) complications, ventilator use for >48 hours (p=0.041) and longer duration of in-hospitalization (p=0.0001) were significantly associated with mortality. Validation of UCDCCC nomogram had a concordance index of 0.70. Hosmer-Lemeshow test was 0.759 (p>0.05), indicating good model fit. Thus, surgical management of patients with low ECOG status and high pre-operative albumin levels should be considered despite advanced disease.

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The Effects of Resident Participation on Patient Morbidity and Mortality in Major Gastrointestinal Oncologic Surgery G. Bellini,[1]* A. Teng,[1] D. Lee,[2] K. Rose.[1] *1. Surgery, Mt. Sinai West-Mt. Sinai St. Luke's, New York, NY; 2. TriHealth, Cincinnati, OH.*

Background: While the effects of resident participation have been documented in various studies, there has yet to be a comprehensive study analyzing resident participation in overall gastrointestinal (GI) oncologic surgery. The aim of this study was to compare outcomes in major GI oncologic cases performed by an attending alone and those performed by an attending and resident. Methods: The ACS-NSQIP database from 2005-12 was utilized to study major (GI) operations (esophagectomy, gastrectomy, pancreatectomy, enterectomy, hepatectomy, and colectomy/proctectomy) in patients with an ICD-9 cancer diagnosis. Major complications and 30-day mortality were then compared in those patients who underwent surgery with an attending alone (AA) to those patients who underwent surgery with an attending and resident (AR). Results: A total of 64,637 patients met criteria for the study; AR n= 48,022 and AA n=16,615. In 76.6% of AR cases, the resident assistance was classified as senior level PGY-4 or higher. On average, operative time was significantly increased in AR cases compared to AA cases (228 ± 130 vs

163 ± 104 min, p<0.001). On multivariate analysis, AR cases were more likely to develop superficial incisional infection (OR 1.3, CI 95% 1.2-1.4, p<0.001) and urinary tract infection (OR 1.2, CI 95%, 1.1-1.4, p<0.001) compared to AA cases. However, on multivariate analysis, resident participation was associated with less likelihood of returning to the operating room (OR 0.9, 95% CI 0.8-0.9, p<0.001) and lower mortality (OR 0.7, CI 95% 0.6-0.8, p<0.001). Conclusion: The majority of major GI oncologic operations in the NSQIP database are performed by an attending with the assistance of a senior level resident. This may be due to the complex nature of GI oncologic operation. Potentially, operative time in cases with resident participation may be increased by teaching or by the complex nature of the operation due to the referral bias to teaching centers. However, even with potentially more complex operations, there was less mortality in cases performed by a resident and an attending.

Multivariate Analysis of Major Complications and Mortality in Attending and Resident Cases

Prognostic Factors	Attending & Resident Cases	
	Adjusted Odds Ratio (95% CI)	P
Return to OR (yes)	0.9 (0.8- 0.9)	<0.001
Superficial Incisional SSI	1.3 (1.2- 1.4)	<0.001
Urinary Tract Infection	1.2 (1.1- 1.4)	<0.001
Operation Time (min) 169-248	2.1 (2.0- 2.2)	<0.001
Operation Time (min) >248	3.8 (3.6- 4.0)	<0.001
Mortality	0.7 (0.6- 0.8)	<0.001

CI= Confidence Interval; OR= Operating Room; SSI=Surgical Site Infection

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Potentially Preventable Readmissions After Complex Cancer Surgery- Analysis of the National Readmissions Dataset S. Zafar,[1]* A.A. Shah,[1] M. Raoof,[3] L.L. Wilson,[1] N. Wasif.[2] *1. Surgery, Howard University Hospital, Washington, DC; 2. Mayo Clinic, Phoenix, AZ; 3. City of Hope, Duarte, CA.*

Introduction Hospital readmissions following surgery are subject to penalties and have become a focus of quality improvement efforts. We aim to describe the burden, timing, and factors associated with potentially preventable readmissions (PPRs) after complex cancer surgery. Methods Data was abstracted from the National Readmissions Dataset (2013). All adult patients undergoing a complex oncologic resection (defined as esophagectomy/ gastrectomy, hepatectomy, pancreatectomy, colorectal resection, lung resection, and cystectomy) were selected. Readmissions occurring within 30 days from discharge were analyzed. Causes for readmissions were categorized in eleven diagnostic groups and tabulated. ICD-9 primary diagnosis codes were reviewed to identify PPRs. Logistic regression analyses were used to identify demographic, clinical and hospital factors associated with PPRs. Results We analyzed 60,970 patients with 92,260 admissions. A 30 day readmission occurred in 14% of patients, and was highest following cystectomy (25%) and lowest for lung resections (9%). Of all readmissions 82% were deemed to be PPRs. Half of PPRs occurred within the first 10 days of discharge. Infections, gastrointestinal complications and respiratory conditions accounted for 59% of PPRs. Other common causes included dehydration/electrolyte deficiencies (11%), exacerbation of comorbidity (9.2%), bleeding (5%), thromboembolism (3.5%), and wound complications (3.2%). Factors associated with an increased likelihood of PPRs include Medicaid compared with private insurance (OR 1.24, 95%CI 0.8-1.7), higher comorbid conditions (OR 1.44, 95%CI 1.32, 1.59), and discharge to a facility (OR 1.9, 95%CI 1.7-2.1). Patients with a prolonged hospital stay or a major complication during the index admission had a 34% (OR 1.34, 95%CI 1.3-1.4), and 64% (OR 1.64, 95%CI 1.5-1.7) higher likelihood of a PPR respectively. Conclusions Most 30 day readmissions after complex cancer surgery are potentially preventable and occur within 10 days of discharge. We identify common causes of readmission and high risk populations to help physicians, administrators and policy makers develop strategies to decrease PPRs.

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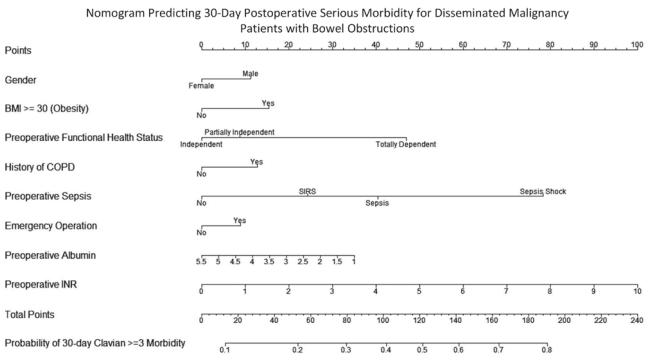
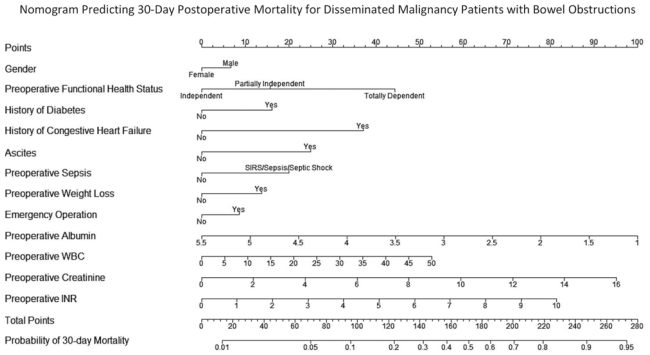
Nomograms to Predict 30-Day Morbidity and Mortality for Patients with Disseminated Malignancy Undergoing Surgery for Bowel Obstruction S. Bateni,* R.J. Bold, F.J. Meyers, A.R. Kirane, R. Canter. *UC Davis Medical Center, Sacramento, CA.*

Introduction: Bowel obstruction (BO), a common surgical condition among patients with disseminated malignancy (DMa) with rates as high as 28-51%, is associated with substantial postoperative morbidity and mortality. Given the need for risk stratification to optimize patient-centered decision making, we sought to construct nomograms predicting acute morbidity and mortality in DMa patients undergoing surgical intervention for BO. Methods: Using the American College of Surgeons National Surgical Quality Improvement Program from 2007-2014, we identified patients with DMa and primary diagnosis of BO who underwent abdominal operations from CPT and ICD-9 codes. Nomograms were developed using logistic regression and validated with bootstrapping. Results: We identified 2,842 DMa patients with a primary diagnosis of BO who underwent an abdominal operation. The mean age was 63.5 (SD±13.1). The majority had independent functional status (82.8%) and low rates of sepsis & shock (5.1% & 1.5%). The most common operations performed were large bowel resections (22.4%), small bowel resections (21.9%), celiotomy & lysis of adhesions (21.2%), and ostomy creation (16.7%). 35.1% of procedures were emergent. The median length of stay was 13 days (0-127 days). Rates of readmission and discharge home were 17.5% and 73.0%, respectively. Rates of 30-day overall morbidity, serious morbidity and mortality were 36.3%, 20.6% and 14.3%. Significant predictors on multivariate analysis for all 3 outcomes included impaired functional status, preoperative sepsis and low albumin, p≤0.05. Nomograms for 30-day overall morbidity, serious morbidity and mortality were developed and validated with concordance indices of 0.61, 0.63 and 0.76. Conclusion: We constructed nomograms to predict risk of 30-day overall morbidity, serious morbidity and mortality in DMa patients undergoing surgical intervention for BO. Given the clinical challenges of caring for patients with incurable malignancy with limited life expectancy, careful evaluation of the risks, benefits and goals of intervention is crucial. These nomograms will contribute to improved patient selection and counseling.



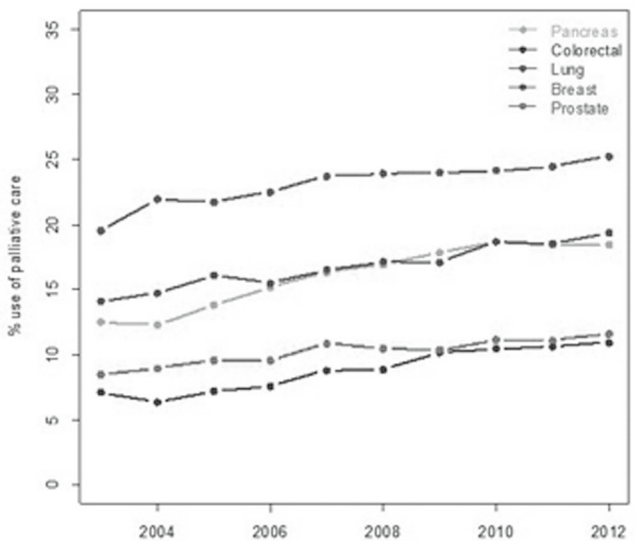


PT336

Trends and Disparities in the Use of Palliative Care for Stage IV Cancer Patients in the United States M. Ali-Mucheru,* D.A. Etzioni, B.A. Pockaj, R. Gray, C. Stucky, Y. Chang, N. Wasif. *Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

Background: Palliative care (PC) provides symptomatic relief to improve the quality of life and survival of patients with metastatic cancer. Little is known about the trends and disparities in the use of palliative care for Stage IV cancer patients in the United States. Methods: Retrospective analysis of the National Cancer Database (NCDB) of patients with Stage IV lung, colorectal, pancreas, breast and prostate cancer from 2003-2012. Multivariable logistic regression analysis was used to identify predictors of use of PC, which is coded as separate from curative intent therapy in the NCDB. Results: A total of 899,422 patients with stage IV lung (58%), colorectal (14%), pancreas (13%), breast (8%) and prostate (7%) cancer were included. Of these, 169,992 (18.9%) patients received PC, which included pain management in 12.5%. For each cancer type an increasing trend in the use of palliative care from 2003-2012 was seen (all p <0.001; Figure 1). In 2012, use of PC was highest for lung (25%) and lowest for colorectal (11%) cancer patients. Utilization was highest in New England (24.41%) and lowest in the Pacific (11.10%) region. Chemotherapy was the modality most often utilized in pancreas (35%) and colorectal (40%) cancer patients whereas radiation therapy was the most utilized in lung (54%), breast (50%), and prostate (59%) cancer patients. Predictors of utilization of PC include receiving care at an academic (OR 1.15, 95% CI 1.13-1.1.8) or comprehensive community program (OR 1.14, 95% CI 1.12-1.16) compared to a community cancer program. Patients who were Black (OR 0.90, 95% CI 0.88-0.92 vs. White), elderly (>65 years OR 0.85, 95% CI 0.83-0.87 vs. <50 years), and of lower educational attainment (OR 0.84, 95% CI 0.82-0.85) were less likely to receive PC. Conclusions: The use of PC for the five leading causes of cancer death is increasing in the United States. However, overall usage remains low (19%) and elderly, African American and low educational attainment patients are less likely to receive such care. Given the benefits of PC, expansion and uniform access of PC services for patients with stage IV disease should be a focus of high quality cancer care.

Figure 1. Trends in palliative care stratified by cancer type



PT337

Receipt of Postmastectomy Radiation Improves Survival Regardless of Time Interval from Diagnosis: Implications for the American College of Surgeons Commission on Cancer Quality Metrics V. Zheleva,* S. Dumitra, R. Nelson, N. Vora, L. Lai. *City of Hope National Medical Center, Duarte, CA.*

Introduction To ensure optimal breast cancer care, the American College of Surgeons Commission on Cancer (ACS CoC) developed quality measures with respect to timing of radiation, endocrine, and chemotherapy. This study evaluates nation-wide compliance to the receipt of postmastectomy radiotherapy (PMRT) in patients with ≥ 4 positive lymph nodes (LN) within 365 days of diagnosis (MASTRT) and assesses the impact of compliance on overall survival (OS). Methods Women diagnosed with invasive breast cancer from 2004 to 2012 were identified in the National Cancer Database. Receipt of RT within 365 days from diagnosis was determined for patients with Stage III (≥4LN) disease post mastectomy to evaluate compliance with the MASTRT measure. Uni- and multivariate logistic regression was used to assess patient, tumor, and treatment factors associated with non-compliance; uni- and multivariate Cox proportional hazard models - to assess factors associated with OS. Results Of the 29,349 women with Stage III disease (≥4LN) post mastectomy, 66.9% received RT within 365 days, while 33.1% were non-complaint (2.2% received RT after 365 days, 30.9% did not receive RT). Compliance with timely RT (≤365days) was associated with improved OS compared to no RT (HR 0.69, 95%CI 0.66-0.72). Survival advantage persisted in patients who received delayed RT (>365days) compared to no RT (HR 0.74, 95%CI 0.64-0.85). In multivariate analysis, factors associated with non-compliance to MASTRT were Medicaid (OR 0.72, 95%CI 0.66-0.78), Medicare (OR 0.80, 95%CI 0.73-0.87) or no insurance (OR 0.63, 95%CI 0.55-0.72), distance to hospital >44 miles (OR 0.69, 95%CI 0.62-0.76), and ER negativity (OR 0.79, 95%CI 0.73-0.86), while adjuvant chemotherapy (OR 4.62, 95%CI 4.26-5.02) was associated with improved compliance. Conclusion The survival benefit of compliance with the ACS CoC quality measure MASTRT for PMRT appears to be based on receipt of RT itself rather than time to RT. Focus on modifiable factors associated with non-compliance, such as insurance type and access to care, may lead to improved quality of care and ultimately OS.

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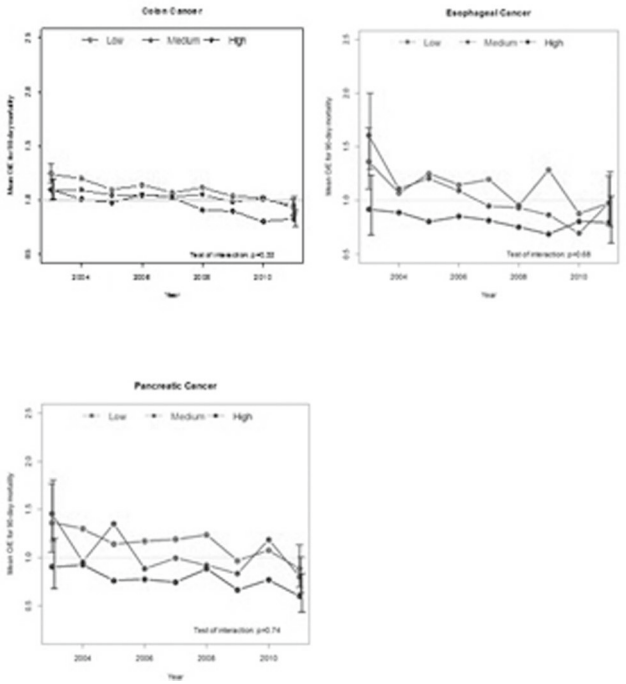
Attenuation of the Volume-Outcome Relationship for Gastrointestinal Cancer Surgery: Is a Push Towards Continued Regionalization Justified? N. Wasif,* Y. Chang, A. Mathur, B.A. Pockaj, R. Gray, D.A. Etzioni. *Surgery, Mayo Clinic Arizona, Phoenix, AZ.*

Introduction Demonstration of a volume-outcome relationship has resulted in regionalization of complex cancer surgery to high volume hospitals. A simultaneous national trend towards improved surgical outcomes brings into question whether the potential benefits of regionalization are still relevant. We hypothesize that the difference in adjusted post-operative mortality between low and high volume hospitals has decreased over time. Methods The National Cancer Database (NCDB) was used to identify patients with colon, esophageal, and pancreatic cancer undergoing curative intent surgery from 2003-2011. Hospitals were divided into low (<25th percentile), medium (25th-75th) and high (>75th percentile) volume groups depending on annual volume of cancer-specific surgery. Year-specific hospital averaged observed/expected (O/E) ratios were calculated for 90-day mortality. Poisson regression was used to model hospital averaged O/E ratios over time. Results Our study population included 343,929 patients with colon (88%), esophageal (5%) and pancreatic (7%) cancer. There were significant (p<0.05) improvements in adjusted 90-day mortality from 2003 and 2011 for all volume categories and cancer types, except in high volume hospitals for esophageal cancer. In 2003, high volume hospitals had significantly better outcomes compared to low volume hospitals for all cancer types, as suggested by lower O/E ratios for 90 day mortality (p <0.05). However, by 2011 the difference in O/E ratios for 90 day mortality was no longer significantly lower for high compared to low volume hospitals (p >0.05); this was true for all three cancer types (Figure1). Conclusions During the period of our study, 90-day mortality after gastrointestinal cancer surgery improved in low, medium and high volume hospitals. However, by 2011 the difference in adjusted post-operative mortality between low and high volume hospitals was not significantly different, likely due to global improvements in operative and peri-operative care. This attenuation of the volume-outcome curve has important implications for policy pertaining to regionalization of cancer care in the US.



PT339

Predictors and Outcomes of Surgical Interventions in Patients with Diffuse Malignant Peritoneal Mesothelioma: Analysis of Data from the National Cancer Data Base L. Bijelic,[1]* K. Darcy,[2] T. Cannon,[1] C. Tian.[2] *1. Surgery, Inova Fairfax Medical Campus, Fairfax, VA; 2. Women's Health Integrated Research Center, Fairfax, VA.*

Diffuse malignant peritoneal mesothelioma (DMPM) is a rare malignancy historically associated with poor outcomes. More recent reports show longer survival for patients treated with radical surgery, usually combined with intraperitoneal chemotherapy. The use of surgical interventions in patients with DMPM has not been extensively studied on a population level. The aim of this study is to study the prevalence and types of surgical interventions in patients with DMPM, the influence of surgery on survival outcomes and the relationship between demographic and clinical factors with surgical treatments and outcomes. This is a retrospective cohort study of adult patients diagnosed with DMPM from 2003 to 2014 and registered in the National Cancer Database (NCDB). Eligible patients had surgical treatment and survival data available. Relationships between demographic and clinical variables, surgical treatments and survival outcomes were evaluated using logistic and Cox modeling and log-rank testing. There were 2,062 eligible patients with a median age of 63. The majority of patients (51%) did not receive any surgery and only 34% received radical surgery. The use of radical surgery was associated with treatment at an academic cancer program, private insurance, younger age, female gender and epithelial mesothelioma subtype. Patients treated with radical surgery had a significantly better overall survival than those who did not receive surgery (38.4 versus 7.1 months, $p<0.0001$). The effect of surgery and chemotherapy on overall survival remained significant in univariate and multivariate modeling (Table 1). The majority of patients in the U.S. are not treated with radical surgery for DMPM. Utilization of surgical treatment varied by clinical and socio-economic factors. Patients who did not have private insurance and those treated in non-academic programs had a lower likelihood of having radical surgery. Treatment with radical surgery was independently associated with improved survival.

Table 1. Variables associated with Overall Survival in DMPM

	Univariate Analysis		Multivariate Analysis	
	HR (95% C.I.)	P value	HR (95% C.I.)	
Age				
Inc each 10 years	1.40 (1.34 – 1.45)	<0.0001	1.29 (0.24 – 1.34)	<0.0001
Sex				
Male	Reference		Reference	
Female	0.59 (0.53 – 0.65)	<0.0001	0.70 (0.63 – 0.79)	<0.0001
Race				
White	Reference		Reference	
Black	0.68 (0.54 – 0.87)	0.002	0.81 (0.63 – 1.03)	0.083
Other	0.68 (0.48 – 0.98)	0.038	0.81 (0.57 – 1.17)	0.262
Unknown	1.50 (0.99 – 2.29)	0.058	1.30 (0.85 – 1.98)	0.231
Histology Subtype				
Epithelioid	Reference		Reference	
Biphasic	2.04 (1.59 – 2.63)	<0.0001	2.43 ((1.89 – 3.14)	<0.0001
Fibrous	2.84 (2.20 – 3.65)	<0.0001	2.34 (1.81 – 3.02)	<0.0001
Mesothelioma, NOS	1.37 (1.23 – 1.53)	0.0001	1.13 (1.01 – 1.27)	0.030
Surgical Treatment				
None	Reference		Reference	
Limited Surgery	0.41 (0.35 – 0.48)	<0.0001	0.53 (0.45 – 0.64)	<0.0001
Radical Surgery	0.34 (0.30 – 0.39)	<0.0001	0.58 (0.49 – 0.68)	<0.0001
Systematic Treatment				
None	Reference		Reference	
Adjuvant	0.47 (0.40 – 0.55)	<0.0001	0.87 (0.73 – 1.05)	0.144
Intraoperative	0.31 (0.25 – 0.37)	<0.0001	0.59 (0.46 – 0.74)	<0.0001
Unknown	0.73 (0.64 – 0.83)	<0.0001	0.95 (0.83 – 1.08)	0.429

PT340

Quality of Life Post-Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: A Prospective Study C. Chia,* G.H. Tan, K. Soo, M. Teo. *Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

Background:Cytoreductive surgery(CRS) and hyperthermic intraperitoneal chemotherapy(HIPEC) for peritoneal carcinomatosis(PC) are increasingly being performed in many institutions worldwide. While many studies have shown a good quality of life(QOL) post surgery, few have been performed prospectively. We conducted a prospective QOL study on all patients undergoing CRS and HIPEC. Methods:All patients who had CRS and HIPEC for PC at our institution from March 2012 to April 2014 were included. A total of 131 procedures were performed. The European Organization for the Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) was administered to the patients at baseline prior to surgery and thereafter at 3, 6 and 12 months. Results: There were 36 males and 95 females. Median age was 54 years old (range 19-76). Median follow up was 1.1years. 2-year overall and disease- free survivals were 88.2% and 42.3% respectively. 36.6% of patients had ovarian or primary peritoneal malignancies; 29% had colorectal primaries; 22.9% had appendiceal primaries, 3.1% had peritoneal mesothelioma and 8.4% had other primaries. The median duration of surgery was 425 minutes (range 200-830). The median PCI score was 10 (range 0-39). 29.8% of patients had a stoma post-operatively. 21.3% had high-grade complications. With respect to the global health status, there was no significant change from pre-operative levels to 3 months post-operatively. However, this score improved at 6 and 12 months. Physical and role functioning scores decreased at 3 months but improved at 6 months. Social functioning scores remained stable at 3 months but improved at 6 months. Emotional functioning scores were the only ones that increased at 3 and 6 months. There was an improvement in almost all symptoms by 6 months, especially the pain scores. Conclusions:Apart from an initial decline in physical and role functioning during the recuperative first 3 months, all patients returned to their baseline or improved in all other functional categories, with most significant improvement in the emotional category. QOL is significantly improved by 6 months post CRS and HIPEC in most patients.

PT341

Clinical Outcome of Patients with Squamous Cell Carcinoma of the Anal Canal (SCCAC) Treated with Radiotherapy (RT) or with Concurrent Chemotherapy (CRT): Mexican Experience

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1. Surgical Oncology, Instituto Mexicano del Seguro Social, CD. de Mexico, Mexico; 2. Instituto Nacional de Cancerologia, México city, Mexico.

Objective. This study was undertaken to evaluate the outcome of patients with SCCAC treated in two Mexican institutions. Methods. Between 1990 and 2014. Patients with histologically confirmed SCCAC Stage I-IIIB were treated at Oncology Hospital. National Medical Center (192 patients) and Mexican National Cancer Institute (28 patients). Patients underwent CT scan of the abdomen and pelvis Chest X-Ray, physical examination, anoscopy. RT was delivered in 7 coplanar fields to the pelvis, superficial and deep inguinal nodes (except T1, N0) at total doses of 50.4 Gy in 25-28 fractions. Boost of 10 Gy in 5 fractions was delivered to perineum. Chemotherapy based in 5FU (1000 mg/m2, day 1-4, 29-32)) + Mitomycin (10 mg/m2, days 1-29) (n=67) or cisplatin. (75 mg/m2, days 1, 29, 57 and 85) (n=51). Outcomes. Local control, overall survival (OS), disease free survival (DFS) and colostomy free survival (CFS). Kaplan-Meier was used to estimate OS and DFS; differences in subgroups was evaluated with log-rank test. Descriptive statistics was done with parametric and no-parametric test. Results. 118 patients were treated with CRT and 102 with RT. Mean age in CRT and RT group was 57 and 62 yrs. Tumor stage according treatment group was: CRT (I: 10, II: 50 and III: 58), RT (I: 6, II, 54 and III: 42). Mean follow up was 163 months. Local recurrence was: 23% in CRT group, whereas 38.2% of RT group (p=0.02). Distant recurrence was 7% in CRT group, conversely 20% in RT group (p=0.004). Colostomy free was 87% in patients treated with CRT, conversely in 77% in the RT group (p=0.20). Overall and disease free 5-year survival according stage in CRT group was (I, 58%, 50%; II, 89%, 89%, and III: 64% and 67%, respectively), conversely in RT group (I: 80%, 80%; II: 70%, 70%, and III: 50% and 56%) (p= 0.004 and 0.003). No differences in outcomes between chemotherapy was observed. Multivariate analysis demonstrated that male, locoregional and distant recurrence are unfavorable factors for survival Conclusion. Results of this large retrospective cohort demonstrated that CRT is superior to enhance local control, CFS and survival

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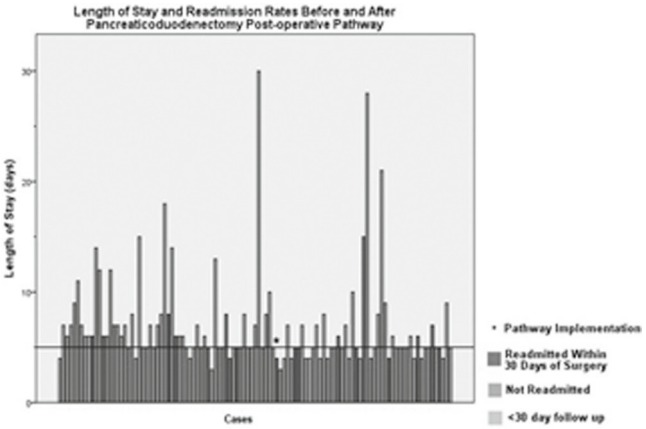
A Standardized Perioperative Care Pathway for Pancreaticoduodenectomy Patients Facilitates Safe Discharge on or Before Postoperative Day Five S.K. Daniel,[1]* G.N. Mann,[2] J.O. Park,[1] V.G. Pillarisetty.[1] *1. University of Washington, Seattle, WA; 2. University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Pancreaticoduodenectomy is a procedure with known high morbidity and mortality, as well as a prolonged length of stay (LOS). We hypothesized that standardization of perioperative care to promote early ambulation and feeding would allow for early and safe discharge. We therefore engaged our multidisciplinary team members to develop a comprehensive perioperative care pathway with an expected discharge on postoperative day five for patients undergoing pancreaticoduodenectomy. Methods: Implementation of our standardized perioperative care pathway was on 6/1/2015. Following IRB determination that this qualified as a quality improvement project, we performed a retrospective chart review and compared cases performed in the year following implementation to those performed the prior year. Data analysis was performed using SPSS. Results: One hundred nine patients underwent pancreaticoduodenectomy during the 2 year period of study, 60 before and 49 following pathway implementation. Complete 30 day follow up data was available for 107 (98%) patients. The groups were similar in terms of preoperative comorbidities. Following pathway implementation, there was a trend towards reduced median (6 to 5 days) and mean (7.4 to 6.3 days) LOS (p=0.191). Overall morbidity was similar between the two group (33% prior vs. 39% after, p=0.560). Readmission within 30 days of date of surgery was 0.14 prior to pathway and 0.21 afterwards (p= 0.322). Patients discharged ≤ 5 days after surgery (n=53) had similar readmission rates to those discharged ≥ 6 days following surgery (n=54) in the combined group of patients (0.17 vs. 0.17; p = 0.966). Furthermore, average date of readmission was similar between patients with LOS ≤ 5 and ≥ 6 (14.4 vs. 15.8 days; p=0.618). Interestingly, epidural placement was associated with increased LOS (p=0.024) and these were placed more often prior to pathway implementation (0.45 vs. 0.08; p<0.001). Conclusions: Implementation of a standardized perioperative care pathway for pancreaticoduodenectomy is safe and facilitates early discharge. Decreased epidural placement may partially explain the decreased LOS.

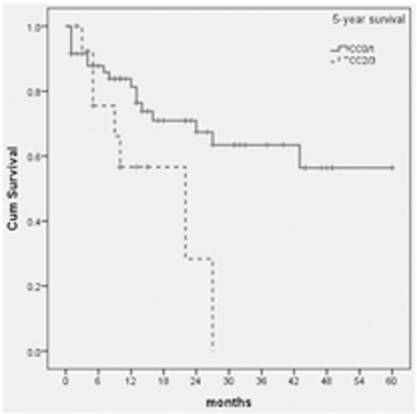


PT343

Cytoreductive Surgery and HIPEC in Elderly Patients: Complete Cytoreduction Remains Feasible and Crucial for Improved Survival S. Naffouje,[2]* G. Salti.[1] *1. Edward Medical Center, Naperville, IL; 2. University of Illinois at Chicago Hospital and Health Sciences System, Chicago, IL.*

Background: Despite their survival benefit in peritoneal surface malignancies, Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) remain aggressive procedures with a notable morbidity rate, rendering this benefit at debate in the elderly population. We aim to evaluate the outcomes of CRS and HIPEC in our 60+ year-old patients, and study the impact of complete cytoreduction on the survival of this population Methods: Patients ≥60 years old who had CRS and HIPEC were included and divided into 2 age groups: 60-69 years (Group 1), and ≥70 years (Group 2) to study the variation in outcomes with age. Primary outcomes were 30-day morbidity and mortality. Clavien-Dindo classification was used for morbidity grading. The impact of completion of cytoreduction (CC) on the 5-year survival of this population was tested using the Kaplan-Meier method. Results: a total of 73 elderly CRS and HIPEC patients were included. 46 patients fell in Group 1, and 27 patients in Group 2. Overall, 31 (42.47%) patients had postoperative morbidities of any grade, 9 (12.33%) were major (grade 3-4), and 3 (4.11%) mortalities (grade 5). Mean Peritoneal Carcinomatosis Index (PCI) was 14.71±9.23, CC0/1 was achieved in 80.82%. The most common pathology of the primary tumor was colorectal adenocarcinoma (CRC) in 29 patients (39.73%) then Pseudomyxoma Peritonei (PMP) in 22 patients (30.13%). There was no difference between groups 1 and 2 in regards to PCI, rate of CC0/1, operative time, blood loss, LOS, or in tumor pathology. Moreover, no difference was detected in postoperative morbidity or mortality. Upon comparison of survival based on CC, CC0/1 patients demonstrated improved 5-year survival compared to CC2/3 overall (41.0 vs. 16.7 mo; p=0.024). This result was reproducible within Group 1 (45.5 vs 16.0 mo) and Group 2 (30.4 vs 16.3 mo) Conclusion: CRS and HIPEC is a feasible, and relatively safe, surgical option for elderly patients. Our data suggest that surgeons should pursue complete cytoreduction even for patients in older age groups. Our survival analysis demonstrates that macroscopic residual disease hinders the patients' survival by 2-3 fold

5-year survival in our elderly patient population (73 patients; ≥60 years-old)
Comparison of the impact of completion of cytoreduction (CC0/1 vs. CC2/3 on the 5-year survival in this population)



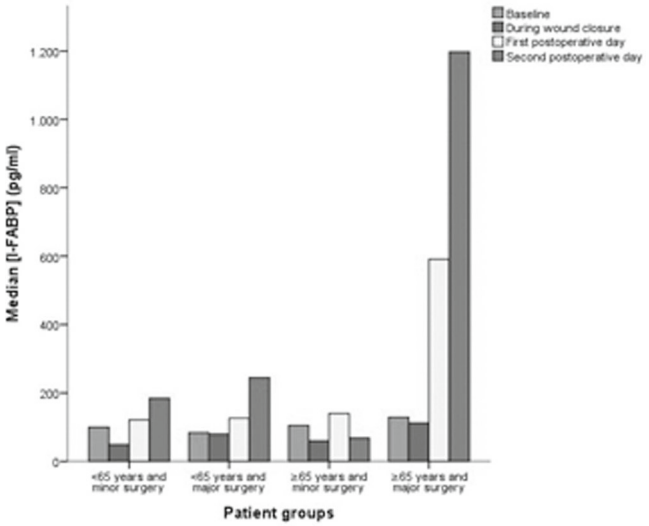
Complete Cytoreduction Y/N	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
0	16.741	3.871	10.722	22.760	22.000	9.046	4.270	39.730
1.0	41.070	3.700	33.819	48.321	.	.	.	.
Overall	37.711	3.484	30.882	44.540	43.000	.	.	.

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	5.110	1	.024

PT344

Compromised Intestinal Integrity Following Surgery in Oncogeriatric Patients S. Stokmans,* J.J. de Haan, H. van der Wal - Huisman, H.J. Hoekstra, E. Heineman, G.H. de Bock, A.R. Absalom, B.L. van Leeuwen. *University Medical Center Groningen, Groningen, Netherlands.*

Background: Postoperative morbidity is increased in frail elderly cancer patients undergoing surgery. Gut wall hypoxia-induced loss of intestinal integrity is hypothesized to be of importance in the development of postoperative complications. A non-invase tool to determine intestinal cell damage is Intestinal Fatty Acid Binding Protein (I-FABP), a protein present in enterocytes and released in the circulation after enterocyte damage. This study aims to investigate the development of intestinal cell damage in young and older cancer patients following surgery. Methods: Prospective cohort study executed between September 2014 and June 2016 in patients undergoing surgery for a solid malignancy. Urine I-FABP levels were measured preoperatively, at wound closure and on the first and second postoperative day. A mixed design ANOVA was performed to compare I-FABP values between patient groups. Results: 119 patients were evaluated, 59 patients <65 years (median 55 years) and 60 patients ≥65 years (median 70 years). Major surgery was performed in 75% of older patients and 46% of younger patients. Urine I-FABP levels were significantly increased on the first and second postoperative day in both age groups ($p<0.01$ in all cases). Interestingly, older patients undergoing major surgery displayed higher I-FABP levels compared with older patients undergoing minor surgery ($p=0.013$) and younger patients undergoing minor ($p=0.01$) and major ($p<0.01$) surgery. No significant differences were observed between the other patient groups (see attached chart). Conclusion: The significant increase of urine I-FABP levels in all patients during the postoperative course indicates that intestinal integrity is disturbed following oncologic surgery in both young and older patients. When both age and surgery severity are taken into account, the strongest I-FABP increase in the postsurgical course is found in older patients undergoing major surgery. Further research is necessary to demonstrate the association between peroperative gut wall hypoperfusion, disturbed intestinal integrity and postoperative morbidity.

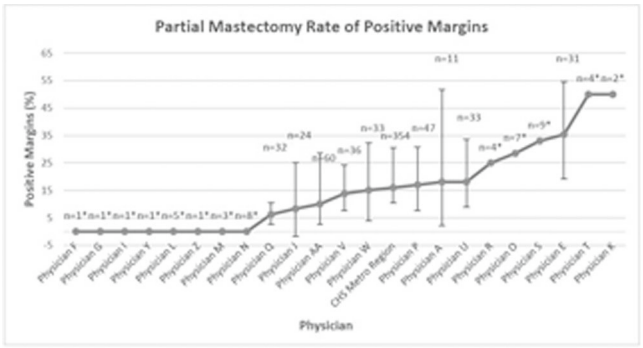


Graph 1: I-FABP over time in 4 patient groups

PT345

Surgeon-Specific Breast Care Metric Reporting Across a Large Cancer Network R.L. White,* K.K. Walsh, P. Palmer, M. Robinson, J. Eddy. *Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC.*

Introduction: Site-based quality metrics have become a common and integral part of clinical care. With the continued move away from fee-for-service and toward value-based payment models, surgeon-specific metrics are becoming more of a focus. Within the breast surgery program across Carolinas HealthCare System, we analyzed surgeon-specific performance on 13 different metrics; some quality-related and others related to surveillance. Methods: Data were gathered through existing cancer registry data as well as through in-depth chart reviews on breast surgeons practicing at eight different institutions in our CoC network over a 6-month time period. Surgeries performed between July 1, 2015 and December 31, 2015 were deemed eligible. Cases were excluded from analysis if patients had received treatment of interest at an outside facility or had substantial comorbidities. Each metric was summarized for each physician as either a proportion or a mean with 95% confidence intervals calculated for surgeons with cases ≥10. Anonymized reports were created and distributed after creating a breast metrics steering committee to review and evaluate the results. This abstract reports on established metrics recommended by the NAPBC. Results: Twenty-seven surgeons were profiled using these 13 metrics with an analyzed case total of 712. Performance on established metrics was excellent: core biopsy rate was 98.9% [89.7-100%], sentinel lymph node biopsy rate was 100% for eligible cases, reconstruction was discussed in 91.2% [50-100%] of cases, and the breast conservation rate for Stage 0, T1 and T2 cancers was 67% [0-100%]. In patients with atypical ductal and atypical lobular hyperplasia, excisional biopsy was discussed in 100% of cases. Margin positivity in partial mastectomies varied across surgeons from 0-50% with a median rate of 16% (Figure). Conclusion: Quality metrics for individual performance will be an ever increasing part of practice as we move toward more value-based payment models. As a system, we have initiated a process to inform surgeons of their own practice metrics with the goal of improving overall performance and patient care.



PT346

Association Between Commission on Cancer-Accreditation and Perioperative Outcomes Following Surgery for Gastrointestinal Malignancies Z. Fong,* D.C. Chang, S.S. Stapleton, G. Jin, A.B. Haynes, J.T. Mullen, J.C. Cusack, G.M. Boland, K.D. Lillemoe, K.K. Tanabe, M. Qadan. *Surgery, Massachusetts General Hospital, Boston, MA.*

Introduction: Commission on Cancer (CoC)-accreditation aims to guide patients with cancer to facilities that provide multidisciplinary, patient-centered, oncologic care. Non-accredited hospitals represent a heterogeneous group, with some hospitals foregoing accreditation, while others are unable to meet minimum requirements. Although accreditation has been associated with improved patient-reported outcomes, its association with perioperative outcomes is unknown. Methods: Using the Nationwide Inpatient Sample (2002-2011) and the American Hospital Association databases, we identified patients undergoing elective esophagectomy, gastrectomy, pancreatectomy, and colectomy for cancer. In-hospital mortality, complications, length of hospital stay (LOS), and cost were analyzed. In addition, outcomes were stratified according to hospital volume. Results: We identified 68,020 patients from 1800 hospitals, of which 41.3% were CoC-accredited. CoC-accreditation was not associated with any differences in adjusted in-hospital mortality rates for esophagectomy (OR 0.9, p=0.743), gastrectomy (OR 1.1, p=0.772), pancreatectomy (OR 0.840, p=0.416) or colectomy (OR 1.1, p=0.323). Similarly, CoC-accreditation was not associated with any differences in complication rate (esophagectomy OR 0.9, p=0.700; gastrectomy OR 1.0, p=0.930; pancreatectomy OR 0.9, p=0.471; colectomy OR 0.9, p=0.168), LOS (esophagectomy +0.8 days, p=0.532; gastrectomy -0.9 days, p=0.190; pancreatectomy +0.2 days, p=0.727; colectomy +0.004 days, p=0.969) or cost (esophagectomy -$5832, p=0.550; gastrectomy -$3927, p=0.190; pancreatectomy -$1317, p=0.760; colectomy -$230, p=0.740) for all 4 procedures. Stratified analysis by volume tertiles found no association between CoC-accreditation and in-hospital mortality among any of the procedures (Figure 1). Conclusion: We found no association between CoC-accreditation and perioperative outcomes among low, medium or high-volume hospitals. Additional studies will determine the effect of CoC-accreditation on oncologic outcomes including cancer-specific and stage-stratified survival rates.

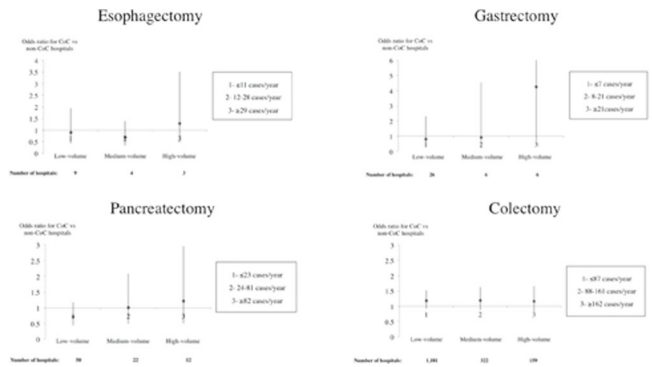


Figure 1. Adjusted in-hospital mortality rates for patients undergoing esophagectomy, gastrectomy, pancreatectomy and colectomy, stratified by low, medium, or high-volume tertiles.

PT347

Failure to Rescue Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy K. Li,* A.A. Mokdad, M.M. Augustine, S.C. Wang, M.R. Porembka, A. Yopp, R. Minter, J.C. Mansour, M.A. Choti, P.M. Polanco. *Surgery, University of Texas Southwestern, Dallas, TX.*

Introduction: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) can significantly improve the survival of patients with peritoneal carcinomatosis (PC). This procedure, however, can result in significant morbidity and mortality. Using a national cohort of patients, this study aims to identify perioperative patient characteristics predictive of failure to rescue (FTR)–mortality following postoperative complications from CRS/HIPEC. Methods: Patients suffering a complication following CRS/HIPEC between 2005 and 2013 were identified in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) dataset. Major complications are those corresponding to Clavien-Dindo grade III or IV. FTR was defined as 30-day mortality in the setting of a complication. Patients who suffered FTR were compared to those who survived a complication (non-FTR). Univariable comparisons were conducted using the Wilcoxon rank-sum test or the Fischer's exact test. Predictors of FTR were identified using a multivariable logistic regression model. Results: 915 eligible CRS/HIPEC cases were identified. 382 patients (42%) developed one or more post-operative complications. 88 (10%) patients suffered one or more major complications. 17 patients died following a complication, amounting to an FTR rate of 4%. FTR patients were more likely than non-FTR patients to have dependent functional status (18% vs 2%, p=0.01), have ASA class 4 status (29% vs 8%, p=0.01), develop ≥3 complications (65% vs 24%, p<0.01), and suffer a major complication (94% vs 20%, p<0.01). The following were independently associated with FTR: major complication (odds ratio [OR] 66.0, 95% confidence interval [CI] 8.4-516.6), dependent functional status (OR 5.9, 95%CI 0.8-41.9), and ASA class 4 (OR 13.4, 95%CI 1.2-146.8). Conclusion: Morbidity associated with CRS/HIPEC is comparable to other complex surgical procedures and has an acceptable low rate of death in this national cohort of patients. Dependent functional status and ASA class 4 are patient factors predictive of FTR; therefore, these patients should be considered ineligible for CRS/HIPEC.

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Laparoscopic Colon Resection for Cancer: Greatest Benefit for the Frail A. Lewis,* M. Raoof, K. Melstrom, S. Sentovich, I.B. Paz. *City of Hope, Duarte, CA.*

Introduction: Colorectal cancer (CRC) is a common ailment among the frail. Frailty is increasingly recognized as an indicator of poor post-operative outcomes. The benefit of laparoscopic approach to colon resection in frail patients is unknown. Methods: A query of the 2011-2014 American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database was performed to identify patients who underwent resection for CRC. An index based on preoperative ASA class, functional status, dyspnea, impaired sensorium, weight loss, transfer from 'care home', prealbumin, creatinine, and hematocrit was calculated to identify patients with frailty. Univariable and multivariable analyses were performed to evaluate 30-day mortality. Nearest-neighbor propensity score matching (PSM) was performed to match patients undergoing laparoscopic and open colon resection. Results: Before matching, a total of 52,087 patients with CRC were identified, of which frailty, as defined as an index score > 5, accounted for 2.63%. Laparoscopic resection was performed in 32.9% of the frail and 53.1% of non-frailty (p < 0.001). Patients were matched on laparoscopy, charlson comborbidity score, frailty, elective setting, type of resection, ostomy, age, sex, race, smoking status, BMI, and use of steroids. After PSM, frail patients accounted for 2.36% and 2.34% of patients undergoing laparoscopic and open colon resection, respectively. Frail patients had a higher 30-day mortality rate with open compared to laparoscopic approach (14.8% vs 6.9%, OR 2.4, 95% CI 1.5-3.7, p < 0.001). The effect of laparoscopy was less evident in non-frail patients (1.7% vs. 1%, OR 1.7, 95% CI 1.4-2.0, p<0.001). Conclusions: Laparoscopic approach to colon resections is likely under-utilized in the frail, and there is no detrimental effect from a laparoscopic approach in the frail population. Further studies are required to clarify the role of laparoscopy in patients with frailty

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Irreversible Electroporation of Non-Hepatic and Non-Pancreatic Cancers: A Single Site Assessment of Feasibility and Outcomes

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Introduction: The use of irreversible electroporation (IRE) is a fairly recent innovation in the surgical management of oncologic disease with promising early results. This ablative technique proposes the ability to locally manage solid neoplasms with both definable tissue selectivity and the absence of thermal necrosis and its sequelae. We have incorporated the use of intra-operative IRE in the treatment of primary and metastatic tumors when attempting to achieve local control in close R1 resections. Our study seeks to evaluate this use of IRE in the treatment of non-pancreatic and non-hepatic cancers and to further assess its utility in margin enhancement. Methods: This is a retrospective chart review of a prospective database at a single tertiary institution. Included were patients with pathologically proven cancer whom underwent IRE from November 2013 through May 2016 at the time of surgical resection of primary and/or metastatic tumors for margin enhancement. Primary tumors included colon, retroperitoneal, mesenteric, pelvic and extremity tumors. Results: 17 patients received intraoperative IRE for margin enhancement of non-hepatic and non-pancreatic lesions. Of these patients, 9 (57.9%) had no recurrence, 2 (11.8%) had local recurrence, and 6 (35.3%) experienced distant recurrence. Median followup was 27 months. 2 patients (11.8%) reported nerve palsies/parasthesias possibly attributable to IRE use due to the proximity to our ablative zone and the affected structures, though also known complications of the surgical resection. Conclusions: We report a local recurrence rate of only 11.8% in patients treated with intra-operative IRE and demonstrated no related intra-operative complications. Intra-operative IRE was not associated with unplanned re-interventions or readmissions within the global 30 day post-operative period. As such, we propose that intra-operative IRE may serve as a viable and safe adjunct in the surgical management of non-pancreatic and non-hepatic cancers in attaining clinically R1 resection margins. This contention would benefit from extensive patient follow up and investigation of prospective data.

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Initial Experience of a Targeted Intraoperative Radiotherapy Program for Early Stage Breast Cancer

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Introduction: Targeted Intraoperative Radiotherapy (TARGIT-IORT) offers exceptional convenience compared to external beam radiotherapy (EBRT) following breast conserving surgery for breast cancer. TARGIT-IORT lacks the long-term follow-up compared to EBRT, but seems to be equivalent for tumor control with decreased toxicities, better cosmetic outcome and increased compliance. This study describes the implementation of TARGIT-IORT at a large academic cancer center. Methods: We conducted a retrospective review of early stage breast cancer patients treated between November 2015 and September 2016 with TARGIT-IORT. American Society for Radiation Oncology (ASTRO) partial breast guidelines were used for inclusion criteria. Results: 56 patients, median age 68, 70% African American successfully were treated. All patients had either DCIS or invasive cancer no greater than 3.0 cm, clinically negative axillary exam, Estrogen and Progesterone Receptor positive, and Her-2 negative. Patients underwent wire localization the day of surgery. Sentinel node biopsy was obtained by peri-areolar injection of Lymphazurin. TARGIT-IORT consisted of 20 Gy delivered directly in the tumor cavity after completion of partial mastectomy and sentinel node biopsy in 93.4% of the cases. The applicator size ranged from 3.5 to 5 cm and the delivery time ranged from 16.2 to 43.9 minutes. Mean operative time was 126 minutes. Of the 39 patients with invasive cancer: 90% were pathologically node-negative, 95% were margin negative. Complications rate was overall 7.2%. All patients with positive or close margins for DCIS was offered re-excision; one received re-excision, one received mastectomy, and two received EBRT. Six patients (11%), required EBRT due to positive margins or positive sentinel node biopsy. Conclusions: TARGIT-IORT is a highly desirable and very convenient alternative to EBRT for early stage breast cancer. With careful selection criteria, it can be offered successfully with very acceptable operative time and low complications. This treatment is also very attractive for poorly complaint patients and does not preclude EBRT if necessary based upon the final pathologic report.

Demographics and treatment characteristics (n=56 patients)

	N (%)
Age years (median)	68
Race Caucasian African-American Others	 15 (26.6) 39 (70.0) 2 (3.4)
Tumor Histology Ductal carcinoma in situ (DCIS) Invasive Ductal Carcinoma (IDC) Others (Mucinous, Lobular, Tubular)	 17 (30.8) 64 (60.7) 5 (8.5)
Operative times in minutes, mean, range	126 (82-188)
IORT setting Pre-pathology At re-excision Dedicated post-pathology procedure	 53 (94.3) 2 (3.8) 1 (1.9)
Radiation therapy modality IORT alone IORT and External beam radiation	 50 (89.2) 6 (10.8)
Pathologic Stage Tis T1a T1b T1c T2 (up to 3 cm)	 17 (30.6) 5 (8.9) 11 (19.6) 15 (26.7) 8 (14.2)
Margins Negative (No tumor at the ink) Positive for IDC Positive for DCIS Close for DCIS, <2 mm	 43 (76.7) 2 (3.4) 2 (3.4) 9 (16.5)
Complications None Surgical site infection Others	 52 (92.8) 3 (5.5) 1 (1.7)

IORT= Intraoperative Radiation Therapy

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Sarcopenia is Associated with Hospital Expenditure in Patients Undergoing Cancer Surgery of the Alimentary Tract

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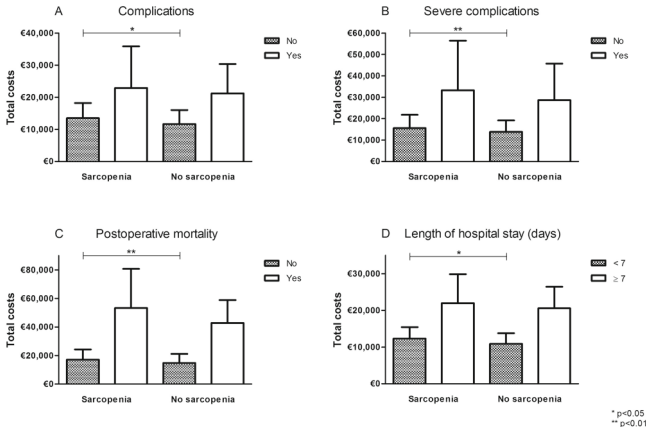
INTRODUCTION: Sarcopenia has been correlated with poor postoperative outcomes, and impaired medium- and long-term survival in surgical cancer patients. Furthermore, it is associated with increased health-care cost in the United States of America. We sought to determine its effect on hospital expenditure in a Western European health-care system, with equal access for all patients. METHODS: Computed tomography-assessed skeletal muscle mass, as well as clinical and financial characteristics were obtained for cancer patients who underwent abdominal cancer surgery in Erasmus University Medical Centre between 2005 and 2015. Patients were classified as (non-) sarcopenic based on the cut-offs established by Martin et al. and patients were divided in sex-specific quartiles for skeletal muscle mass. The relationship between sarcopenia and hospital costs was assessed using linear regression analysis and Mann-Whitney U-tests. RESULTS: In total, 524 patients were included with a median age of 65 (interquartile range 58-72). Most patients were male (60.7%). The majority of patients had an ASA classification of 1 or 2 (80.2%). Most patients underwent a resection for colorectal cancer (35.3%), while 157 (30.0%) underwent surgery for colorectal liver metastases, 126 (24.0%) for primary liver tumours, and 56 (10.7%) for pancreatic or periampullary cancer. Almost half of our cohort (44.7%) had sarcopenia. Total hospital costs for these patients were significantly higher than for patients without sarcopenia (€17,843 versus €15,015; $p<0.001$) and decreased per sex-specific quartile of skeletal muscle mass. Significantly higher costs were observed in patients without (severe) postoperative complications or prolonged (≥7 days) hospital stay (figure) and in patients undergoing hepatopancreatobiliary cancer surgery in particular. In linear regression analysis, presence of sarcopenia was associated with a cost increase of €5,255 ($p=0.001$). CONCLUSION: Sarcopenia was independently associated with increased hospital costs. Reduction of sarcopenia might therefore reduce hospital costs in an era of incremental health-care costs and an increasingly ageing population.



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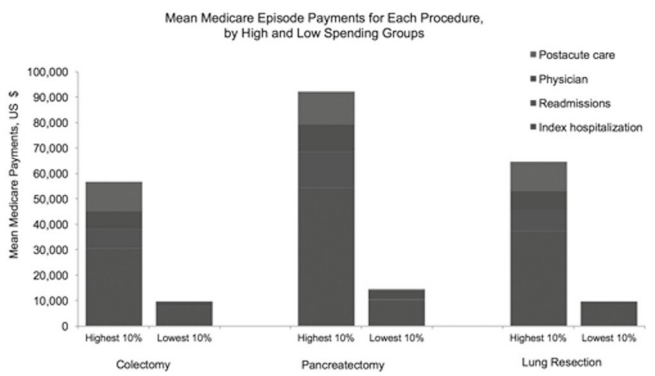
Understanding Variation in Costs of Cancer Resection S.P. Shubeck,* J. Thumma, E.C. Norton, J. Dimick, H. Nathan. *Department of General Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: The Affordable Care Act has spurred a shift in responsibility for healthcare costs from payers to providers. Based on extensive studies of cost variation in medical oncology populations, bundled payment programs for oncology have been adopted by CMS and private insurers. Although surgery drives a large portion of total cancer care expenditures, cost concentration in surgical oncology populations is poorly understood. We sought to better characterize variation in costs of cancer resection. Methods: Using 100% Medicare claims data for 2010-2013, we identified patients (pts) aged 65-99 years undergoing colectomy (Col), pancreatectomy (Panc), or lung resection (Lung) for cancer. We calculated price-standardized Medicare payments for index hospitalization, physician services, post-acute care, and readmissions for the entire "surgical episode" from the index admission through 30 days after discharge. Predictors of payments were analyzed by multivariable linear regression. Results: High-cost pts were more likely than low-cost pts to have multiple comorbidities (Col: 53% vs 45%, Panc: 56% vs 49%, Lung: 54% vs 40%) and experience more serious complications (Col: 11% vs 9%, Panc: 13% vs 10%, Lung: 10% vs 7%). Medicare expenditures for pts in the highest versus lowest decile of payments were 6x higher for Col ($56,788 vs $9,532), 6x higher for Panc ($92,078 vs $14,568), and 7x higher for Lung ($92,078 vs $14,568). Index hospitalization payments comprised 48-57% of the difference in total payments between highest and lowest deciles with post-acute care services and readmissions contributing to a lesser extent (Figure). Medicare patients in the highest decile of spending accounted for a disproportionate share of aggregate costs: 26% in colectomy, 27% in pancreatectomy, and 29% in lung resection. Conclusion: There is substantial cost concentration among Medicare beneficiaries undergoing cancer resection: 1/10 of patients account for 1/3 of the total costs. Spending is primarily driven by the index hospitalization including expenses related to complications, especially in multimorbid pts. Bundled payments for surgical oncology procedures must appropriately account for patient complexity.



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Race Is Not an Independent Predictor of Pancreatic Cancer Survival O. Moaven,* J. Richman, S. Reddy, T. Wang, M. Heslin, C. Contreras. *Department of Surgery, University of Alabama at Birmingham, Birmingham, AL.*

Introduction: Pancreatic adenocarcinoma (PA) is an aggressive malignancy. It is unknown whether racial background contributes patient survival after resection. Methods: We retrospectively analyzed the National Cancer Database of the American College of Surgeons, years 1998-2012. Unadjusted chi-square, student's t-tests and multivariate generalized additive models were used to compare the differences between white vs. African American patients (AAp) in patient characteristics and outcomes including overall survival, short term survival, and unplanned readmission after resection. Results: We identified 67704 patients with resectable PA who were offered resection. AAp refused surgery more frequently than white patients (14.6% vs. 10.7%, p<0.01). Resection was performed on 60208 patients; AAp comprised 9.8% of the population (n=5927). Overall, AAp were younger (mean age 62.7 vs. 66.0 years, p<0.01), more likely to have additional comorbidities (37.4% vs. 31.8%, p<0.01), more likely to live in areas with lower income (percent in lowest quartile 45.2% vs. 14.5%, p<0.01), less educated (percent in lowest quartile 34.6% vs. 13.5%, p<0.01), and more likely to not have insurance (5.5 vs. 2.3%, p<0.01). AAp were more likely to have well or moderately differentiated tumors (65.9% vs. 61.7%, p<0.01) and slightly more frequent nodal metastasis (61.2% vs. 59.5%, p=0.013). In unadjusted analyses, AA had a modestly increased hazard for all-cause mortality (HR=1.04; 95% CI: 1.01-1.07, p=0.02), and higher risk for all-cause mortality within 90 days after surgery (10.5% vs. 9.3%, OR=1.14; 95% CI 1.04-1.25. p=0.01). There were no significant differences in 30-day mortality or readmission. After adjustment for patient, tumor and facility factors, race was not significantly associated with all-cause mortality (HR= 1.02, 95% CI 0.98-1.07, p=0.35) or 90-day mortality (OR 1.06, 95% CI 0.91-1.24, p=0.14). Conclusions: While race is linked with socioeconomic and clinicopathologic parameters, a multivariable model demonstrates that race does not independently contribute to survival and readmission. Further studies are required to address the disproportionate refusal of resection in AAp with resectable tumors.

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Evaluation of Quality of Life Following Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Colorectal Origin R.M. Dodson,* H.D. Mogal, K. Votanopoulos, P. Shen, E.A. Levine, k. Duckworth, G. Russell, R. McQuellon. *Wake Forest Baptist Medical center, Winston-salem, NC.*

BACKGROUND: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy(HIPEC) for peritoneal metastases of colorectal origin can alleviate symptoms and prolong survival not achievable by systemic therapy alone. The purpose of this study was to monitor outcomes following HIPEC for colorectal cancer (CRC) including morbidity and quality of life (QOL). METHODS: Retrospective analysis of a prospective maintained QOL trial of patients from 2000-2015 that underwent HIPEC for peritoneal metastases from CRC. QOL instruments included: the Short Form-36 (SF-36), Functional Assessment of Cancer Therapy + colon subscale(FACT-C), Brief Pain Inventory(BPI), Center for Epidemiologic Studies Depression Scale (CES-D), and ECOG performance status at baseline, 3, 6, and 12 months post-HIPEC. Clinicopathologic factors, morbidity, and mortality were analyzed RESULTS: 285 patients (47% female) with a mean age of 53.2 +/- 12.9 years were analyzed. Overall 1-year survival was 70.1%; median survival was 18.2 months. Minor morbidity was 39.7%; major morbidity was 28.8%; 30-day mortality was 4.6%. 118 patients participated in the QOL trial. Significant detriments in physical measures of QOL (BPI, worst pain, sleep, FACT-C, trial outcome index, physical function, physical and functional well-being) were found at 3 months, but returned to baseline at 6 months. Mental/emotional measures (CES-D, emotional well-being, emotional health, and role emotional) improved after CS+HIPEC. CONCLUSIONS: HIPEC for CRC is associated with morbidity and impairment of QOL. However, recovery with good overall QOL typically occurs at or before 6 months. Long term survival with good QOL is frequently found after HIPEC for CRC.

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Perioperative Mortality Following Palliative Operations: Understanding the Continued Impact of the Palliative Triangle

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BACKGROUND:For patients with advanced malignancy, mortality alone is suboptimal to evaluate treatment success following palliative operations. Shared decision making involving the patient, family, and surgeon, is an approach shown to more effectively palliate cancer-related symptoms. Understanding the causes of post-operative mortality is critical to better counsel patients and family in the pre- and post-operative setting. METHODS:Operations were identified from a prospectively maintained palliative surgery database at a tertiary care center, 2003-2013. Recorded data included symptoms requiring palliation and contributing factors leading to death. Patients were followed for ≥90 days or until death. RESULTS:Palliative operations to relieve symptoms or improve were performed on 162 patients. Primary tumor types included 56 pancreatic(34.6%), 19 colorectal(11.7%), 13 gastric(8.0%), 12 melanoma(7.4%), and 62 other(38.3%). Symptoms improved in 133 patients(81.1%) overall; 25 patients(15.4%) developed new symptoms in follow-up, a median 182 days after operation. Median overall survival was 264 days. Nine patients(5.6%) died within 30 days and 21 additional patients(12.9%) died within 90 days. Causes of death at 30 versus 90 days were from postoperative complication(n=1, 11.1% vs. n=3, 14.3%), disease progression(n=1,11.1% vs. n=14, 66.7%;p=0.014), or decision made among the patient, family, and surgeon to stop active treatment(n=7, 77.8% vs. n=4, 19.0%;p=0.0042). Mortality within 30 days was associated with less frequent symptom improvement compared to mortality at 30 to 90 day(n=1,11.1% vs. n=11,52.4%;p=0.049). CONCLUSIONS:Decisions regarding pre- and post-operative palliative surgical care are best made within the dynamic relationship described by the palliative triangle. A majority of 30-day mortality was associated with interactions of the palliative triangle, while disease progression accounted for most 90-day deaths. Patients who survived the immediate postoperative period reported durable improved quality of life. Understanding differences in outcome measures will be crucial as surgical quality is scrutinized in palliative surgery patients.

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Health Insurance and Pancreatic Cancer Treatment and Outcomes

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Background: Along with racial disparities, health insurance disparities are important factors affecting the treatment and outcome of many cancers and include differences in screening, surgical resection and/or the use of adjuvant therapy. The purpose of this study is to investigate the role of health insurance on the treatment and survival in pancreatic cancer (PDAC) patients. Methods: 4564 patients diagnosed with PDAC from 2004-2013 were identified from the Tennessee Cancer Registry and were stratified into 5 groups based on insurance: Private, Medicare, Military, Medicaid, and uninsured. Univariate analysis and multivariate (MV) regression models were used to test the association of insurance with surgical resection, adjuvant therapy, overall survival (OS) and cost. Results: Uninsured and Medicaid patients were more often black and presented with later stage disease while those with Private insurance were most likely to be resected (58%) among stage 1 and 2 patients. Resected patients had similar R0 resection rates and lymph node (LN) positive disease as well as overall costs across the insurance groups. By MV analysis, patients with Medicare and military insurance had a higher likelihood of being resected compared to the uninsured (OR 2.52, 1.07, 5.9 and 3.30, 1.26,8.6, respectively) with a trend for those with private insurance (OR 2.19, 0.94, 5.08) but no difference in those with Medicaid. There was no difference among the insurance groups in the use of adjuvant chemotherapy (ACT). Cox-proportional hazards regression revealed no difference in OS in resected patients among the different insurance groups or by race. Factors associated with decreased OS survival included increasing age, stage, LN status, and grade. The use of ACT but not chemoradiation was associated with a significant improvement in OS. (Table). Conclusion: Uninsured and Medicaid patients tend to present with later stage disease, and are less likely to undergo surgical resection. The use of ACT, overall cost and OS, however, is similar among insurance types. These results are in contrast to other cancers suggesting that in more aggressive cancers without effective screening, disparities in health insurance may play a lesser role.

Factor	HR	95% CI	p-value
Age	1.29	1.04-1.61	0.02
Insurance (ref = uninsured)	ref	ref	ref
Medicaid	1.74	0.78-3.88	0.17
Medicare	0.87	0.49-1.52	0.63
Military	1.37	0.58-3.24	0.47
Private	0.96	0.55-1.66	0.88
Male gender (ref = female)	0.99	0.80-1.23	0.95
Black race (ref = white)	0.98	0.73-1.30	0.87
Tumor size	1.23	1.09-1.39	0.001
LN pos (ref = LN neg)	2.00	1.40-2.86	<0.001
Margin pos (ref=margin neg)	1.28	0.97-1.70	0.08
Grade (ref = 1)	ref	ref	ref
Grade 2	1.44	0.99-2.11	0.06
Grade 3	1.91	1.28-2.85	0.002
Adjuvant Chemotherapy	0.50	0.39-0.65	<0.001
Adjuvant Chemoradiation	1.04	0.81-1.33	0.74

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Virtual Colorectal Cancer Surveillance: Bringing Scope Rates Back on Target

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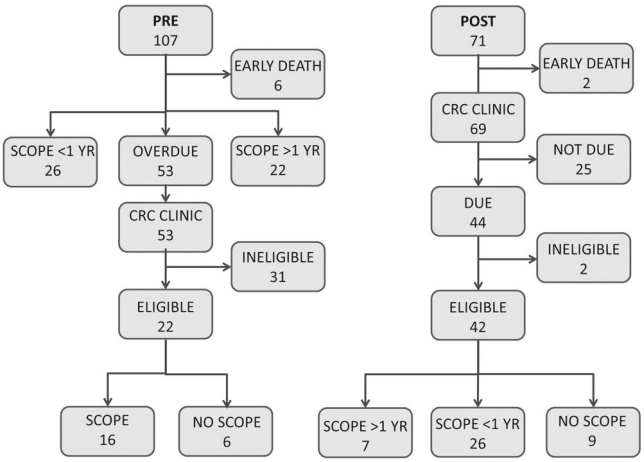
Background: For colorectal cancer, post-resection surveillance endoscopy is recommended within the first year to detect recurrent and metachronous cancer. We aimed to improve our Veterans Affairs facility's low rate of endoscopic surveillance (currently 34%). Methods: We identified opportunities for improvement in current endoscopic surveillance processes system then developed and tested an intervention. We implemented a gastroenterology-managed virtual surveillance clinic with standardized processes and clarification of provider roles within our inter-professional team. The primary outcome measure was the proportion of eligible patients who underwent endoscopy 1 year after resection, which we compared pre- and post-intervention. The secondary outcome was the proportion of patients with endoscopy completed at any time after resection. Results: The virtual surveillance clinic was implemented in August 2014. A total of 178 patients underwent colorectal cancer resection between January 2010 and April 2016 (107 pre-intervention, 71 post-intervention). Post-intervention patients underwent cancer resection after clinic establishment or within the prior year (eligible for primary outcome). Of these, 42/71 remained eligible for one-year surveillance endoscopy. Sixty-two percent (26/42) underwent endoscopic surveillance within one year versus 34% pre-intervention ($p<0.01$). Including patients with delayed endoscopies after the one year mark, seventy-nine percent of post-intervention patients (33/42) underwent surveillance endoscopy. The pre-intervention group included 107 patients who had their cancer resection more than a year prior to clinic establishment (eligible for secondary outcomes only). By the time of the intervention 22/107 patients were still overdue and remained eligible for endoscopy, and 73% (16/22) underwent surveillance endoscopy. Conclusions: Implementation of a virtual surveillance clinic with clearly defined processes and established provider roles increased guideline-concordant endoscopic surveillance after colorectal cancer resection. This approach may serve as a model for managing long-term cancer surveillance needs using existing resources and workflows.



Performance of surveillance colonoscopy at one year among patients with resected colorectal cancer pre- and post-implementation of virtual surveillance clinic

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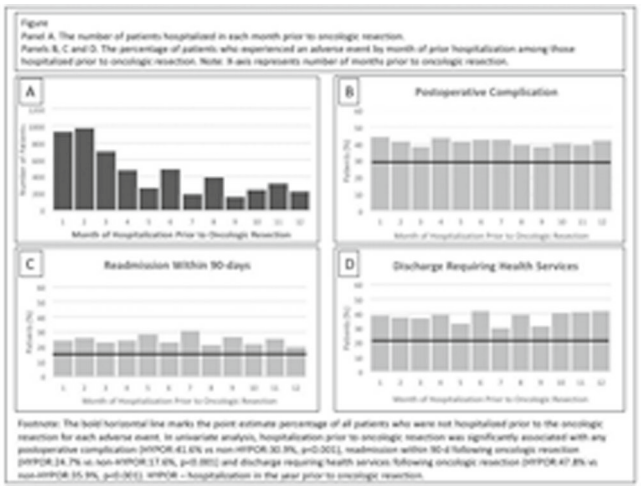
Hospitalization in the Year Prior to Oncologic Resection Increases Risk of Adverse Events C. Sharoky,* K. Collier, C. Wirtalla, A. Sinnamon, M. Neuwirth, R. Roses, D.L. Fraker, G. Karakousis, R.R. Kelz. *Hospital of the University of Pennsylvania Center for Surgery and Health Economics, Philadelphia, PA.*

Introduction: Increased vulnerability in the period after inpatient hospitalization has been cited as a cause of medical readmissions, however little is known about the effects of prior hospitalization on surgical outcomes. This study examined whether hospitalization in the year prior to oncologic surgery was associated with adverse events. Methods: Patients ≥18y with stomach, pancreas, colon or rectal cancer who underwent resection in California and New York (2008-2010) met inclusion criteria. Patients with hospitalization in the year prior to oncologic resection (HYPOR) were identified. Patients with cancer-related prior hospitalizations were excluded. Independent multivariable logistic models were used to examine the association of HYPOR with inpatient mortality, postoperative complications, discharge needs, and subsequent readmissions. Separate analyses were performed to determine whether outcomes changed based on temporal proximity of HYPOR to surgical admission. Results: Of 32,356 patients, 16.9% (n=5,452) were HYPOR. HYPOR patients were older (Median 72y vs 67y, p<0.001), had more Elixhauser comorbidities (4 vs 3, p<0.001) and were more likely to have public insurance (67.5% vs 55.0%, p<0.001) compared to non-HYPOR. The distribution of HYPOR by month can be seen in the Figure. HYPOR was not associated with inpatient mortality. Rates of postoperative complications, discharge requiring health services, and readmission within 90 days were higher in HYPOR patients (see Figure). On multivariable analysis, HYPOR was significantly associated with increased odds of postoperative complications (OR 1.29 [CI 1.20-1.37]), discharge requiring health services (OR 1.47 [CI 1.37-1.58]) and readmission within 90 days (OR 1.47 [CI 1.36-1.58]). Time interval (in months) from HYPOR to resection was not associated with the examined outcomes. Conclusions: Patients hospitalized in the year before oncologic surgery are at increased risk of postoperative complications, discharge requiring health services, and readmissions. This study identifies a cohort of cancer patients who may benefit from additional preoperative counseling and prehabilitation services prior to oncologic surgery.



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Use of Palliative Care Among Patients Admitted for Cancer Z. Enumah, F. Gani, J.K. Canner, F. Johnston.* *Johns Hopkins University, Baltimore, MD.*

Background: Although a growing body of literature recommends the initiation of palliative care (PC) early in the continuum of cancer care, the use of PC remains variable. We sought to describe the use of PC and to identify factors associated with the use of inpatient. Methods: Patients admitted with a primary diagnosis of gastrointestinal and / or thoracic cancer were identified using the National Inpatient Survey (NIS). Multivariable logistic regression analysis was performed to identify patient and hospital level characteristics independently associated with the use of PC. Results: A total of 380,862 patients were identified who met inclusion criteria. Median age of all patients was 67 years (IQR: 58-76) with 45.2% (n=171,960) of patients being female. During their inpatient stay, 37,632 (9.8%) patients received a PC consult. Patients who received PC were more likely to have a longer length-of-stay (LOS >14 days: 10.5% vs. 7.9%) and were more likely to develop a postoperative complication (31.4% vs. 46.1%, both p<0.001). Overall inpatient mortality was 7.4% (n=28,138) and was significant higher among patients who received PC than those who did not (33.2% vs. 4.6%, p<0.001). On multivariable analysis, increasing patient age (age≥75 years: OR=2.33, 95%CI: 2.16-2.51), insurance status (Medicare vs. private: OR=0.66, 95%CI: 0.64-0.69), socioeconomic status (high vs. low: OR=1.12, 95%CI: 1.08-1.15) and preexisting comorbidity (CCI>6: OR=2.55, 95%CI: 2.44-2.65) were independently associated with greater odds of receiving PC (all p<0.001). Similarly, patients who received care at large (reference small: OR=1.30, 95%CI: 1.25-1.35) or urban-teaching hospital (reference rural: OR=1.43, 95%CI: 1.37-1.50) demonstrated greater odds of receiving PC (both p<0.001). Interestingly, patients who underwent a major surgical procedure during their inpatient admission demonstrated 76% lower odds of receiving PC (OR: 0.24, 95%CI: 0.23-0.24, p<0.001). Conclusions: Among patients admitted for cancer, PC services were used in 9.8% of patients with less than 0.5% of surgical patients receiving PC during their inpatient admission. Further research is require to delineate the barriers to the use of PC among high-risk patients.

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Extended Postoperative Recovery Leads to Worse Long-term Oncological Outcomes Y. Sekigami,[2] E.C. Poli,[1]* R. Rajeev,[2] T. Gamblin,[2] K.K. Turaga.[1] *1. General Surgery, University of Chicago, Chicago, IL; 2. Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Curative cancer surgery remains the cornerstone of treatment of localized malignancies. Extended post operative recovery (eLOS) is associated with debility and immunosuppression. We hypothesized that eLOS is associated with worse long term oncological outcomes. Methods: The NCDB participant user file from 2004-13 was utilized to identify patients with localized gastrointestinal malignancies undergoing curative cancer resections. Quartiles (Qx) of length of stay (LOS) were calculated based on histology and site specific indicators. Survival modeling was performed using

cox-proportional hazards and conditional models were created. Alpha of 0.05 was set for statistical significance. Results: Of 1,616,215 patients in the cohort, 577,860 patients were included who met inclusion criteria. Majority of patients were ≥65 years (56%) with a predominance of colon cancer (70%). The median length of stay (LOS) varied from 5 days (partial hepatectomy) to 10 days (esophagectomy). After adjusting for age, gender, stage, and site of disease, increasing length of stay was significantly associated with worse oncological survival with a dose response effect (Q1 HR 1.0, Q2 1.12 (1.10-1.14) p<0.001, Q3 1.42 (1.41-1.44) p<0.001 and Q4 1.82(1.80-1.85), p<0.001). Conditional overall survival for patients who survived 3, 6 and 12 months after surgery, was worse with eLOS (p<0.001). Conclusions: Longer than expected length of stay after an index curative cancer operation leads to worse overall oncological outcomes. This effect persists even after excluding patients who suffer delayed post-operative mortality within 12 months after the operation. More research needs to be done to determine if this outcome is related to perioperative immunosuppression.

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Impact of Insurance on Physical and Psychological Concerns of Breast Cancer Patients: Results of a Comprehensive Distress Screening Program S. Dumitra,* V. Jones, C. Vito, J. Rodriguez, C. Bitz, E. Polamero, R. Obenchain, M. Loscalzo, L. Lai, L. Kruper, S. Warner. *City of Hope, Duarte, CA.*

INTRODUCTION: Understanding patient stress is critical to cancer care. This study examines self-reported biopsychosocial impacts of insurance concerns on patients with breast cancer. METHODS: From March 2014-February 2016, patients underwent an electronic 48-point distress screen during their initial surgical clinic visit. Biopsychosocial distress was self-reported on a five-point Likert scale. Respondents indicating distress were also asked if and how they would like to receive help. The impact of insurance concerns on biopsychosocial distress was assessed using chi-square. RESULTS: Of the 344 patients screened, 26.7% patients had insurance concerns. There was no difference in ethnicity or education amongst those with and without insurance concerns. Distress over insurance correlated with financial concerns (p<0.001) and concern for affording medications (p<0.000). Those with insurance concerns reported more sleeping problems (67.7 vs. 55.0%, p=0.018). Patients with insurance concerns reported more problems managing emotions (81.5 vs 64.2%, p<0.000), worrying about the future (88.9 vs. 72.9%, p<0.000) and anxiety (91.8% vs 88.3%, p=0.065) but not depression. Patients with insurance concerns also had concerns about understanding treatment options (65.2 vs. 41.2%, p<0.000) and concerns about side effects of treatments (65.2 vs. 56.7%, p=0.009). Patients with insurance concerns were more likely to seek help regarding insurance (p<0.000), medication (p<0.000) and pain (p=0.004) but not for other issues despite reporting higher rates of distress. CONCLUSION: Patients with health insurance concerns report more biopsychosocial distress than their counterparts. This study highlights insurance-related disparities amongst breast cancer patients and identifies patient groups that would benefit from automatic supportive care.

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Mind the Gap: A Case for Interdisciplinary Cooperation in the Treatment of Early Stage Breast Cancer W. Guerrero,[1]* D. Layman,[2] A. Wise,[2] W. Gilman,[2] E. Izaguirre,[3] M. Farmer,[3] M. Fleming.[4] *1. Department of Surgery, University of Tennessee Health Science Center, Memphis, Memphis, TN; 2. College of Medicine, University of Tennessee Health Science Center, Memphis, Memphis, TN; 3. Department of Radiation Oncology, University of Tennessee Health Science Center, Memphis, Memphis, TN; 4. Division of Surgical Oncology, University of Tennessee Health Science Center, Memphis, Memphis, TN.*

Partial breast radiation (pBR) allows women with early-stage breast cancer to avoid the more widespread side effects of external beam radiation (eBR). Radiation catheters (RCs) are placed after lumpectomy. If the conformation of the cavity along the axis of a wire placed for wire localized lumpectomy (WLL) does not match the orientation of the catheter, an air gap may result. If the gap is large enough, pBR cannot be delivered; the patient will require eBR. We sought to determine how choices made in each phase of care affect the success of pBR therapy. This is a retrospective case-control study. We reviewed all patients for whom pBR was planned at a single institution between January 2008 and June 2016. Clinicopathologicand outcomes data were recorded. There were 164 patients who desired pBR. They were all female; average age at presentation was 62.2 years (IQR 57.2, 67.7). Most patients presented with Stage I disease (67%, n=110) or DCIS (27%, n=45). Median follow up was 34.4 months. Twenty-five patients (15%) required RC revision; seven catheters (4%) were exchanged and 18 catheters (11%) were pulled altogether; these patients required eBR. Patients who underwent WLL were equally likely to have an air gap as those without wire localization (RR 1.1; 95% CI 0.5, 1.9, p=0.99). However, in the presence of an air gap, patients who had not undergone WLL were far more likely to have their RC pulled (OR 50.9; 95%CI 8.3, 250, p<0.0001) than patients who had undergone WLL (OR 15.3; 95% CI 2.7, 86.4, p=0.006). The presence of an air gap was highly correlated with catheter revision (OR 31.15; 95% CI 8.86, 94.07, p<0.0001) and inability to initiate pBR therapy (OR 10.08; 95% CI 3.4, 31.7, p<0.0001). The presence of an air gap is a major factor in the administration of pBR. We observed that while WLL alone does not prevent the formation of an air gap, it does confer relative protection from RC removal necessitating eBR. Successful administration of pBR requires coordination between radiology, surgery, medical physics, and radiation oncology

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Continuous Evolution in Complex Surgical Procedures: Lessons Learned from a Peritoneal Surface Malignancy Center A. Ben-Yaacov,* J. Dux, A. Zendel, D. Zippel, M. Venturero, A. Nissan. *Department of Surgery and Surgical Oncology, Chaim Sheba Medical Center, Givataym, Israel.*

BACKGROUND: Integration and assimilation of novel surgical procedures requiring a learning period referred as "learning curve". Mostly, learning curves of individual surgeons or institutions are defined by the completion of a finite number of cases. We hypothesize that in complex procedure this model may not apply and the process requires continues improvement and a plateau of the "learning curve" may never be reached. METHODS: A retrospective analysis of prospectively maintained database of a single group performing cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) between the years 2007 to 2016. A total number of 275 patients with peritoneal surface malignancy were treated. A total number of 269 patients were analyzed for the following outcomes: operative time, estimated blood loss (EBL), completeness of cytoreduction score, intensive care unit stay, hospital stay, post-operative complications and mortality. Statistical analysis was employed to assess these parameters for each specific year from 2007 to 2016 and to show weather there is a continuous improvement or a plateau phase on the learning curve of these complex procedures. RESULTS: The number of cases performed each year increased from 13 in 2007 to 80 cases in 2016. There was a linear decrease in operative time and average EBL from 9.2 hours in 2007 to 4.9 hours in 2016, and 1400 ml to 441 ml respectively(P<0.05). Continuous increase in percentage (%) of CC score 0 from 61.5% In 2007 to 89% in 2016. There was a linear decrease in ICU and hospital stay from 5 days to 1 day, and 22 days to 15.5 in respectively (p<0.05). There was no significant decrease in 3-4 complications. However, peri-operative mortality decreased from 5 (4.3%) cases between 2007-2012 to 2 (1.8%) cases between 2013-2016, (P<0.001). We could not deify a point of time or cumulative number of cases to indicate plateauing of a learning curve. CONCLUSIONS: In complex procedures such as CRS and HIPEC there is no clear distinction between a learning curve and optimal performance. There is however, according to our results, a continuous and linear trend of improvement in almost every aspect studied

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Identification and Introduction of Key Complex General Surgical Oncology Principles for Incoming Fellows B. Bednarski,* B. Badgwell, T.A. Aloia, J.E. Lee, E.G. Grubbs. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: As general surgical education evolves, questions remain regarding resident preparedness for surgical fellowships, including Complex General Surgical Oncology (CGSO). To address potential knowledge gaps in key concepts of CGSO and facilitate transition to fellowship, a novel introductory course was designed, implemented and evaluated at a single institution. Methods: A needs assessment survey for faculty was created to identify which key content areas in CGSO [anatomy, minimally invasive surgery, palliative surgery (PS), end of life care, specialized imaging techniques (SIT), multidisciplinary care (MDC), and neoadjuvant therapy (NT)] would benefit early fellow education. Content areas were revisited in small group discussions with

current CGSO fellows. Results were used to create a one-day course curriculum. A retrospective pre-post survey using a 5-point Likert scale [Novice (1) to Expert (5)] was used to assess knowledge gained. Results: Twenty-six of 45 faculty (57.8%) completed the needs assessment and identified three essential content areas: NT, MDC, and PS. Small group discussions with 10 CGSO fellows supported these topics and the addition of SIT, communication skills (CS) and management of difficult clinical conversations (MDCC). The curriculum content was developed to include case-based interactive lectures on SIT, NT and MDC. A separate session was dedicated to the content areas of PS, CS and MDCC using lectures, small group discussion and role-play. Eleven fellows (7 CGSO, 3 Breast and 1 Endocrine) attended the course. Retrospective pre-post assessments revealed improved knowledge in SIT, PS, CS, and MDCC with median score increases from 3 (pre) to 4 (post) on the Likert scale for each category, while median scores for NT and MDC were unchanged (4 to 4). Conclusions: CGSO faculty and fellows identified content areas where increased education could improve the transition from residency to CGSO fellowship. The opportunity exists to enhance the foundation of knowledge early in fellowship through innovative, needs-based curriculum. Follow up studies will assess the impact of the curricular content on the fellows' early clinical experience.

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Post Liver Transplant Cancer Risk in Patients Receiving Antibody-Based Immunosuppression Induction R. Mangus, R. Graham,* M. Maluccio. *Surgery, Indiana University School of Medicine, Indianapolis, IN.*

Introduction: Solid organ transplant patients have an increased risk of cancer in the post-transplant period because of their immunosuppressed state. Many transplant centers are now augmenting early immunosuppression with antibody based immunosuppression-induction. This study is a retrospective analysis of cancer incidence in 1685 liver transplant patients who all received immunosuppression induction with rabbit antithymocyte globulin over a 15 year period. Methods: A thorough review of the electronic medical record was conducted for all patients. Any diagnosis of cancer required clinical documentation and confirmation with review of a pathology report. Cox regression analysis was employed to assess long term patient survival. Patients with hepatocellular carcinoma (HCC) were analyzed separately from those patients without a history of HCC. Results: There were 1685 liver transplant patients included in this analysis with mean follow up of 75 months. There were 10% of patients who had any history of non-HCC cancer at the time of transplant. Among these non-HCC patients, 16% developed de novo post-transplant cancer. Among patients with HCC at transplant, 10% had any history of non-HCC cancer at the time of transplant, with a 15% incidence of de novo cancer post-transplant. Risk factors for post-transplant non-HCC cancer include White race (18%, $p<0.01$), older age (23% for age 60 and older, $p<0.001$), history of alcoholic liver disease (19%, $p=0.03$), and smoking (19%, $p=0.02$). There was an increased risk with increased pack-years (27% for more than 40 pack-years, $p<0.001$). 10-year Cox regression patient survival demonstrates lower survival for patients with any pre- or post-transplant history of cancer, though this does not reach statistical significance. Conclusion: These results suggest that patients who develop HCC prior to liver transplant do not have a higher risk of post-transplant de novo non-HCC cancer. There is an increased risk of cancer in these post-transplant patients, but the risk is not higher than that previously reported for solid organ transplant patients who did not receive immunosuppression induction.

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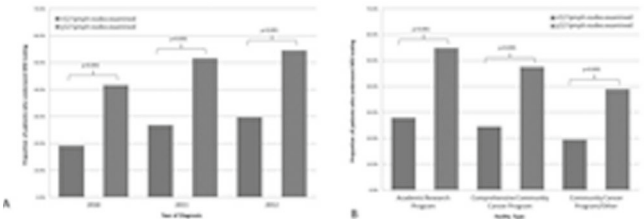
Underuse of Microsatellite Instability Testing and Predictors of High Microsatellite Instability Disease Among Young Colorectal Cancer Patients in the United States T. Shaikh,* E.A. Handorf, M. Hall, J.E. Meyer, N.F. Esnaola. *Fox Chase Cancer Center, Philadelphia, PA.*

BACKGROUND: The purpose of this study was to identify predictors of non-adherence to MSI testing in young CRC patients and identify factors associated with an increased risk of high microsatellite instability (MSI-H) disease. METHODS: Patients 18-49 years old diagnosed with invasive colorectal adenocarcinoma between 2010-2012 and known MSI testing status were identified using the National Cancer Data Base. Univariate associations between patient/tumor/facility/treatment characteristics and MSI testing status/results were analyzed using chi-square tests. Multivariable logistic regression was used to identify independent predictors of receipt of MSI testing, as well as MSI-H status among those tested. RESULTS: Among 17,218 patients identified, only 7,422 (43%) underwent MSI testing; the proportion of patients tested increased between 2010 (36%) and 2012 (48%; $p<0.001$). Higher educational level, early stage disease, and number of regional lymph nodes examined >12 were independently associated with MSI testing, whereas older age (40-49), Hispanic ethnicity, Medicare/Medicaid/uninsured insurance status, non-academic/research facility, facility location, rectosigmoid/rectal tumor location, non-mucinous histology, unknown grade, non-receipt of definitive surgery were associated with underuse. Among 6,358 tested patients with known MSI status, 531 (8%) patients had MSI-H disease. Lower income, history of previous cancer, and stage II disease were independently associated with MSI-H status, whereas older age (40-49), female sex, advanced comorbidity, non-metropolitan facility status, facility location, more distal tumor location, non-mucinous histology, unknown or lower tumor grade, and non-receipt of chemotherapy were inversely associated with MSI-H status. CONCLUSION: Despite long-standing national guidelines, significant underuse of routine MSI testing in young patients diagnosed with colorectal cancer persists. Interventions are warranted to improve adherence to guideline-based care in these patients, particularly among those at increased risk of MSI-H disease.

Figure: Association between number of regional lymph node examined and receipt of MSI testing in patients who underwent colectomy according to year of diagnosis (A) and facility type (B)



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Timing and Extent of Surgical Resection for Recurrent Retroperitoneal Well-Differentiated Liposarcoma N. Ikoma,* C. Roland, Y. Chiang, K.E. Torres, J. Cormier, N. Somaiah, K.K. Hunt, B.W. Feig. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Objectives: Recurrence after surgical resection of retroperitoneal well-differentiated liposarcoma (RP WDLPS) is common, and is a treatment challenge. We aimed to investigate the effect of timing and extent of surgical resection for recurrent RP WDLPS. Methods: The departmental sarcoma database was reviewed to identify patients with RP WDLPS who underwent surgical resection (salvage surgery) for 1st recurrent disease at the MD Anderson Cancer Center from 1994-2010. Medical records were reviewed to identify patient/treatment factors. Associations between clinicopathologic variables and overall survival (OS) as well as disease free survival (DFS) were examined. Results: We identified 45 patients who underwent surgical resection of RP WDLPS for 1st recurrent disease; median age was 54 years, and 42% were male. Sixty percent had recurrent tumors ≥10 cm, and 67% had multifocal tumors. Concomitant organ resections were performed in 17 (38%) of patients, and 24% of patients (4/17) had tumor invasion of resected organs. Median OS after salvage surgery was 7.4 years, and the 5-year OS was 70.4%. Median DFS after salvage surgery was 1.4 years, and the 5-year DFS was 21%. Multivariate analysis revealed that organ invasion (either at the primary surgery [HR 10.39, 95% CI 2.49-43.40; p=0.001] or at the salvage surgery [HR 4.17, 95% CI 1.13-15.47]) was associated with shorter OS after salvage surgery. Time between the date of recurrence and the date of salvage surgery of less than 6 months was associated with shorter DFS after salvage surgery (HR 2.41, 95% CI 1.15-5.05; p=0.02). Disease free interval (time from primary resection to the 1st recurrence, <1 year vs. ≥1 year) was not associated with OS or DFS. Organ resection was not associated with OS or DFS, but was associated with longer hospital stay ≥14 days (HR 16.2, 95% CI 1.73-151.8; p=0.015). Conclusions: In patients with resected recurrent RP WDLPS, organ invasion is a rare event and concomitant organ resection is associated with increased length of stay; therefore, organ resection should be avoided unless invasion is suspected. Early reoperation after recurrence may not always be the most beneficial approach.

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Quality of Life (QoL) and Pain in Primary Retroperitoneal Sarcoma (RPS): Preliminary Data from a Prospective Observational Study M. Fiore,* D. Callegaro, S. Lenna, R. Miceli, C. Brunelli, C. Colombo, N.N. Rampello, P.G. Casali, A. Caraceni, A. Gronchi. *Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy.*

Background: Prospective QoL data are lacking for patients undergoing surgery for RPS. Methods: Patients operated on between March 2014 and January 2016 for primary RPS were prospectively recruited. QoL was evaluated by EORTC QLQ-C30 and QLQ-CR29 questionnaires; pain status was investigated by Brief Pain Inventory (BPI-SF) and DN4 (neuropathic pain). Lower limb impairment was studied by Lower Extremity Functional Scale (LEFS) (score 80/80: no impairment). Baseline results before surgery are reported. Results: Sixty consecutive patients were enrolled. Median tumor size was 23 cm; 30 were right-sided, 28 left-sided, 2 located in the pelvis. Histology was as follow: dedifferentiated liposarcoma (53%), well differentiated liposarcoma (27%), leiomyosarcoma (13%), other (7%). Preoperative treatments were administered in 25% (7 RT, 6 CT, 2 CT+RT). In a scale from 0 to 100, median Global Health Status Score was 58.3 (interquartile range, 41.7-70.8); Physical Functioning Score 86.7 (73.3-93.3); Role Functioning Score 100 (66.7-100); Emotional Functioning Score 66.7 (50.0-79.2); Cognitive Functioning Score 83.3 (83.3-100); Social Functioning Score 100 (66.7-100). Median scores for most QLQ-30/CR-29 symptoms were zero, except for fatigue (22.2), insomnia (33.3), pain (16.7), and urinary symptoms (16.7). Sixty-eight percent of patients had some pain. Among them, 50% referred also neuropathic symptoms (even though no patient scored DN4≥4/10); median LEFS score was 65.5/80 (45.5-76.25). In a scale from 1 to 10, mean pain intensity for BPI-SF items varied from 1.16 (pain in this moment) to 2.27 (worst pain in previous 24 h). Mean average pain within the previous 24 h was 1.84. Ten patients (16.7%) reported pain with a score ≥5. Lower limb was the most common site of pain (21.6%); other affected areas were abdomen, flank/back. Ten patients (16.7%) needed daily pain-killers. Conclusion: At baseline, RPS patients reported reduced score of global health status. Main symptom are fatigue and insomnia. Mild pain is reported by the majority of patients. Functional impairment and mild neuropathic symptoms in the lower limb are documented also before surgery.

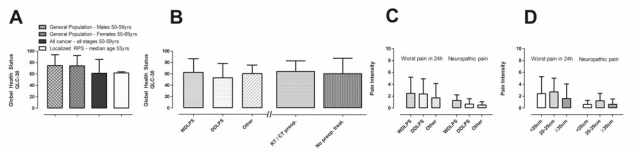

Fig. 1 Panel A, Comparison between EORTC QLC-30 reference values, all-cancer patients (Acta Oncologica, 2014; 53: 958–965) and present series of RPS. Panel B-D, Global Health Status and pain according to histotypes and tumor size and preoperative treatments.

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Defining the Incidence and Clinical Significance of Lymph Node Metastasis in Soft Tissue Sarcoma E. Keung,[1]* Y. Chiang,[1] J. Cormier,[1] R. Voss,[2] K.E. Torres,[1] G.N. Mann,[1] K.K. Hunt,[1] B.W. Feig,[1] C. Roland.[1] *1. MD Anderson Cancer Center, Houston, TX; 2. University of California, San Diego, San Diego, CA.*

Introduction: The reported incidence and clinical significance of lymph node metastasis (LNM, N1) in soft tissue sarcoma (STS) across disease sites is inconsistent. Recent studies have focused on extremity/trunk STS (ETSTS). We sought to define the subgroup of patients with LNM at initial sarcoma diagnosis across all disease sites and histologic subtypes. Methods: We identified and categorized 79,783 patients diagnosed with STS from the National Cancer Data Base (1998-2012) by nodal stage. Pathologically-confirmed LNM (pN1) were identified in 1204 patients (1.5%) and 1511 patients (1.9%) had clinically-suspicious but not pathologically-confirmed LNM (cN1). Survival analyses were performed by Kaplan-Meier method. Results: Of the 2715 patients (3.4%) with pN1 or cN1 LNM at presentation, 1160 (42.7%) had synchronous distant metastasis (M1). LNM was identified in a small proportion of non-ETSTS patients (5.8% head & neck, 5.3% intrathoracic, 5.5% intra-abdominal & 2.0% ETSTS; Table 1). Angiosarcoma (6.5%), epithelioid (12.8%), clear cell (16%), and small cell sarcoma (19.9%) had the highest incidence of patients with LNM, although liposarcoma, fibrous histiocytoma, and leiomyosarcoma accounted for the greatest number of patients with LNM (213, 347 & 333, respectively; Table 1). For patients with pN1M0 disease, median overall survival (OS) was 26.2 months and varied by histologic subtype. Among patients with pN1M0 STS, angiosarcoma, leiomyosarcoma, clear cell sarcoma, small cell sarcoma and fibrous histiocytoma were associated with worse median OS (19.4, 20, 23.8, 27.7 and 28.1 months, respectively) compared to epithelioid sarcoma and liposarcoma (48.2 and 59.3 months) (p<0.001). Conclusion: Despite clinical suspicion, pathologic lymph node evaluation in STS is inconsistently performed. LNM occurs across anatomic disease sites and is not evenly distributed across histologies. Although patients with M1 disease do poorly regardless of LN status, in those with M0 disease, LNM predicts worse OS in a histology-dependent manner.

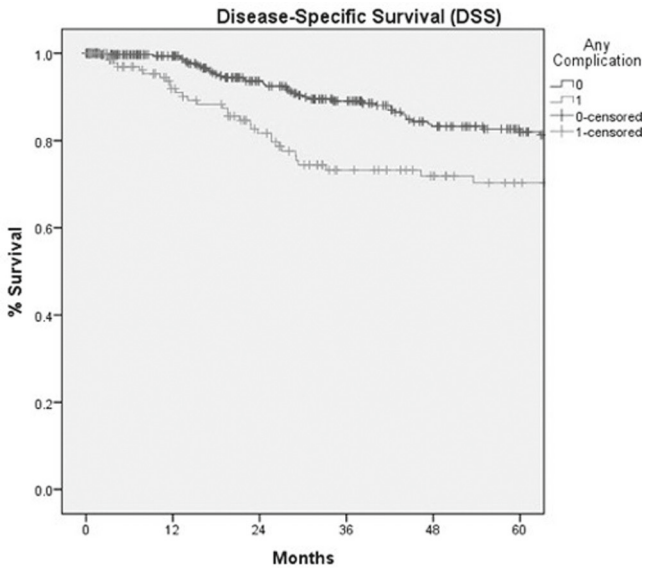
Percent of Patients with Lymph Node Metastases (pN1 and cN1 Disease) by Sarcoma Tumor Histology and Disease Site

Histology	Disease site % of all patients with LNM (Number of patients with LNM)				
	All Sites 3.4 % (2715)	Head/Neck/Face 5.8% (128)	Intrathoracic 5.3% (192)	Intraabdominal/Visceral 5.5% (1018)	Extremity/Truncal 2.0% (977)
Small cell sarcoma	19.9 % (110)	5.0 % (1)	11.1 % (2)	27.1 % (101)	6.5 % (12)
Clear cell sarcoma	16.0 % (85)	18.8 % (3)	18.8 % (3)	23.5 % (11)	15.0 % (68)
Epithelioid sarcoma	12.8 % (137)	14.3 % (7)	21.3 % (10)	15.2 % (43)	11.1 % (77)
Angiosarcoma	6.5 % (234)	6.3 % (70)	7.0 % (78)	9.6 % (39)	4.3 % (47)
Sarcoma NOS	6.0 % (509)	7.1 % (45)	9.9 % (63)	9.1 % (218)	3.6 % (173)
Alveolar soft part sarcoma	4.5 % (14)	0 % (0)	0 % (0)	9.3 % (3)	3.8 % (9)
Spindle cell sarcoma	4.3 % (166)	4.7 % (16)	5.5 % (19)	6.8 % (71)	2.8 % (60)
Giant cell sarcoma	4.2 % (184)	9.6 % (24)	10.8 % (27)	5.9 % (41)	2.9 % (92)
MPNST	3.3 % (47)	3.9 % (6)	4.5 % (7)	4.5 % (13)	2.5 % (21)
Synovial sarcoma	3.0 % (117)	4.7 % (11)	5.6 % (13)	4.1 % (39)	2.5 % (73)
Leiomyosarcoma	2.7 % (347)	3.1 % (22)	3.9 % (28)	4.4 % (231)	1.3 % (66)
Fibrous histiocytoma	2.6 % (333)	4.2 % (45)	4.9 % (53)	5.1 % (70)	1.8 % (165)
Myxo/Myxo sarcoma	1.7 % (11)	0 % (0)	0 % (0)	4.2 % (4)	1.4 % (7)
Liposarcoma	1.4 % (213)	2.2 % (9)	2.2 % (9)	2.9 % (125)	0.7 % (70)
Fibrosarcoma	1.4 % (77)	3.6 % (13)	4.2 % (51)	2.0 % (15)	0.8 % (34)
DFSP	0.2 % (6)	0.4 % (1)	0.4 % (1)	0.2 % (1)	0.2 % (3)

PT371

The Oncologic Impact of Postoperative Complications Following Resection of Truncal and Extremity Soft Tissue Sarcomas J.S. Broecker,[1] C.G. Ethun,[2]* D.K. Monson,[3] A. Lopez-Aguiar,[2] N. Le,[2] M.R. McInnis,[2] N.B. Reimer,[3] S. Oskouei,[3] K. Delman,[2] C.A. Staley,[2] S.K. Maithel,[2] K. Cardona.[2] *1. Emory University School of Medicine, Atlanta, GA; 2. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 3. Department of Orthopaedic Surgery, Emory University School of Medicine, Atlanta, GA.*

Introduction: Postoperative complications (POC) negatively impact oncologic outcomes in various malignancies; there is limited data regarding their effect in soft tissue sarcomas (STS). The aim of this study was to determine the impact of POC on long-term survival after resection of truncal and extremity STS. Methods: All patients who underwent resection for a primary truncal or extremity STS at a single institution from 2000-2015 were included and analyzed. Primary outcome was disease-specific survival (DSS). Results: Among 546 STS pts, mean age was 55yrs and 54% were male. Mean tumor size was 9.6cm, and the majority were deep (88%) and high-grade (88%) tumors. The most common subtype was undifferentiated pleomorphic sarcoma (39%). POC occurred in 159(29%) pts, of whom 55% had surgical site infections and 57% had major complication (≥Clavien-Dindo III). Neoadjuvant therapy was given to 55% and 44% of pts with and without a POC, respectively (p=0.02). Pts with POCs were older (61vs53 years), had more comorbidities (50vs38%), longer operative time (127vs93 minutes), higher grade tumors (93vs86%), and were more likely to receive neoadjuvant radiation (42vs33%) (all p<0.05). There was no difference in receipt of adjuvant therapy between POC and no POC groups (62%vs53%, p=0.07). Median follow-up for survivors was 37 months. The 5-year DSS for the entire cohort was 79%. In comparison to pts who had no POC, POC pts had a worse DSS (70%vs82%, p=0.001; Fig.1). Predictors for decreased DSS on UVA included POC (HR=2.12, 95%CI:1.37-3.28; p=0.001), advanced age, neurovascular/bone resection, positive margin, high grade, neoadjuvant and adjuvant therapy (all p<0.05). POC (HR=1.85, 95%CI:1.18-2.90; p=0.008) remained an independent predictor for reduced DSS on MVA, along with age (HR=1.19, p=0.03), high-grade (HR 4.2, p=0.04), neurovascular/bone resection (HR=1.76, p=0.02), and neoadjuvant therapy (HR=1.91, p=0.009). Conclusions: Postoperative complications following resection of truncal and extremity STS are associated with worse DSS. Efforts to optimize modifiable risk factors and decrease the rate of post-operative complications warrant further investigation.



Disease-Specific Survival (DSS) following Resection of Truncal and Extremity Soft TIssue Sarcoma (STS)

PT372

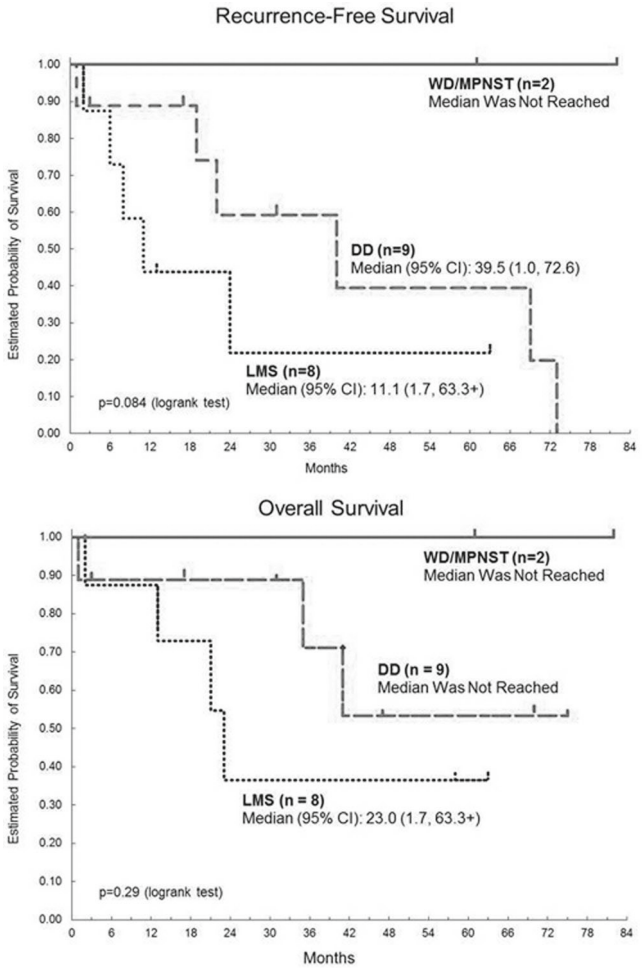
CD40 Stimulation Improves Upon Imatinib in Gastrointestinal Stromal Tumor J. Zhang,* S. Zeng, B. Medina, J. Loo, G. Vitiello, N. Param, F. Rossi, R. DeMatteo. *Surgery, MSKCC, New York, NY.*

Introduction: Targeted therapy with imatinib mesylate and other tyrosine kinase inhibitors (TKI) is effective in treating gastrointestinal stromal tumor (GIST), but is not curative. Agonistic CD40 antibody (αCD40) immunotherapy has shown promise in some cancers. Since CD40 is highly expressed in GIST, we sought to determine whether αCD40 could improve upon imatinib therapy in GIST. Methods: Human GIST surgical specimens were analyzed for CD40 expression by flow cytometry (n=50). $Kit^{V558\Delta/+}$ mice that develop intestinal GIST were treated with αCD40 and imatinib. Results were analyzed by flow cytometry, tumor weight, histology, immunohistochemistry (IHC), and western blot. Results: In human GISTs and $Kit^{V558\Delta/+}$ murine tumors, CD40 was expressed primarily on tumor-associated macrophages (TAMs) and Kit^{+} tumor cells, and imatinib decreased CD40 expression on tumor cells. In $Kit^{V558\Delta/+}$ mice, αCD40 alone had no anti-tumor efficacy, but when combined with imatinib, improved the anti-tumor response. With the addition of αCD40 to imatinib, tumor weight decreased 37% (p=0.0197), histologic changes were more pronounced, and Ki67 staining decreased 89% (p=0.02). The addition of αCD40 to imatinib enhanced T cell cytotoxicity by increasing the ratio of intratumoral CD8:CD4 T cells (2.5 vs. 1.3, p=0.004) and by increasing IFN-γ secretion by CD8 T cells (10.1 vs. 5.5%, p=0.008) and NK cells (9.3 vs. 6.4%, p=0.04). αCD40 also increased TAM activation as measured by percent of TAMs expressing CD11c (94 vs. 85%, p=0.02) and CD80 (21 vs. 7%, p=0.0002). Surprisingly, the addition of αCD40 to imatinib further decreased tumor cell signaling via phospho-Kit, suggesting a potential relationship between the CD40 pathway and Kit signaling in GIST. Conclusions: Agonsitic CD40 therapy improved the effects of imatinib in GIST via activation of T cells and macrophages and decreased tumor cell signaling. This study indicates the potential benefit of combining αCD40 with imatinib in patients with GIST.

PT373

Pancreaticoduodenectomy in the Surgical Management of Primary Retroperitoneal Sarcoma: A Multi-Institutional Case Series W.W. Tseng,[1]* D. Callegaro,[2] S. Bonvalot,[3] C.G. Ethun,[4] K. Cardona,[4] R. Canter,[5] K. Dhanireddy,[7] F. van Coevorden,[6] D. Tsao-Wei,[7] A. Gronchi.[2] *1. Surgery, Section of Surgical Oncology, University of Southern California, Keck School of Medicine, Los Angeles, CA; 2. Istituto Nazionale dei Tumori, Milano, Italy; 3. PSL University, Institut Curie, Paris, France; 4. Emory University, Winship Cancer Institute, Atlanta, GA; 5. UC Davis Medical Center, Sacramento, CA; 6. Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, Netherlands; 7. University of California, Keck School of Medicine, Los Angeles, CA.*

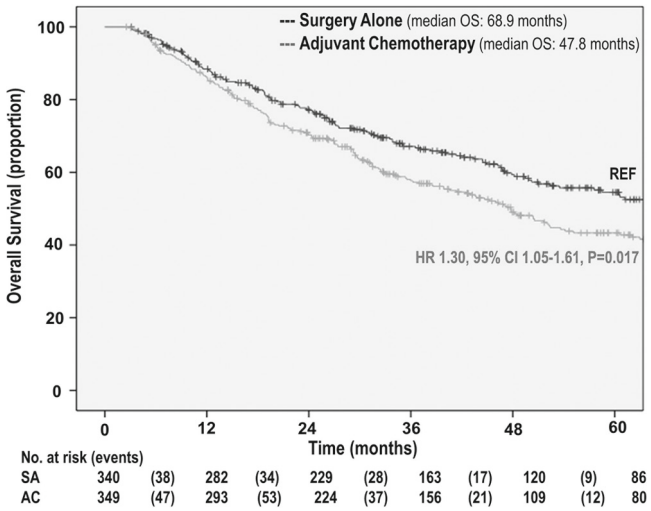
INTRODUCTION: In retroperitoneal sarcoma (RPS), complete resection is the mainstay of treatment. The optimal extent of resection must balance adequate disease control with potential for morbidity. In this study, our objective was to examine the complication rates and clinical outcome for primary RPS patients who underwent pancreaticoduodenectomy (Whipple procedure) done to achieve complete resection. METHODS: Data for study patients were collected retrospectively from 6 sarcoma referral centers and combined for analysis. RESULTS: 19 cases in which a Whipple procedure was done for primary RPS resection were identified, which represents 3% of all resections done during the same time period. Histologic subtypes included dedifferentiated liposarcoma (DD, n = 9), leiomyosarcoma (LMS, n = 8), well differentiated liposarcoma (WD, n = 1) and malignant peripheral nerve sheath tumor (MPNST, n = 1). The average tumor size was 19.3 cm (median: 15, range: 4-55). In addition to the pancreas and duodenum, an average of 2.8+/-1.4 other organs were resected en bloc. Negative margins were achieved in the majority of patients (14/17, 82%; 2 unknown). Complications occurred in almost half of patients (9/19, 47%) and in 6 (31%) these were considered major, including 2 patients with hemorrhage and 1 with myocardial infarction. Pancreatic leaks occurred in 26% of patients. Two patients died within 60 days of surgery. With a median follow-up of 57.9 months, locoregional recurrence developed in 67% of DD and 0% of LMS patients, whereas distant metastasis was observed in 11% of DD and 50% of LMS patients (p = 0.15). Both patients with other histologic subtypes (WD, MPNST) remained disease-free. Plots for recurrence-free and overall survival are shown (Figure). CONCLUSIONS: Although infrequent, when a Whipple procedure is done for primary RPS resection, resection of additional organs is often required and the overall complication rates are moderate. Consistent with reported data, clinical outcome is dependent on histologic subtype. The necessity for pancreaticoduodenectomy should take into account all of these considerations and be individualized to each patient.



PT375

Contemporary Reappraisal of the Efficacy of Adjuvant Chemotherapy in Resected Retroperitoneal Sarcoma J. Datta,* B.E. Ecker, M. Neuwirth, R. Geha, D.L. Fraker, R. Roses, G. Karakousis. *Surgery, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.*

Background: While margin-negative resection remains the cornerstone of therapy for retroperitoneal sarcoma (RPS), the impact of adjuvant chemotherapy (AC) on overall survival (OS) remains poorly understood. Methods: The National Cancer Data Base was queried for patients undergoing curative-intent resection of primary non-metastatic RPS (2004-2013). Multivariable modeling identified factors associated with AC receipt. Cox regression identified covariates associated with OS, and AC and surgery alone (SA) cohorts were matched 1:1 by propensity scores based on these covariates. In the propensity-score matched cohort, OS was compared by Kaplan-Meier estimates. Results: Of 3,892 resected RPS patients, 90.0% and 10.0% received SA and AC, respectively. Predictors of AC receipt included younger age, non-Caucasian race, hospital location, histologic grade, adjacent organ invasion, and histologic subtype. The propensity score-matched cohort comprised 767 patients (SA n=377; AC n=390); at a median follow-up of 59.2 (IQR 35.0-85.3) months, median OS of the propensity-matched cohort was 53.6 (IQR 22.4-119.5) months. Utilization of AC was associated with significantly worse long-term survival (median OS: 47.8 vs. 68.9 months, p=0.017; HR 1.30, 95% CI 1.05-1.61). AC was not associated with improved OS in margin-positive (R1/R2) resection, high-grade (G2/G3) and larger (>10 cm) tumors, or in any histologic subtype. When stratified by histologic subtype, an absolute but non-significant association with improved median OS was observed with AC in patients with spindle cell sarcoma (63.8 [AC] vs. 20.7 [SA] months, p=0.122), giant cell sarcoma (65.2 [AC] vs. 53.5 [SA] months, p=0.685, and synovial sarcoma (not reached [AC] vs. 15.5 [SA] months, p=0.084). Conclusions: Data from a large nationwide oncology database do not support adjuvant chemotherapy regimens following curative-intent resection of RPS, even in subgroups at high risk of failure (e.g., R1/R2 resection, high-grade or large tumors).



Comparative effect of surgery alone versus adjuvant chemotherapy on overall survival in propensity-matched cohorts with resected retroperitoneal sarcoma.

PT376

Flap Reconstruction Versus Primary Closure in the Management of Soft Tissue Sarcoma of the Extremities: A Comparison of Postoperative Complications J. Slump,[1]* P.C. Ferguson,[2] J.S. Wunder,[2] A.M. Griffin,[2] H.J. Hoekstra,[1] E. Bastiaannet,[3] S.O.P. Hofer,[2] A.C. O'Neill.[2] *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. University of Toronto, University Health Network and Mount Sinai Health System, Department of Surgery, Divisions of Plastic and Orthopaedic Surgery, Toronto, ON, Canada; 3. University of Leiden, Leiden University Medical Center, Department of Surgery, Leiden, Netherlands.*

Introduction: While reconstruction plays an essential role in the operative management of many extremity soft tissue sarcomas (ESTS), the effect of reconstructive flap closure on the post-operative complication rates remains unclear. This study assessed the complications of ESTS resections followed by either flap reconstruction or primary closure and determined the risk factors for complications. Methods: Eight hundred and ninety four patients undergoing ESTS resection with either primary closure or flap reconstruction between 2005 and 2015 were included in this retrospective study. Post-operative complication rates and risk factors for complications were compared between the surgical techniques, using univariate and multivariate logistic regression analyses. Results: Comparable post-operative complication rates were observed between flap reconstruction (38%) and primary closure (30.9%) in multivariate analyses (OR 0.99, CI 0.69-1.42, p=0.96). Pre-operative radiation and distal lower leg tumours were found to be the strongest independent predictors for wound complications in primary closure of defects (OR 3.42 p<0.01 and OR 2.0, p=0.02 respectively). BMI>30 (OR: 2.35, p=0.02), having comorbidities (OR 1.75, p=0.048) and stage 4 tumours (OR 4.51, p<0.01) were important predictors of complications in patients with flap reconstruction. Conclusion: While flap reconstruction may increase the complexity of ESTS resection, it does not significantly increase the risk of post-operative complications. Predictors of complications differ between treatment groups with tumour variables being most significant risk factors in primary closure while patient characteristics including comorbidities, BMI and stage 4 tumours are the strongest predictors in flap reconstructions.

Table 1 - Factors associated with complications, stratified for flap reconstruction or primary closure (multivariable analyses with all significant factors from univariable analyses included)

	Flap reconstruction		Primary closure	
Risk factor	Multivariable OR (95%CI)	p-value	Multivariable OR (95%CI)	p-value
Comorbidities	1.75 (1.01-3.04)	0.048*	1.29 (0.81-2.09)	0.28
Body Mass Index ≥ 30	2.35 (1.12-4.93)	0.02*		
Age ≥ 70 years			1.63 (0.84-3.16)	0.15
Tumour stage IV	4.51 (1.61-12.58)	0.004*	1.79 (0.66-4.87)	0.25
Prior surgery			1.06 (0.50-2.23)	0.88
Pre-operative radiotherapy			3.58 (2.19-5.88)	<0.001*
Maximal tumour diameter ≥ 10 cm			1.40 (0.85-2.31)	0.19
Superficial tumour depth			1.30 (0.55-3.08)	0.55
Distal lower extremity tumour location			2 (1.11- 3.57)	0.02*

*Significant predictor of post-operative complications in multivariate analyses

PT377

Tumor-Targeting S. typhimurium A1-R is More Effective than Traditional and Targeted Chemotherapy in Multiple Sarcoma Subtypes in Patient-Derived Orthotopic Xenograft (PDOX) Mouse Models I.A. Elliott,[1]* T. Murakami,[2] M. Zhao,[2] Y. Zhang,[2] T. Kiyuna,[2] Y. Hiroshima,[3] K. Igarashi,[2] K. Kawaguchi,[2] T. Russell,[4] J. Crompton,[1] S.M. Dry,[1] A. Singh,[1] R. Hoffman,[2] F.C. Eilber.[1] *1. Surgery, University of California, Los Angeles, Los Angeles, CA; 2. AntiCancer Inc., San Diego, CA; 3. Yokohama City University, Yokohama, Japan; 4. Veterans Affairs Los Angeles Health Services Research & Development Center of Innovation, Los Angeles, CA.*

Background: Sarcomas are rare, aggressive, often chemoresistant, and their histologic diversity has precluded meaningful clinical trials. The development of novel systemic therapies is an unmet clinical need. PDOX mouse models enable testing of therapies against a tumor's unique biology, thus sparing patients toxicity and lost time. Bacterial therapy for sarcoma dates back to Coley's use of S. pyogenes in the 1890's, and there is currently renewed interest in this approach; in addition to direct targeting of tumor tissue, it may also promote tumor immunogenicity. We report that tumor-targeting Salmonella typhimurium A1-R is more effective than traditional and molecular-targeted chemotherapies in several bone and soft tissue sarcoma PDOX mouse models. Methods: Sarcoma resection specimens from four patients were implanted orthotopically in nude mice. Upon reaching 500mm^3, 3mm^3 sections were passaged orthotopically and therapies tested. S. typhimurium A1-R (AntiCancer, Inc., San Diego, CA), with attenuated virulence due to Leu-Arg auxotrophy, was injected weekly for 4 weeks at 2.5-5.0x10^7 CFU. Chemotherapy was given in standard regimens. Tumor volume(mm^3)=length×width^{2}x½. Results: In an undifferentiated pleomorphic sarcoma PDOX model, A1-R i.t. decreased tumor growth from 10.1 to 2.4 fold (p=0.046). In Ewing sarcoma, A1-R i.v. decreased growth from 2.6 to 1.0 fold (p<0.001), and outperformed doxorubicin, palbociclib, and lisitinib (3.0, 1.2, and 1.7-fold change in tumor volume, respectively). In follicular dendritic cell sarcoma, A1-R i.p. decreased growth from 19.6 to 3.1 fold (p<0.001), and outperformed doxorubicin and NVP-BEZ235 (8.8 and 17.1-fold growth). In osteosarcoma, A1-R i.t. decreased growth from 6.2 to 0.7 fold (p<0.001), and outperformed ifosfamide, everolimus, and sorafenib (2.7, 2.2, and 3.7-fold growth, respectively). Conclusion: S. typhimurium A1-R is effective against a range of sarcoma subtypes, and outperformed traditional and targeted therapies in PDOX mouse models. Further investigation into the mechanism, safety, and efficacy of this promising therapy is warranted.

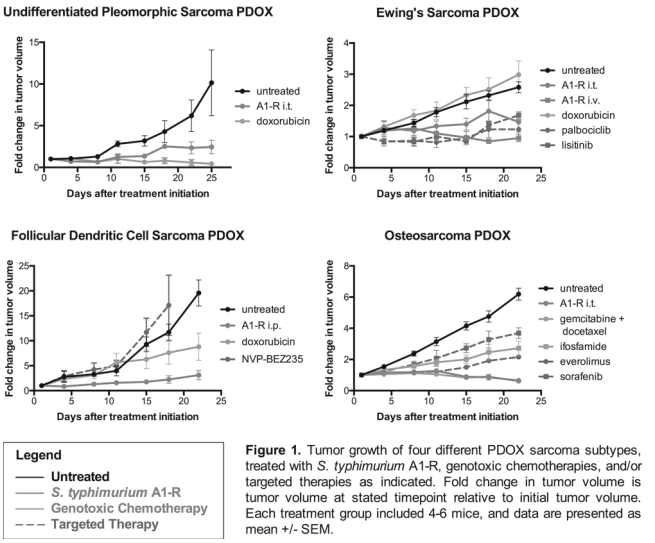


Figure 1. Tumor growth of four different PDOX sarcoma subtypes, treated with *S. typhimurium* A1-R, genotoxic chemotherapies, and/or targeted therapies as indicated. Fold change in tumor volume is tumor volume at stated timepoint relative to initial tumor volume. Each treatment group included 4-6 mice, and data are presented as mean +/- SEM.

PT379

MHC-I Loss and High Treg:CD8 Ratio are Associated with Worse Survival in Gastrointestinal Stromal Tumor (GIST) M.J. Cavnar,* N. Cohen, K. Seier, M. Gönen, V. Balachandran, C. Curtin, M. Keohan, W. Tap, C. Antonescu, R. DeMatteo. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: We have previously shown that human GISTs contain activated CD8$^+$ T cells, regulatory T cells, and macrophages. MHC-I is a marker of self that is associated with the CD8$^+$ T cell infiltrate, and loss of expression is associated with worse prognosis in some tumors. The association of immune cells and MHC-I with outcome in GIST has not been established. METHODS: A tissue microarray was constructed using three 0.6mm cores per patient from primary (Prim-GIST; n=76) or metastatic (Met-GIST; n=54) GISTs resected from 1982 to 2005. We performed immunohistochemistry for a panel of immune markers. Slides were digitized and color deconvolution was used with ImageJ/Fiji to quantify mean cell count per core [CD3 (all T cells), CD4, CD8, FoxP3 (regulatory T cells)], % area [CD68 (macrophages)], and intensity (MHC-I). Markers were correlated to overall and disease-specific survival (OS, DSS), calculated from the time of surgery. Survival analysis was done using continuous univariate analysis and the Kaplan-Meier method for markers with significant association. RESULTS: The median age was 62, with 55% male. 10yr OS and DSS was 48% and 69% in Prim-GIST and 32% and 34% in Met-GIST (p<0.05). Prim-GISTs had lower median FoxP3 count (2.7 vs. 4.8, p=0.016) and lower MHC-I intensity (84.6 vs.141.8, p=0.01) than Met-GISTs. There were no differences for the other markers. For Prim-GISTs, univariate analysis showed that a low MHC-I intensity was associated with worse OS and DSS. Using a cutoff point corresponding to loss of MHC-I expression, 10yr OS and DSS were 32% and 57% for MHC-I^{low} vs. 58% and 77% for MHC-I^{high} (p=0.0087, 0.012, respectively; Figure). Univariate analysis showed that for both groups, a high ratio of FoxP3 to CD8 count was associated with worse OS and DSS (p<0.05), although the relationship was stronger for Met-GIST. Using a cutoff ratio of 1 in Met-GIST, median OS and DSS were 7% and 15% for a high ratio vs. 37% and 48% (p=0.007, 0.04; Figure). CONCLUSIONS: Low MHC-I expression was associated with worse OS and DSS after resection of Prim-GIST, while a high FoxP3$^+$ to CD8$^+$ ratio was associated with worse OS and DSS in both Prim-GIST and Met-GIST.

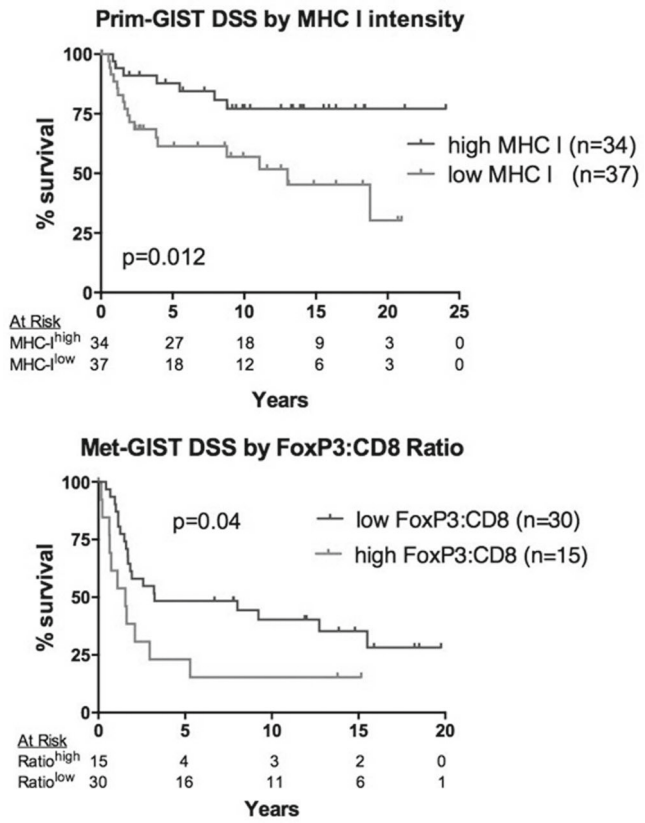


Figure: DSS in GIST stratified by immune markers
Top, DSS in primary GIST stratified by MHC-I expression.
Bottom, DSS in metastatic GIST stratified by FoxP3:CD8 ratio.

PF380

Rectal Gastrointestinal Stroma Tumor (GIST) in the Era of Imatinib: Organ-Preservation and Improved Survival M.J. Cavnar,* L. Wang, V. Balachandran, H. Trenholm, C. Curtin, C. Antonescu, W. Tap, M. Keohan, S. Singer, L. Temple, J. Garcia-Aguilar, R. DeMatteo, P.B. Paty. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: About 5% of GISTs originate in the rectum. Historically, radical resection of rectal GIST including abdominoperineal resection (APR) or pelvic exenteration was common. Neoadjuvant imatinib (Neo-IM) may downsize rectal GISTs and allow organ preservation with local excision or low anterior resection, while adjuvant imatinib (Adj-IM) may reduce risk of recurrence. Little is known about the outcome of rectal GIST in the era of imatinib. METHODS: Using a prospectively maintained database, we retrospectively analyzed 47 primary localized rectal GISTs treated at our center from 1982 to 2016, stratified by when imatinib became available in 2001. Overall, disease-specific, and recurrence-free survival (OS, DSS, and RFS) were analyzed by the Kaplan-Meier method. RESULTS: Rectal GISTs represented 47 (7.1%) of 663 primary GISTs. There were 17 patients prior to 2001 and 30 subsequently. The 2 groups had similar follow-up (median 3.9yrs), age (median 57yrs), gender (68% male), and Miettinen risk (76% high risk). Tumors were slightly smaller at diagnosis in the IM era (median 4.0 vs. 5.0 cm, p=0.029). Median distance to the anal verge was 4.0cm in both groups (p=0.3). Radiation was not used in the IM era (0 vs. 9 patients, p<0.0001). In the IM era, 24 of 30 patients were treated with imatinib, of whom 21, 10, and 9 received Neo-IM, Adj-IM or both. Neo-IM and Adj-IM were given for a median of 8.4mo and 2.8yrs, respectively. For patients treated with Neo-IM, the median size change was -28% (-55% to +18%), post-treatment mitotic rate was 0 (0-12), and pathologic response was 80% (0-100%). 10yr OS, DSS, and RFS were 91%, 100%, and 82% in the IM era, compared to 24%, 43%, and 27% (p≤0.0002; Figure). Organ preservation was more common in the IM era (p<0.0001) - local excision (60 vs. 29%), LAR (37 vs. 12%), and APR/exenteration (3 vs. 59%). Positive margins were similar between groups at 30%. There were less local (0 vs. 41%) and distant recurrences (10 vs. 65%) in the IM era (p≤0.0002). CONCLUSIONS: The use of imatinib is associated with organ preservation and improved oncologic outcome in rectal GIST.

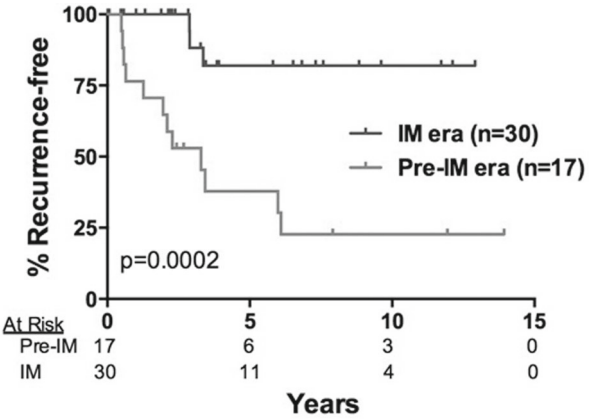


Figure: RFS in Rectal GIST

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Identifying Patients Most Likely to Benefit from Salvage Surgery for Recurrent or Metastatic Uterine Leiomyosarcoma A.M. Holder,[1]* Y. Chiang,[1] K.E. Torres,[1] J. Cormier,[1] V. Ravi,[2] G.N. Mann,[1] K.K. Hunt,[1] B.W. Feig,[1] C. Roland.[1] *1. UT MD Anderson Cancer Center, Department of Surgical Oncology, Houston, TX; 2. UT MD Anderson Cancer Center, Department of Medical Oncology, Houston, TX.*

Introduction: Uterine leiomyosarcoma is an aggressive tumor that, once recurrent or metastatic, can rarely be cured. The aim of this study was to determine prognostic factors that could identify which patients are most likely to benefit from surgical intervention for recurrent or metastatic disease. Methods: 91 patients who presented with recurrent (n=30), metastatic (n=60), or both recurrent and metastatic (n=1) uterine leiomyosarcoma and underwent surgical intervention at our institution between 1990 and 2014 were identified. We excluded 1 patient whose operative note was not available for review. Patient clinical characteristics and pathologic features reviewed included age at presentation, use of hormone replacement therapy, perioperative therapies, extent and type of resection, margin assessment, and outcomes. Disease-specific survival (DSS) and progression-free survival (PFS) were assessed from time of first surgical intervention, and univariate and multivariate analyses were performed. Results: Median age at diagnosis was 53 years. At median follow-up of 32.7 months from surgical resection, median DSS was 37.3 months, and median PFS was 18.6 months. On multivariate analysis, factors associated with reduced PFS were inability to achieve R1 resection (HR 4.62 [1.65-12.92]), progression on preoperative chemotherapy (HR 2.06 [1.14-3.73]), and liver metastases (5.78 [1.62-20.63]). Conclusions: Patients with local or distant recurrence of uterine leiomyosarcoma require a multidisciplinary approach that includes chemotherapy and surgical intervention optimally timed in those patients most likely to benefit. Our study suggests patients least likely to benefit from salvage surgery are those with inability to achieve R1 resection, progression on preoperative chemotherapy, and liver metastases.

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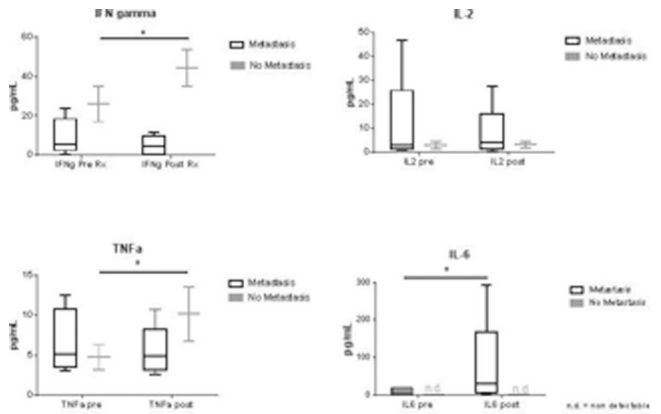
Changes in Serum Th1 Cytokine Expression Predict Metastasis in Soft Tissue Sarcoma Patients Treated with Sorafenib and Radiotherapy S.J. Judge,* M. Yanagisawa, A.O. Olusanya, A.R. Kirane, S.W. Thorpe, R.J. Bold, A.M. Monjazeb, R. Canter. *University of California, Davis, Sacramento, CA.*

Introduction We previously demonstrated that neoadjuvant sorafenib and radiotherapy (RT) are associated with elevated pathologic response rates in patients with locally advanced soft tissue sarcoma (STS) undergoing surgical

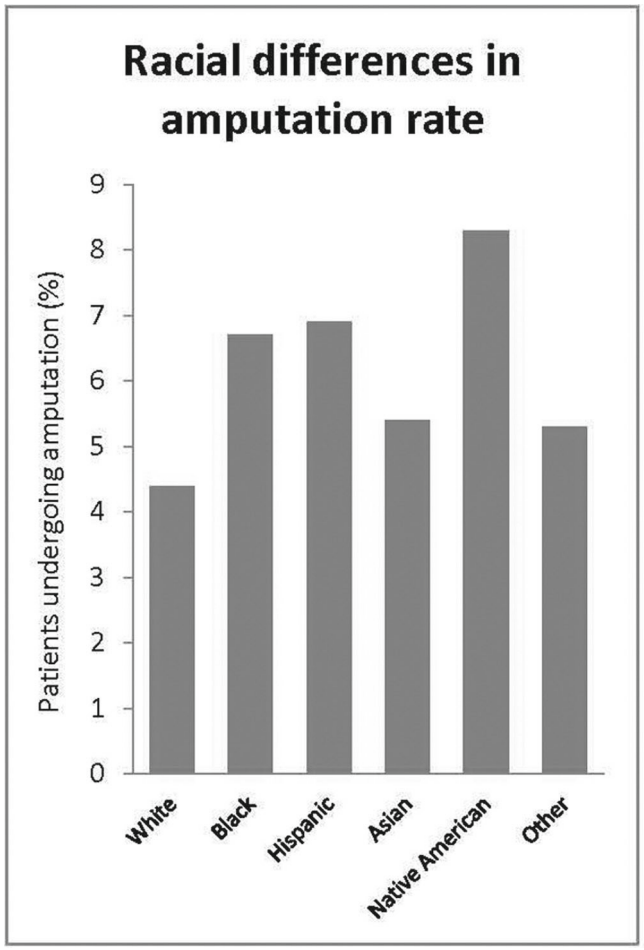
resection with curative intent. Given the potential immunomodulatory effects of neoadjuvant therapy, we sought to analyze the prognostic/predictive value of changes in serum cytokine expression during treatment with oncologic outcome. Methods From July 2009 to November 2011, eight patients with intermediate or high grade STS >5 cm or low grade STS >8 cm (maximal dimension) received sorafenib and conformal RT in a dose escalation phase I trial (NCT00864032). Levels of serum cytokines, including interferon-gamma (IFN-γ), interleukin-2 (IL-2), interleukin-6 (IL-6), and TNF-alpha (TNF-α) were measured before and after therapy, then analyzed to predict metastasis formation and overall survival. Parametric and non-parametric statistics were used as appropriate. Results As reported previously, we enrolled eight patients (5 female, median age 44, 3 myxoid/round cell liposarcoma, 3 high grade pleomorphic, 2 other). Median tumor size was 16 cm (range 6-26) and all were located in the lower extremity. With a median follow-up of 56 months, five distant recurrences and three disease-specific deaths were observed. Comparing patients who remained metastasis-free to those who did not, IFN-γ increased during neoadjuvant therapy (25.9±12.7 to 44.3±13.4 pg/mL versus 9.4±9.2 to 5.1±4.8 pg/mL, P=0.05), TNF-α increased (4.8±2.2 to 10.2±4.9 pg/mL versus 6.8±4.0 to 5.5±3.2, P=0.002), and IL-6 was unchanged (undetectable before/after treatment versus 9.5±8.2 to 75.7±122.8, P<0.001). There were no significant differences in IL-2 levels before/after treatment between metastatic and non-metastatic patients (Figure 1). Conclusion In this select cohort of STS patients, changes in serum cytokine levels during neoadjuvant therapy were predictive of subsequent oncologic outcome after completion of primary therapy. If validated, these findings may identify important immune biomarkers for tailored approaches to combined modality therapy in STS patients.



PF383

Race is Predictive of Limb Amputation in Extremity Soft Tissue Sarcoma H. Player,* O.S. Eng, M. Raoof, P.H.G. Ituarte, J. Femino, W. Chow, L. Lai. *Surgical Oncology, City of Hope, Duarte, CA.*

INTRODUCTION: Socioeconomic disparities impact the quality of cancer care. A challenge in the surgical management of extremity soft tissue sarcoma (ESTS) is limb preservation, which can affect quality of life. We sought to investigate the impact of a patient's race or ethnicity on limb preservation. METHODS: This is a retrospective study of patients with ESTS from the Surveillance, Epidemiology, and End Results (SEER) database. Patients under 18 years of age and those with metastatic disease were excluded. Univariable analysis was performed using chi-square test. Multivariable model was developed using step-wise multivariable logistic regression. RESULTS: Of the 7,650 eligible patients, 94.9% underwent limb-preservation and 5.1% underwent amputation. On univariable analysis, factors predictive of amputation included younger age (p<0.001), male sex (p=0.028), black race or Hispanic ethnicity (p=0.001) (graph), unmarried (p=0.035), Medicaid or uninsured (p<0.001), moderate or high grade tumors (p<0.001), tumor size greater than 5 cm (p<0.001), and lack of radiation treatment (p<0.001). In an adjusted model, older age (OR 0.99, CI 0.99-1.00, p=0.014) and receipt of external beam radiation (OR 0.25, CI 0.19-0.32, p<0.001) were protective against amputation. However, patients who were male (OR 1.24, CI 1.00-1.53, p=0.048), Hispanic (OR 1.42, CI 1.08-1.89, p=0.013), or black (OR 1.43, CI 1.04-1.98, p=0.030) were more likely to undergo amputations. Tumor characteristics (size and grade) were not significantly different between the two groups on multivariable analysis. CONCLUSIONS: After adjusting for tumor characteristics, black and Hispanic minorities remain at significantly increased risk of amputation.



In direct comparison to white patients, the rate of amputation was 1.50 times higher for blacks and 1.55 times higher for Hispanics.

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Surgical Complications Following Surgery for Retroperitoneal Soft Tissue Sarcoma (RSTS): Risk Factors and Impact on Long-term Outcomes G. Lahat,* F. Gerstenhaber, N. Lubezky, E. Nizri, O. Merimsky, R. Nakache, J. Klausner. *Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.*

Background: Post Operative morbidity following surgery for RSTS is not infrequent. Our aim was to identify specific risk factors for a complicated post operative course and to evaluate its possible association with adverse long term outcomes. Methods: Medical records of RSTS patients who had complete macroscopic resection at our institution were reviewed. Subjects were stratified by occurrence of surgical complications. Univariable and multivariable analyses were performed to identify risk factors for postoperative morbidity and to assess post operative complications as a predictor of adverse oncological outcomes. Results: Two hundred and twenty one patients were identified and are included in the study cohort. Median follow-up was 26 months (range, 5-166 months). One hundred and forty- four tumors were primary (65%), 71 were high grade (32%), median tumor size was 15 cm (8 range, 8-67 cm). One hundred and seven patients (48%) had a post operative complication; 22 patients (10%) required at least one invasive therapeutic procedure, surgical re-intervention was necessary in 30 patients (13.5%). Sixty- day post operative mortality rate was 2% (n=4). Multi visceral resection^2 emerged as a significant risk factor for post operative morbidity (p=0.025), whereas, age, gender, tumor size, tumor grade, tumor histology, recurrent status, and significant comorbidities had no association with post operative complications. Recurrence occurred in 68 patients (31%); at 5 years, overall survival was 62.2%

(95% CI, 52.3-81.1). Post surgical morbidity emerged as a negative predictive value for survival; 5- year OS rate of patients with post operative morbidity and of patients with no complications were 70.1% vs. 50.2%, respectively (p=0.05). Conclusions: Post operative morbidity following surgery for RSTS is increased with multi visceral resection. Our data also imply that a complicated course may be associated with adverse oncological outcomes. Nevertheless, until more effective therapies become available extensive surgical resections should be performed when indicated.

PF385

Effect of Nephrectomy for Retroperitoneal Sarcoma on Postoperative Renal Function D. Kim,* Z. Li, R. Gray, S. Bagaria. *Surgery, Mayo Clinic, Jacksonville, FL.*

Introduction Retroperitoneal sarcoma (RPS) is a rare mesenchymal malignancy that has a high rate of local recurrence. Surgery remains the cornerstone of treatment with an R0 resection offering the best chance for cure. Removal of the kidney may improve local recurrence, however, the risk of chronic kidney disease (CKD) may discourage one from performing a nephrectomy. Here, we aim to evaluate our experience with long-term post-operative renal function in patients who underwent a nephrectomy for RPS. Methods A retrospective review was conducted of patients presenting with the diagnosis of a RPS from 1990 to 2014 at Mayo Clinic Florida and Mayo Clinic Arizona. Patients who underwent nephrectomy were included. The primary outcome measured was CKD stage as calculated by glomerular filtration rate (GFR). The stages of CKD are 1 (GFR = 90+), 2 (GFR = 60-89), 3 (GFR = 30-59), 4 (GFR = 15-29), and 5 (GFR <15 or on dialysis) Results Retrospective review identified 57 patients who underwent nephrectomy for a RPS, of which 6 patients were excluded for lack of preoperative GFR. Of the 51 patients in our study cohort, GFR decreased by an average of 38 ± 23 ml/min/1.73m^2 and 35 (69%) of patients demonstrated progression of their renal impairment. A total of 10 (50%) patients with CKD stage 1 progressed to CKD stage 3. A total of 20 (95%) patients with CKD stage 2 progressed to CKD stage 3 or 4. A total of 3 (30%) patients with CKD stage 3 progressed to stage 4, of which two progressed to CKD stage 5. Conclusion A nephrectomy as part of an en-bloc resection will be associated with an expected decrease in GFR. Patients with a preoperative CKD stage of 3 are at greater risk of developing end stage renal disease. However, the risk of CKD should not limit the willingness to perform an en-bloc nephrectomy in the treatment of RPS for patients with normal to mildly reduced preoperative renal function.

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Clinicopathological Characteristics and Outcomes Analysis of Dermatofibrosarcoma Protuberans with Fibrosarcomatous Transformation E.C. Sorenson,* M. von Mehren, S. Movva, J.M. Farma. *Surgery, Fox Chase Cancer Center, Philadelphia, PA.*

Background: Dermatofibrosarcoma protuberans with fibrosarcomatous transformation (DFSP-FS) is an uncommon variant occurring in 10–30% of patients with DFSP. Although it is thought that DFSP-FS portends a poor prognosis, due to its rarity the actual prognostic significance of DFSP-FS remains unclear. We investigated the clinicopathological characteristics and outcomes of DFSP-FS in comparison with DFSP. Methods: We retrospectively identified patients at our institution from 1990–2015 who underwent surgical resection of primary or recurrent DFSP or DFSP-FS. Logistic regression and Kaplan-Meier estimates were used to analyze clinicopathological characteristics and survival predictors for DFSP and DFSP-FS. Results: 48 DFSP and 20 DFSP-FS patients matched the inclusion criteria. Clinicopathological characteristics are shown in Table 1. Overall, 58% of patients required an additional operation (range, 1–4) in an attempt to achieve R0 resection of the primary tumor. Compared with the DFSP group, DFSP-FS patients were older at diagnosis (median, 47 vs 41 years; p=0.05), had larger primary tumors (median, 6.8 vs 2.1 cm; p=0.02), and were more likely to have R1 status after final excision of the primary tumor (35 vs 6%; p=0.01). At at median follow-up of 46 months, DFSP-FS patients were more likely than DFSP patients to recur (40 vs 8%; p=0.002), with a median recurrence at 21 months vs 108 months, respectively. For the entire cohort, 5-year recurrence-free survival (RFS) was shorter with a close (<1 cm) or positive surgical specimen margin compared with a negative margin (68 vs 87%, p=0.01). Five-year RFS and overall survival (OS) were worse for patients with DFSP-FS compared with DFSP (RFS: 45 vs 94%, p=0.0004; OS: 87 vs 97%, p=0.02). Age, sex, race, anatomic location, tumor size, and number of primary re-excisions were not predictive of RFS or OS. Conclusions: Our sizable series of patients with DFSP-FS demonstrates a high R1 resection rate and worse RFS and OS compared with classical DFSP patients. Although it may entail multiple operations, an aggressive approach to attain a negative surgical margin is warranted for patients with DFSP-FS.

Clinicopathological characteristics of patients with DFSP and DFSP-FS.

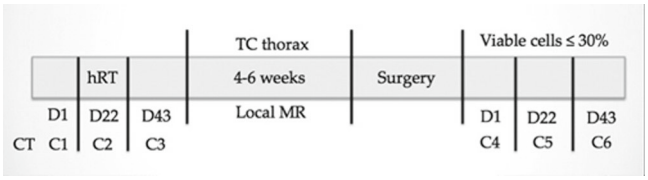
	DFSP	DFSP-FS	*p*-value
Number of patients	48	20	
Median age at diagnosis	41 (19–69)	47 (18–81)	0.05
Sex			
Female	29 (60%)	5 (25%)	0.3
Male	19 (40%)	15 (75%)	
Race			
White	35 (73%)	10 (50%)	0.8
Black	8 (17%)	10 (50%)	
East Asian	4 (8%)		
Other / Unknown	1 (2%)		
Anatomic location			
Trunk	28 (58%)	12 (60%)	0.5
Lower extremity	10 (21%)	2 (10%)	
Upper extremity	6 (13%)	2 (10%)	
Head or neck	4 (8%)	4 (20%)	
Median size of initial lesion	2.1 (0.4–15)	6.8 (2.5–21)	0.02
Initial lesions requiring re-excision	28 (58%)	9 (45%)	0.9
Final margin status of initial lesion			
Negative	36 (75%)	9 (45%)	0.01
Close (<1cm)	8 (17%)	2 (10%)	
Positive	3 (6%)	7 (35%)	
Unknown	1 (2%)	2 (10%)	
Recurrence			
Local	3 (6%)	5 (25%)	0.05
Distant	1 (2%)	3 (15%)	0.4

PF387

Neoadjuvant Hypofractionated Radiotherapy and Chemotherapy in High-grade Extremity Soft Tissue Sarcomas R.S. Sobreira Batista,* S. Aguiar JR, C.A. Mello, M. SILVA, A. Lopes. *Colorectal and Sarcomas, AC Camargo Cancer Center, SAO PAULO, Brazil.*

Introduction: Neoadjuvant radiotherapy (RT) and chemotherapy (CT) are used to treat large high-grade extremity soft tissue sarcomas aiming to treat metastatic disease earlier and sterilize margins to provide R0 surgery. However, pre-operative RT increases wound complication rates (rWC) not allowing or delaying adjuvant CT. Hypofractionated neoadjuvant RT (hRT) can be offered in this scenario, concomitant to CT. Methods: This is a non-controlled, single-arm, phase II clinical trial. Patients over 18 years with high-grade soft tissue sarcoma in the girdles or extremities were eligible. Three neoadjuvant CT (ifosfamide and doxorubicin) cycles were offered adding hRT in the second cycle of CT (doxorubicin only). Viable cells of the surgical specimen were evaluated and the patients with a count of less than 30% continued to receive an additional 3 CT cycles as adjuvant treatment. Results: Since Feb/2015 to Aug/2016 7 female and 4 male were enrolled. Six lesions were high than 10cm and 8 were localized in limbs. The most commons subtypes were synovial, pleomorphic and lyposarcoma (3 cases each). Occurred three WC cases and one of them didn't receive adjuvant CT. In four patients a complete pathological response in surgical specimen was founded. Four patients had toxicity grades III/IV due the neoadjuvant chemotherapy; the most common hematologic (n=3). All of then completed the full treatment. A dose reduction was needed in four patients. There were no deaths. Five patients received more three ciclos of chemotherapy as complementary adjuvant scheme based on pathological response data. Conclusion: Neoadjuvant hRT and CT may be an

option to treat patients with high-risk sts with acceptable WC rates. This early results have shown high rates of pathological complete response.



PF388

Use of Preoperative Radiotherapy Versus Surgery Alone in the Treatment of Retroperitoneal Sarcoma B. Turner,* L. Hampton, C. Robertson-More, M. Quan, L.A. Mack, A. Bouchard-Fortier. *University of Calgary, Calgary, AB, Canada.*

Introduction: Retroperitoneal sarcomas (RPS) represent an uncommon and heterogeneous group of malignancies with a high recurrence rate following resection. Preoperative radiotherapy (RT) is increasingly being used in the hope of sterilizing margins and decreasing local recurrence (LR) following resection. In this study, we sought to compare LR, disease free survival (DFS) and overall survival (OS) in patients treated with/without RT before resection of RPS. Methods: All patients with a diagnosis of RPS within the Alberta Cancer Registry treated with curative-intent surgery from Feb 1990 – Oct 2014 were identified. Data on patient demographics, tumor factors (location / size/ histology/ grade), treatment, recurrence and survival were abstracted by primary chart review. (EMR where available, paper charts where needed). Descriptive statistics were used for treatment patterns. Kaplan-Meier curves were used for survival analysis, examining OS and local DFS. Cumulative local recurrence rate was analyzed with two-tailed Fisher's exact test. Results: Complete data were available on 83 patients. Overall, 43 patients (51.8%) had curative intent surgery without adjuvant chemotherapy or RT and 38 patients (45.8%) had preoperative RT (median 50 Gy in 25 fractions) followed by curative intent surgery. Two patients had post-operative adjuvant radiation and were not included in analysis. After a median follow up of 24.7 months (0.57-242.4), LR occurred in 24 patients (55.8%) of the surgery alone group and in 12 patients (31.6%) in the RT/surgery group (p=0.005). Median DFS after surgery alone was 29.3 months, and for RT/surgery was 34.3 months (HR: 1.8; 95% CI [0.93 - 3.50], p=0.087). Median OS after surgery alone was 58.8 months, and after RT/surgery was 66.1 months (HR:1.69; 95% CI [0.0.91 - 3.15], p=0.10). Conclusions: In this univariate analysis, preoperative radiation was associated with a statistically significant reduction in local recurrence. However, there was no significant difference in local DFS or OS. Pending the results of current randomized trials, it remains prudent to offer preoperative radiation for patients with RPS for whom a curative intent surgery is planned.

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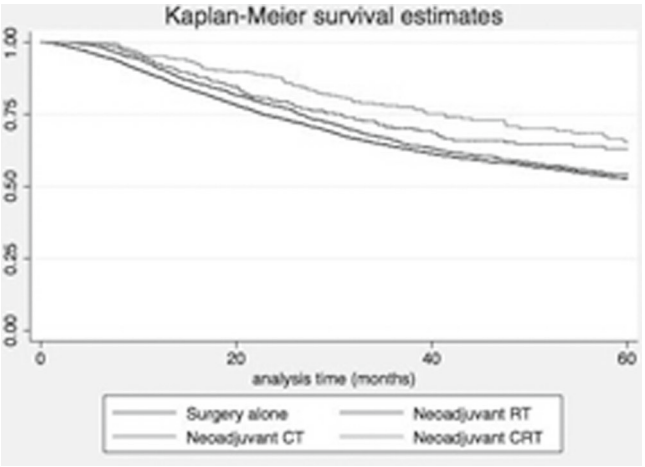
Neoadjuvant Therapy for Operable Stage IIB/IIC/III Extremity Soft Tissue Sarcoma: Analysis of the National Cancer Data Base M. Seaton,* E. Reardon, S. Ahmad, N. Hanna. *Surgery, University of Maryland Medical Center, Baltimore, MD.*

BACKGROUND: The optimal multimodality therapy for operable Stage IIB, IIC, and III extremity soft tissue sarcomas is unclear. In 2016, the National Comprehensive Cancer Network guidelines for treatment of these tumors included surgery alone, neoadjuvant radiation therapy (RT), neoadjuvant chemotherapy (CT), or neoadjuvant chemoradiation therapy (CRT). The purpose of this study was to compare 5-year survival among patients who received these 4 different modalities. METHODS: We performed a cohort study using data from the National Cancer Database. All subjects who had surgery for clinical Stage IIB, IIC, or III soft tissue sarcoma of the upper or lower extremity between 1998 and 2011 were included. Multivariate Cox-proportional hazards regression (adjusted for age, clinical stage, tumor grade, and treatment facility type) and Kaplan-Meier survival estimates were used to compare 5-year survival between treatment groups. RESULTS: A total of 7,328 subjects were included in the analysis. Of these, 4,839 received surgery, 1,744 received neoadjuvant RT, 358 received neoadjuvant CT, and 387 received neoadjuvant CRT. Compared to surgery alone, neoadjuvant RT was associated with a 12% lower risk of death (HR_{adj}: 0.88, p=0.008) and neoadjuvant CRT was associated with a 34% lower risk of death (HR_{adj}: 0.66, p<0.001). Neoadjuvant CT was not associated with a significantly different risk of death compared to surgery alone (HR_{adj}: 0.85, p=0.116). CONCLUSIONS: These findings suggest that neoadjuvant RT and neoadjuvant CRT are associated with improved survival among patients with operable Stage IIB, IIC, and III extremity sarcomas.



PF390

The Timing of Radiation Therapy and Surgical Resection for Soft Tissue Sarcomas and the Impact on Wound Complications: A Meta-analysis A. Christiansen, A. Marsh, N. Hussain, S. Shaheen, E. Paulus.* *Surgery, CMU College of Medicine, Saginaw, MI.*

Background: Radiation therapy (RT) is used in combination with surgical resection in the treatment of soft-tissue sarcomas (STS). An understanding of the timing of RT relative to surgery and outcomes has not been well defined. This systematic review analyzes the effect of timing of RT on outcomes in the treatment of STS of the extremities. Methods: Literature searches through MEDLINE, PubMed, and the Cochrane Database that included patients with STS of the extremities treated with neoadjuvant or adjuvant RT were performed. Primary and secondary outcomes analyzed included wound complications and 5-year local recurrence. Methodological quality assessments were made using the Cochrane Tool for randomized trials and the Newcastle-Ottawa Scale for observational studies. Results: Fifty-seven articles were retrieved from the initial search. A total of 8 studies (2 randomized trials, 6 retrospective cohort) and 1,191 patients were included in the systematic review and meta-analysis. 678 patients received neoadjuvant while 713 had adjuvant RT. Early wound complications were infection, dermatitis and re-operation. Late wound complications included fibrosis, edema, joint stiffness, bone changes, atrophy, limb shortening and telangiectasia. Overall patients with neoadjuvant RT were 8% less likely to develop local recurrence compared to adjuvant (95% CI 0.55-1.54, I^2 = 43%, p = 0.75); this failed to reach significance by the random-effects model. Significance was reached for local recurrence with the fixed-effects model (95% CI 0.55-0.99, I^2 = 0.99, p = 0.05). Although not significant, patients treated with neoadjuvant RT had a 56% greater risk of developing early complications (95% CI 0.94-2.60, I^2 = 48%, p = 0.09) but only a 2% greater risk of developing late complications (95% CI 0.20-5.28, I^2 = 91%, p = 0.98). Conclusions: Based on the results of this review, neoadjuvant RT does not significantly increase the risk of early or late wound complications. This group may demonstrate a decreased rate of local recurrence at five years. These findings must be interpreted with caution because of heterogeneity and bias in the available studies.

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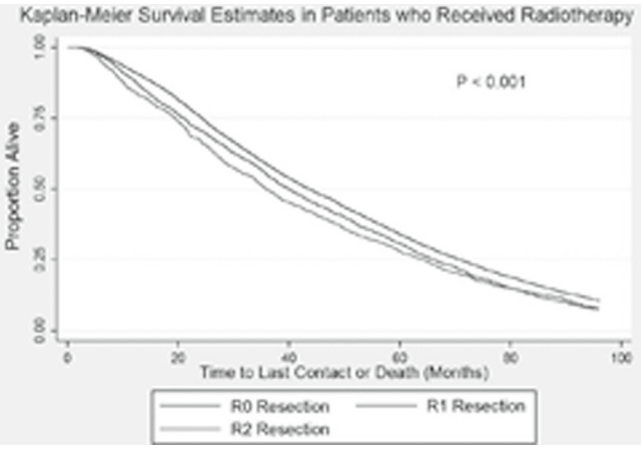
Neoadjuvant Radiotherapy is Independently Associated with R0 Resection in Extremity Soft Tissue Sarcoma: An NCDB Analysis A.A. Gingrich,* S. Bateni, A.M. Monjazeb, S.W. Thorpe, A.R. Kirane, R.J. Bold, R. Canter. *Surgery, University of California, Davis, Sacramento, CA.*

Background: Neoadjuvant radiotherapy (RT) is increasingly advocated in the management of soft tissue sarcoma (STS) because of well-defined fields and the ability to sterilize surgical margins surrounding the pseudocapsule. As

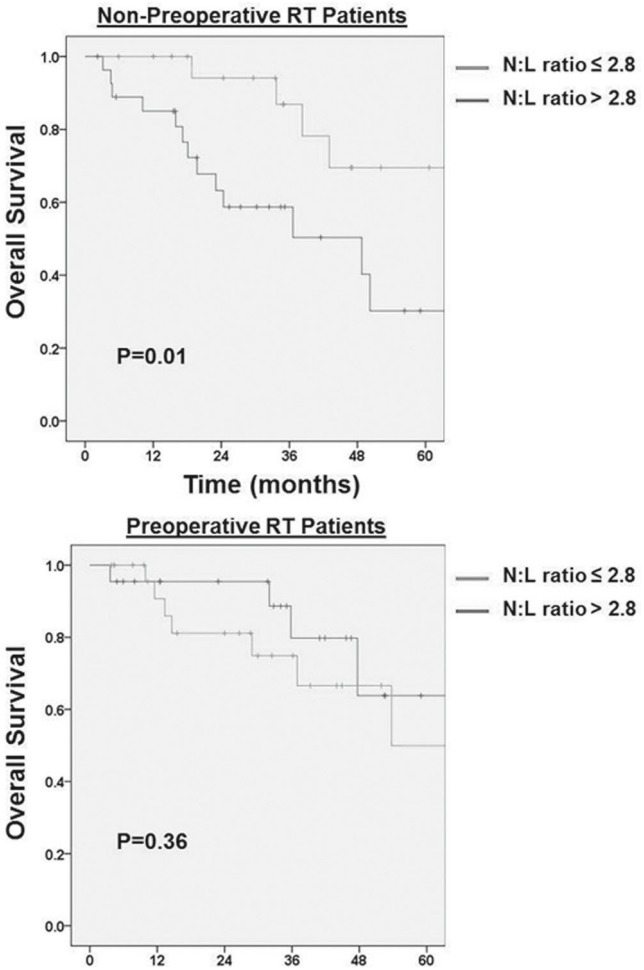
data in support of this hypothesis are limited, we sought to characterize the impact of neoadjuvant RT on rates of R0 resection and overall survival (OS) in extremity STS patients undergoing surgery. Methods: From January 2003 - December 2012, we identified patients with a diagnosis of extremity STS from the National Cancer Database. Excluding patients with age <18 years, not undergoing surgery, metastases at diagnosis, intraoperative RT, and missing/unknown data such as sequence of RT, our final cohort consisted of 27,968 patients. Using Chi-square analysis, logistic regression, and Cox-proportional hazard analysis, we determined rates of R0 resection among preoperative, postoperative and no RT cohorts as well as predictors of R0 resection and OS. Results: Overall, the mean age was 59.5 (SD 0.10) years; 45.9% were female. Median tumor size was 10.5cm, with a range from <1mm – 98.9cm. The most prevalent histologies were sarcoma NOS (20.3%), leiomyosarcoma (14.6%), and undifferentiated pleomorphic sarcoma (13.5%). 51% of patients did not receive RT, 11.83% received pre-operative RT and 37.17% received post-operative RT. Rates of R0 resection for preoperative RT, postoperative RT, and no RT cohorts were 90.1%, 74.9%, and 79.9%, respectively (P<0.001). Independent predictors of achieving R0 resection included facility type (OR 1.36, 95% CI 1.20-1.55), histologic subtype, tumor size (OR 0.992, 95% CI 0.99-0.994), Charlson score (OR 0.92, 95% CI 0.84 – 0.99), and preoperative RT (OR 1.83, 95% CI 1.61-2.07). On Cox-proportional hazard analysis, pre-operative RT was not associated with improved survival, but R0 resection was (see Figure). Conclusions: Pre-operative RT independently predicts higher rates of R0 resections in patients with extremity STS undergoing surgical resection. Given the benefits of margin negative resection in STS, further examination of the relationship between preoperative RT and oncologic outcome is warranted.



PF392

Serum CRP and Neutrophil:Lymphocyte Ratio Do Not Predict Survival in Soft Tissue Sarcoma Patients Receiving Neoadjuvant Radiotherapy M. Yanagisawa, S.J. Judge, C. Li, N. Wang, S.W. Thorpe, A.R. Kirane, R.J. Bold, A.M. Monjazeb, R. Canter.* *UC Davis, Sacramento, CA.*

Introduction: Serum C-reactive protein (CRP) and neutrophil:lymphocyte (N:L) ratio have previously been identified as independent predictors of overall survival (OS) in soft tissue sarcoma (STS) patients undergoing surgical resection with adjuvant therapy. Given the potential for neoadjuvant radiotherapy (NRT), to alter the inflammatory milieu of the host, we sought to analyze the prognostic/predictive value of these inflammatory markers in STS patients in which a large proportion received NRT. Methods: From November 2007 to December 2015, 98 patients with intermediate or high grade STS of all anatomic sites were identified from a prospective tumor registry database. Clinical, pathological, and treatment variables, including CRP and N:L ratios pre- and post-NRT were analyzed for their association with OS. Parametric and non-parametric statistics were used as appropriate. Results: Median age was 62.8 (range 6.1-87.9), and 46% were female. 55% of tumors were extremity, 20% trunk, and 18% retroperitoneal, while median tumor size was 9.5 cm (range 0.7-60.0). Undifferentiated pleomorphic sarcoma was most common (36%), followed by liposarcoma (18%), leiomyosarcoma (8%), and other. 80% of tumors were high grade, and 50% received NRT. Baseline characteristics were similar between the NRT and non-NRT cohorts with the exception of site (extremity 75% NRT vs. 35% non-NRT, P=0.0002). NRT and non-NRT cohorts also demonstrated similar baseline CRP levels (median 0.4 vs 0.7, P=0.10) and N:L ratios (median 2.8 vs. 3.4, P=0.16). Multivariate analysis of all patients revealed histologic grade, tumor size, and baseline N:L ratio to be significant predictors of OS. Subgroup analysis of NRT patients demonstrated no significant association of baseline N:L ratio (see Figure), baseline CRP, post-treatment N:L ratio or CRP with OS. Conclusion: Our data suggest that the utility of baseline CRP and N:L ratio as predictors of poor clinical outcome may not apply to STS patients receiving neoadjuvant RT. Patients with elevated CRP and N:L ratio at diagnosis appear to be good candidates for neoadjuvant RT.



PT393

Fellowship-Trained VATS Thoracic Surgeon Reports Half the Incidence of NSCLC Nodal Upstaging Compared to Reports from the STS Database E. Simmerman,* B. Bateson, N. Bekele, C. Schroeder. *General Surgery, Augusta University Medical Center, Augusta, GA.*

Introduction: The incidence of NSCLC nodal upstaging is reported between 10-25%. Lymph node dissection is critical to detect upstaging of lung cancer. This study compares the incidence of nodal upstaging when clinical staging is performed by the radiologist versus a fellowship-trained general thoracic surgeon performing lymph node dissections. Methods: This is a retrospective chart review of procedures performed by a single thoracic surgeon at a tertiary care center. Lymph node sampling procedures included Video Assisted Thoracoscopic Surgery with Mediastinal Lymph Node Dissection and Mediastinoscopy performed from July 2014-May 2016. A median of 4.2 stations per patient were sampled. A thoracic surgeon reviewed each PET scan preoperatively, providing a lung cancer clinical staging. The surgeon's clinical staging was compared to the radiologist's clinical staging. These were compared to the pathologic staging from lymph node sampling to determine hilar and mediasti-

nal upstaging. Results: 74 cases were reviewed including 13 mediastinoscopy, 8 combined VATS and mediastinoscopy, and 53 VATS operations. Surgeries were performed with intent to stage and treat NSCLC. After eliminating infectious and metastatic processes, 42 operations were performed for NSCLC. 175 lymph node stations were sampled for a total of 354 lymph nodes, of which 4 lymph nodes were positive. Only 1 (2.4%) lung cancer was up-staged from N0 to N1 and 1 (2.4%) lung cancer was upstaged from N0 to N2. A recent study of the STS database reported a nodal upstaging incidence of 11.6% in the VATS group and 14.3% in the open group. When compared to this study we report a much lower incidence of NSCLC upstaging of 4.8% (p=0.225). Surprisingly the specificity and NPV of the thoracic surgeon and the radiologist clinical staging was similar with specificity of 87% and NPV of 99%. Conclusions: We report half the incidence of NSCLC nodal upstaging when compared to reports from the STS database. The combination of clinical staging and a consistent, systematic lymph node dissection by the fellowship-trained VATS thoracic surgeon may result in improved staging and treatment of NSCLC.

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Gastrectomy with Extended Lymphadenectomy: A North American Perspective A. Gosselin-Tardif,* J. Lie, I. Nicolau, J. Cools-Lartigue, L. Feldman, J. Spicer, C.L. Mueller, L. Ferri. *General Surgery, McGill University Health Center, Montreal, QC, Canada.*

Purpose: Despite evidence of the oncological benefits of extended (D2) lymphadenectomy in gastric cancer from many Asian studies, there is persistent debate over its use in the West, mainly due to perceived high rates of mortality and morbidity. The lack of consensus is further fueled by limited data on this topic originating from North America. This study evaluates the safety and efficacy of D2 dissection in a high-volume North American center. Methods: A prospectively entered database of all gastrectomies at a single referral center from 2005-16 was reviewed for demographic data, tumor characteristics, peri-operative outcomes, and pathological results. Wedge resections and palliative operations were excluded. Data are presented as median (IQR); M-W U or Fisher's exact tests determined significance (*p<0.05). Results: Of 366 gastrectomies over this period, 206 met the inclusion criteria. Age was 70 (18) yrs and 65% were male. Type of gastrectomy included: Distal in 118 (57%); Total in 69 (34%); Proximal in 19 (9%). D2 dissection was performed in 151 (73%), the rest having D1. Post-op complication rates were similar (36% D1 and 37% D2), with an equivalent rate of severe (Clavien-Dindo >2) complications (D1=22%: D2=18%). Anastomotic leak rate did not differ (D1=6%: D2 =5%). Length of stay was 8 (7) days in both groups. Same-admission or 30 day mortality was 2.9% (6/206) for the entire cohort, and did not differ between D1 and D2 (3/55 vs 3/151). Of the 175 cases of adenocarcinoma, D2 patients had significantly higher clinical stage (63%>Stage1 vs 24%>Stage1)* and lymph node yield (30(19) vs 14(11))*. There was no difference in complete resection (R0) rate (D1=97% vs D2=92%). A laparoscopic approach was employed in 32% (45/141) of D2 adenocarcinoma patients, resulting in equivalent oncologic outcomes compared to the open approach: lymph node yield of 31(13) and an R0 resection rate of 91%. Conclusion: This study supports the use of D2 lymphadenectomy, by either open or laparoscopic approach, in high volume North American centers as a safe and effective oncologic procedure for gastric cancer, with equivalent complication rates and superior lymph node yield to traditional D1 dissection.

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Expression and Immune and Clinical Correlates of Immune Checkpoint Ligands in NSCLC J.M. Obeid,[1]* D.H. Deacon,[1] Y. Hu,[1] G. Erdag,[2] C.L. Slingluff,[1] T.N. Bullock.[1] *1. University of Virginia, Charlottesville, VA; 2. Johns Hopkins Medicine, Baltimore, MD.*

Background: PD-1/PD-L1 checkpoint blockade antibodies can be therapeutic for patients with non-small-cell lung cancer (NSCLC), especially those expressing the ligand PD-L1. The clinical relevance of other immune checkpoint molecules/ligands such as TIGIT/CD155, LAG3/MHC-II and TIM3/GAL9 for NSCLC is not known. We hypothesize that CD155, MHC-II and GAL9 are expressed in PD-L1^{HI} NSCLC tumors, and that their expression in tumor cells is associated with improved patient prognosis. Methods: Tissue microarrays from 151 anti-PD-1-naïve NSCLC tumors were assessed by immunohistochemistry for CD8^{+} T-cell density and tumor expression of checkpoint ligands PD-L1, MHC-II, GAL9, and CD155. Results: Eighty-three percent of patients had stage I or II disease. Patients with no follow and those with stage IIIB ad IV disease were included in the survival analysis (N=122). Neither the expression of PD-L1 nor GAL9 correlated with DFS. Patients with tumors expressing higher levels of CD155 have worse DFS independent of PD-L1 expression, age, stage and tumor histology (HR=1.24, p=0.046, multivariate cox proportional-hazards). In contrast, tumor expression of MHC-II tends to correlate with better patient DFS in multivariate analysis (HR=0.79, p=0.056). Increased CD8^{+} T-cell infiltration correlates with expression of PD-L1 and MHC-II (p=0.002 and p=0.001 respectively, Spearman correlations). High expression of at least two of the three other checkpoint ligands was identified in 42/76 (55%) tumors with high expression of PD-L1 and 25/72 (35%) of the PD-L1 negative tumors (p=0.015, chi-square test of proportions). Conclusion: These data support our hypothesis that MHC-II is associated with improved prognosis, but interestingly show that CD155 is associated with poorer prognosis. These data indicate that immune inhibiting checkpoints are often co-expressed with PD-L1, but differentially associated with CD8 infiltration. Understanding checkpoint ligand expression in individual tumors will be critical to guide future combination checkpoint blockade immunotherapy.

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NSCLC Sensitivity to JAK2 Inhibition and Identification of PD-L1 as a Potential Target of JAK Inhibitor-Based Therapy M. Stack, D. Bryan,* S. Pitroda, G. Liu, L. Chen, H. Liang, X. Huang, P. Roach, G. Oshima, N. Khodarev, R. Weichselbaum, M. Posner. *University of Chicago, Chicago, IL.*

Introduction Recent therapies for advanced lung cancer include targeted therapies and immune checkpoint inhibitors. We investigated the effects of JAK2 inhibitor SAR302503 (SAR), targeting therapy resistant tumor cells and suppressing PDL1, thereby modulating immune checkpoint therapy response. Methods Western analysis was used to characterize effects of SAR on JAK2-dependent signaling. Sensitivity of NSCLC cell lines to SAR and conventional therapy was characterized via clonogenic survival analysis. Survival data was correlated with gene expression data from the Cancer Cell Line Encyclopedia and Ingenuity Pathway Analysis (IPA). Flow cytometry quantified PDL1 expression in cell lines following combinations of IFNγ stimulation and SAR. Preclinical studies were performed with mice bearing Luis Lung Carcinoma (LLC) and nude mice bearing NSCLC tumors. Results Selective JAK2 inhibitor SAR suppressed JAK/STAT signaling with decreased expression of pStat1 and pStat3 and suppression of clonogenic ability. A subgroup of NSCLC with intrinsic resistance to conventional radio/chemotherapy was sensitive to SAR. SAR sensitivity significantly correlated with expression of interferon-stimulated genes (ISGs), most significantly IRF7, IRF9 and ISG15, and IPA revealed enrichment of ISG pathways. TSP-IRDS, a genomic predictor of radio- and chemo-resistance, predicted response to SAR with 83% sen. and 88% sp. (p=0.042). A significant positive correlation was found between ISG and PD-L1 expression in published datasets of NSCLC patients. SAR suppressed IFN-inducible PDL1 expression in a dose-dependent manner and was able to sensitize LLC to anti-PDL1 treatment in preclinical animal models. Conclusions The above findings suggest dual implications of JAK2 inhibitors; as a potential second line monotherapy for treatment resistant patients, and in combination with PD1/PDL1 immune checkpoint inhibitors.

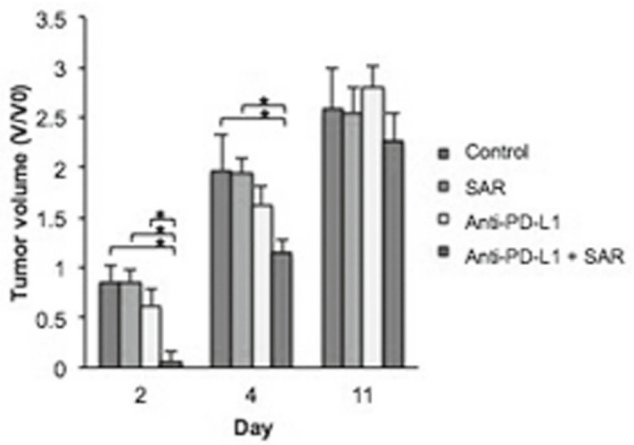


Figure 1: Relative tumor volume following treatments by anti-PDL1, SAR, or their combination as compared to control-treated C57BL/6 mice.

PT397

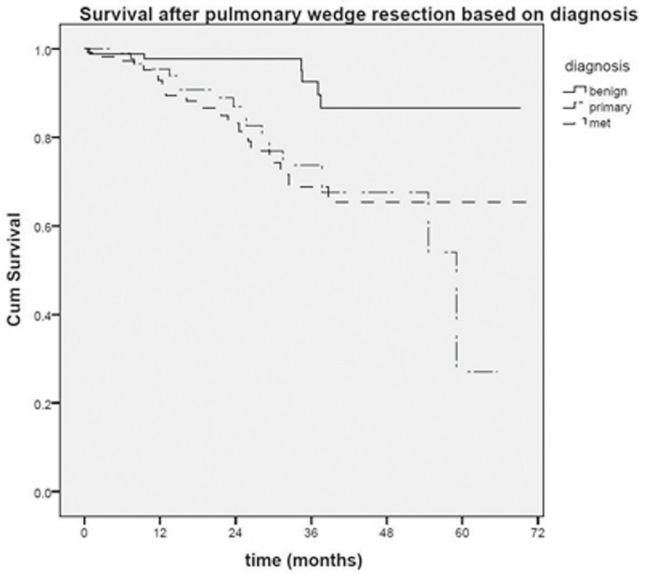
Positive Radial Resection Margin After Esophagectomy for Esophageal Cancer Patients Treated at a Tertiary Center and Its Impact on Survival P. Shah,* M. Cameron, J. Frakes, J.P. Fontaine, D. Coppola, S. Hoffe, K. Almhanna, J.M. Pimiento. *Surgical Oncology, H Lee Moffitt Cancer Center, Tampa, FL.*

Introduction: Although residual tumor at the radial margin can be expected to have a significant impact on the recurrence or overall survival of patient with node negative esophageal cancer (EC), its impact on recurrence and overall survival of patients with node positive EC has not been well characterized. Methods: A retrospective review of patients who underwent esophagectomy for EC at a single institution over a 16 year period (1999-2015) was performed. Pre-operative clinical parameters, stage as well as oncologic management were reviewed and the impact of positive radial margin on overall survival of pre-treatment node positive tumors was analyzed using descriptive statistics. Results: The study group consisted of 437 patients (46%) with pre-treatment stage IIB or III out of 945 patients with EC undergoing esophagectomy. The mean age of patients in this group was 63 years with male predominance (85%). Neoadjuvant therapy (NAT) was administered to 87% of patients. Trans-thoracic resection was performed in 86% and Trans-hiatal in 14% of patients. Positive radial margin on final pathology was identified in 14 patients (3.2%); none of these had squamous histology. Neither the surgical approach nor the use of NAT was found to be associated with radial margin positivity (p=0.6). The median overall survival was significantly lower in the patients with positive radial margin when compared to the rest of the cohort (13.6 months vs 41.2 months, p=0.004). Moreover, when focused only on patients with post treatment pathologic T3 and T4 disease, margin positive disease remained associated with worse survival (p=0.004). However, when final N status is included in multivariate analysis margin positivity loses significance. Conclusions: Residual tumor at radial margin after an esophagectomy for EC is associated with worse overall survival. This finding was significant regardless of the pathologic T stage; however, pathologic nodal staging was the most important factor for prognostication in locally advanced EC. Adenocarcinoma is the predominant pathology identified in patients with positive radial margin and concurrent node positivity.

PF398

Indications and Outcomes with Robotic-Assisted Pulmonary Wedge Resections T. Buckley,[2] F.O. Velez-Cubian,[2] R. Gerard,[2] C.C. Moodie,[1] J.R. Garrett,[1] J.P. Fontaine,[1] E.M. Toloza.[1]* *1. Thoracic Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida Morsani College of Medicine, Tampa, FL.*

INTRODUCTION: Pulmonary wedge resection (WR) is performed for known or suspected lung malignancy if lobectomy is not indicated or is refused by the patient. We studied whether lung nodule pathology correlated with perioperative outcomes. METHODS: We retrospectively analyzed data from all patients (pts) who underwent robotic-assisted lung WR(s) from September 2010 to May 2016 by one surgeon, but excluded pts who had WR followed by completion segmentectomy or lobectomy. We grouped pts by pathology (primary lung cancer [LC], pulmonary metastasis [PM], or benign [BN]) and compared operative times, estimated blood loss (EBL), perioperative complications, chest tube days, hospital length of stay (LOS), and in-hospital mortality, using Chi-square, analysis of variance, Student's t-test, or Kruskal-Wallis test, with $p \leq 0.05$ as significant. RESULTS: Among 292 total pts (mean age 67yr) were 95 LC pts, 109 PM pts, and 88 BN pts. Mean number of WRs was 2.0±0.1 in LC pts, 2.2±0.2 in PM pts, and 1.8±0.1 in BN pts ($p \geq 0.06$). Mean nodule size in LC pts (1.9±0.1cm) was similar as in PM pts (1.6±0.1cm; $p>0.05$), but larger than in BN pts (1.4±0.1cm; $p<0.05$). Median operative time in LC pts (127±6min) was similar as in PM pts (115±5min; $p>0.05$), but longer than in BN pts (104±5min; $p<0.01$). Blood transfusion was the only intraoperative complication, occurring in 1.1% of LC pts, 0% of PM pts, and 2.3% of BN pts (p=0.29). No conversion to thoracotomy occurred. Median EBL in LC pts was higher than in PM pts (100±16mL vs. 50±10mL; $p<0.01$), but similar as in BN pts ($p>0.05$). Postoperative complications occurred in 46.0% of LC pts, 16.5% of PM pts, and 23.9% of BN pts ($p<0.05$). Prolonged air leak (>5d) was most common, occurring in 26.3% of LC pts, 2.8% of PM pts, and 11.4% of BN pts ($p<0.01$). No in-hospital mortality occurred. Median hospital LOS in LC pts (4±0.5d) was longer than in PM pts (2±0.4d; $p<0.01$) and BN pts (3±0.5d; $p<0.05$). The 3-yr overall survival (OS) was similar for LC and PM pts (73.7% vs. 68.8%; p=0.87), which was less than for BN pts (92.5%; p=0.003). CONCLUSIONS: PM pts have similar 3-yr OS and similar (or better) perioperative outcomes to LC pts after robotic-assisted lung WR.



PF399

Risk Factors Associated with Suicide in Esophageal Malignancy B. Bateson,* A. Talukder, A. Jones, A. Lawson, E. Kruse. *Surgical Oncology, Augusta University Medical Center, Augusta, GA.*

Increased suicide risk among cancer patients has been well documented. To date there has been no specific examination of suicide rates and factors associated with suicide in esophageal cancer. The aim of this study is to examine suicide incidence and associated factors in esophageal cancer patients. The Surveillance, Epidemiology, and End Results (SEER) Database of the National Cancer Institute was queried to identify patients with esophageal cancer. The study included mortality and demographic data from 1973 to 2013. Comparison data with the general US population was used from the Centers for Disease Control and Prevention's National Center for Injury Prevention and Control using the Web-based Injury Statistics Query and Reporting System (WISQARS). Standardized mortality ratios (SMRs) and their 95% confidence intervals (95% CIs) were calculated and multivariable logistic regression models generated odds ratios (ORs) for the identification of factors associated with suicide for esophageal malignancy. Overall 177 suicides among 79,559 patients were identified. Of the patients committing suicide, 161 (91%) were over 80 years old. A statistically significant higher suicide rate was identified in patients with cervical esophageal and gastroesophageal (GE) malignancies. There was no statistically significant difference in suicide rate with respect to marital status, surgical intervention, stage at diagnosis, age at diagnosis, and median household income. The SMRs for patients with esophageal cancer were 17.19 for females (95% CI, 9.04-29.87), 4.7 for males (95% CI, 4.03-5.48), 1.5 for African-Americans (95% CI, 0.61-3.12), 8.37 for Caucasians (95% CI, 7.14-9.75), and 5.5 for Others (95% CI, 2.89-9.56). On multivariable analysis, Male gender and Caucasian race were found to be associated with suicide with OR 4.97 (95% CI 2.70-9.15) and OR 2.14 (95% CI, 1.3-3.48) respectively. Identification of evidence-based risk factors associated with suicide among patients with esophageal cancer is an important step in developing screening strategies. This study identifies Caucasians, males, and those with cervical esophageal and GE malignancies with significantly increased odds of committing suicide.

TABLE 1. Incidence of Suicide Among Patients With Esophageal Cancer by Demographic Characteristics

Cancer Site	No. of Suicides	Person-Years	Suicide Rate per 100,000 Person-Years	SMR	95% CI
Esophagus					
Population	177	127100	12	7.28	6.27 - 8.43
Sex					
Female	11	31973	0.24	17.19	9.04 - 29.87
Male	165	95127	1.20	4.7	4.03 - 5.48
Age,y					
≤ 39	0				
40 - 49	6	9049	0.46	1.95	0.79 - 4.05
50 - 50	2	1804	0.77	4.82	0.81 - 15.92
60 - 69	4	3982	0.70	5.93	1.59 - 12.12
70 - 79	4	3668	0.76	5.19	1.65 - 12.53
≥ 80	161	106412	1.05	4.88	4.17 - 5.68
Race					
African American	6	14565	0.29	1.5	0.61 - 3.12
White	159	105865	1.04	8.37	7.14 - 9.75
Other	11	6375	1.20	5.5	2.89 - 9.56
Unknown	1		-	-	

PF401

Impact of Squamous Histology on the Response to Treatment and Long-term Outcomes of Patients with Distal Esophageal Cancer
P. Shah,* M. Cameron, J. Frakes, J.P. Fontaine, D. Coppola, S. Hoffe, K. Almhanna, J.M. Pimiento. *Surgical Oncology, H Lee Moffitt Cancer Center, Tampa, FL.*

Introduction: Squamous cell carcinoma (SCC) has been traditionally linked to a better response to treatment and overall survival when compared to adenocarcinoma (AC) of the esophagus. Recent advances in staging, neoadjuvant therapy (NAT) and increasing surgical management of patients with esophageal cancer (EC) have led to improved overall survival of these patients. The aim of this study is to analyze the impact of squamous histology on treatment response and long term outcomes in patients with distal EC. Methods: A retrospective review of patients who underwent esophagectomy for EC at a single institution over a 16 year period (1999-2015) was performed. Pre-operative clinical parameters, stage as well as oncologic management were compared between SCC and AC of the distal esophagus and the difference in response to treatment and overall survival were analyzed using descriptive statistics. Results: Esophagectomy was performed on 945 patients with EC of which 839 patients (89%) had distal EC. The mean age of this group was 63 years and majority were males (87%). Histology was SCC for 78 patients (9.4%) and AC for 747 patients (90.6%). Pretreatment clinical stage was similar between the two groups (p=0.16). NAT administration was also similar between these groups (p=0.13). Although SCC patients had higher rate of complete response (54% v/s 36%, p=0.01) we found no difference in the overall survival after surgery (33 months for SCC v/s 40 months for AC, p=0.72) irrespective of whether they received NAT (p=0.95) or not (p=0.55). Conclusions: Squamous cell histology had a favorable impact on the rate of pathologic response for patients with distal EC; however, this improvement did not alter their overall survival. This could provide an insight into the decreasing significance of histology in the management and expectations from treatment of EC while emphasizing the continuing need for multimodality therapy to assure good outcomes in these patients.

PT403

Gastric Linitis Plastica: Have We Moved Beyond Surgical Palliation?
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Introduction: Diffuse type gastric cancer (DGC), especially linitis plastica (LP), is associated with poor survival. Despite curative-intent surgical resection and improvement in perioperative therapy, doubt remains whether long term survival is possible in this aggressive disease. Methods: A retrospective review of the GC database at a comprehensive cancer center was reviewed from 2000 to 2016. Patient demographics, tumor characteristics, and treatment were evaluated. Patients with DGC were assessed. LP was defined as patients with DGC who had circumferential infiltration of the gastric wall for at least a third of the stomach length. Descriptive statistics were used to compare DGC and LP groups; survival was assessed by the Kaplan-Meier method. Results: Of 209 resected GC patients, 114 had diffuse histology; the majority were of the signet ring cell subtype. 38 (33.3%) had LP and 76 (66.7%) had DGC without linitis. LP patients were more likely to present at a later stage, with 27/38 patients (71%) with stage III and 4/38 patients (10.5%) with stage IV compared to 16/76 (21.1%) and 2/76 (2.6%) in the DGC group, respectively, p< 0.001. All patients underwent gastric resection with a minority for palliative intent including 6 patients found to have metastatic disease on exploration. R0 resection was achieved in 26 patients (68.4%) with LP. Median OS was 31.5 months for the cohort and 13.6 months for LP patients (p < 0.001); survival in LP patients did not improve with R0 resection. When survival was stratified by stage, patients with stage II LP still had a lower median OS than DGC (18.4 vs. 51.2 months, respectively, p=0.015), though there was no survival differences in stage III and IV. Only half of patients with LP received preoperative chemotherapy or chemoradiation, perhaps due to need for surgical palliation of symptoms; receipt of preoperative therapy was not associated with survival in this subgroup. Conclusion: Gastric LP is associated with a poor prognosis. Early diagnosis and adherence to multimodal therapy may improve survival after surgical resection. Development of novel agents and improvement in neoadjuvant therapy is needed to improve outcomes in this aggressive disease.

PT404

Effects of an Oral Elemental Nutrition Supplement in Gastric Cancer Patients with Adjuvant S-1 Chemotherapy After Gastrectomy: A Phase II Study (OGSG1108)
J. Matsuyama,[1]* H. Imamura,[2] J. Fukui,[3] K. Nishikawa,[4] J. Kawada,[5] T. Kawase,[2] Y. Kurokawa,[6] T. Shimokawa,[7] T. Satoh.[6] *1. Department of Surgery, Yao Municipal Hospital, Yao city, Japan; 2. Toyonaka Municipal Hospital, Toyonaka city, Japan; 3. Kansai Medical University Hospital, Hirakata city, Japan; 4. National Hospital Organization Osaka National Hospital, Osaka city, Japan; 5. Kaizuka City Hospital, Kaizuka city, Japan; 6. Osaka University, Graduate School of Medicine, Department of Gastroenterological Surgery, Suita city, Japan; 7. Wakayama Medical University, Wakayama city, Japan.*

Abstract Background An adjuvant chemotherapy with S-1 is the standard treatment for patients (pts) with stage II/III gastric cancer (GC) who have undergone curative gastrectomy in Japan, and it is suggested that the survival benefit may be obtained by continuity and satisfactory adherence of S-1. Prior study has reported body weight loss might be an important risk factor for a decrease in compliance to adjuvant chemotherapy with S-1. We conducted a phase II study to examine whether postoperative administration of an oral elemental diet (ED: Elental) increases adherence of S-1 therapy in GC pts after gastrectomy. Methods Pts with pathological stage II/III GC who underwent curative gastrectomy were enrolled. Treatment consisted of S-1 administration for 4 consecutive weeks, repeated every 6 weeks (1 course) until 1 year after surgery, and ED administration for at least until 4 courses of S-1. They received 300kcal of ED plus their regular diet, starting from the day the patient started a soft rice or equivalent diet after surgery. The primary endpoint was feasibility of the 1 year administration of S-1 therapy. Secondary endpoints were dietary adherence, nutrition-related blood parameters, relative performance (RP) of S-1 administration and adverse events. Results This study included 82 pts, 27 total gastrectomy (TG) and 55 distal gastrectomy (DG), in 16 hospitals. The feasibility and the median RP of 1-year administration of S-1 was 69.0% (95%CI 56.9-79.5, p=0.022), 87.5% (60.7-100), respectively. The median compliance rate of ED at 4 courses of S-1 was 81.5% (74.4-88.5). There were a total of 18 hematological and 11 non-hematological adverse events of grade3 or higher. The mean rate of body weight loss was 4.3% (TG 5.1%, DG 3.7%), but there was no significant difference in nutrition-related blood parameters in subgroup analyses among types of gastrectomy. Conclusion Nutritional support for gastric cancer patients receiving adjuvant chemotherapy contributes to increase compliance of S-1 and potential effect on survival may be expected. Clinical trial information: UMIN000006872.

PT405

Is Adjuvant Chemoradiotherapy Better than Perioperative Chemotherapy for Resectable Gastric Cancer? M.J. Selleck,[1]* B. Jabo,[2] J.W. Morgan,[3] C.A. Garberoglio,[1] M.E. Reeves,[1] J.P. Namm,[1] N.L. Solomon,[1] S.S. Lum,[1] M. Senthil.[1] *1. Division of Surgical Oncology, Loma Linda University, Loma Linda, CA; 2. School of Public Health, Loma Linda University, Loma Linda, CA; 3. School of Public Health, Loma Linda University; Surveillance, Epidemiology, and End Results (SEER) Cancer Registry, Cancer Registry of Greater California and California Cancer Registry, Sacramento;, Loma Linda, CA.*

Background: Adjuvant chemoradiotherapy (CRT) and perioperative chemotherapy (PC) have been shown to improve overall survival compared to surgery alone in resectable gastric cancer, but these two treatments have never been compared in a randomized trial. We sought to evaluate the effects of CRT and PC on survival among patients who underwent definitive gastric resection. Method: A retrospective review of California SEER data (2007-2013) was performed to compare survival for stage I-III gastric and gastroesophageal junction adenocarcinoma patients treated with surgery and either CRT or PC. Kaplan-Meier analyses were used to evaluate median and 3-year overall survival (OS). Propensity score weighted (age, sex and race/ethnicity) and covariate (T-stage, histology type, signet ring histology, location, and extent of lymphadenectomy) adjusted Cox regression was used to assess mortality hazard ratios (HR). Comparative analyses were conducted for all patients, for clinically node positive (CN+) patients, and by pathologic node (PN) status. Results: Of 1,028 eligible patients, 762 and 266 patients received CRT and PC respectively. Median follow up was 57 months. Median survival for the PC group was 40 months, compared to 57 months for the CRT group (p=0.025); HR=1.33 (95%CI=1.11-1.60). Among CN+ patients, median survival was similar for PC (N=100, 38%) and CRT (N=156, 21%) (45 vs 39 months, p=0.99). The majority of CN+ patients had PN positive (PN+) disease (PC N=64, 60% and CRT N=140, 90%). PN+ status in the PC group was associated with poorer OS compared to the CRT PN+ group (3-year OS=36% vs 51%, p=0.022); HR=1.79 (95%CI=1.20-2.64). While only 40% of patients in the PC group received postoperative chemotherapy, the outcome differences persisted irrespective of receipt of postoperative chemotherapy. Conclusions and Relevance: CRT was associated with better OS in resected gastric cancer patients as compared to PC. In the absence of clinical node positive disease, CRT should be considered as the adjuvant treatment of choice. The observed outcome differences between these two treatment approaches warrant further investigation.

Covariate adjusted mortality hazard ratios for perioperative chemotherapy versus adjuvant chemoradiotherapy weighted for propensity score for all patients.

Covariates	HR	95% CI
Treatment		
Adjuvant Chemoradiation	1	
Preoperative chemotherapy	1.33	1.11-1.60
T stage		
T1-T2	1	
T3-T4	1.63	1.35-1.97
Histology Type		
Intestinal	1	
Diffuse	2.33	1.55-3.47
Not otherwise specified	1.45	1.09-1.96
Signet Ring		
No	1	
Yes	1.41	1.14-1.74
Location		
Distal	1	
Proximal	1.15	0.95-1.39
Extent of lymphadenectomy		
<15	1	
15-25	1.20	0.98-1.46
26+	0.61	0.45-0.78

Propensity score weighted (age, sex and race/ethnicity).
HR: Hazard Ratio; CI: Confidence Interval

PT406

Adjuvant Chemotherapy Following Neoadjuvant Chemoradiation and Surgery for Esophageal Cancer: Does It Improve Outcome? E. Gabriel,* J. Kim, E. Al-Sukhni, M. Brady, R. Shah, K. Attwood, S. Hochwald, M. Kukar. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Data is limited regarding the benefit of adjuvant chemotherapy (ACT) for patients with esophageal cancer who have been treated with neoadjuvant chemoradiation (nCRT) followed by surgery. While large database analyses reported benefits in overall survival (OS) from ACT, these studies have biases. The purpose of this study was to determine if ACT is associated with improved outcomes using a more granular dataset. Methods This was a single institution study of patients undergoing esophagectomy, 2005-2015. A propensity adjusted analysis was performed to compare patients treated with ACT following nCRT and surgery (ACT+) compared to nCRT and surgery only (ACT-). Results 276 patients were identified; 70 (25.4%) had a complete pathologic response (cPR) and were excluded. Of the remaining 206 patients, 43 (20.9%) received ACT. 92.7% without cPR had adenocarcinoma. Reasons for ACT included minimal/poor response to nCRT (60.5%), pathologic nodal disease (32.6%), positive margins (4.7%) and undetermined (2.3%). Reasons for no ACT included moderate response to nCRT (82.3%) or post-operative complications (29.3%), with 11.6% having both of these factors. Between the ACT- and ACT+ groups, there were no significant differences in median age (60.3 vs 61.2), ASA or ECOG, comorbidities (including COPD, CAD, HTN, DM), histology, pathologic T or N stage, nCRT regimen, surgery type/approach or post-operative complications. There was no significant difference in median OS (ACT- 39.4 vs ACT+ 28.3 months, p=0.19). On propensity adjusted analysis, there were no significant differences in OS for ACT+ compared to ACT- (HR 1.41, 95% CI 0.83-2.40, p=0.21), disease-specific survival [(DSS) HR 1.47, 95% CI 0.83-2.60, p=0.19] or recurrence-free survival [(RFS) HR 1.23, 95% CI 0.72-2.10, p=0.46]. Conclusions ACT following nCRT and surgery did not have any benefit on survival outcomes with propensity adjusted analysis. Although our study demonstrates bias in the selection criteria for ACT in those patients undergoing nCRT and esophagectomy, its use is not supported by our data. Further prospective randomized studies are warranted to define the role of ACT in this setting.

PT407

Association of Racial and Socioeconomic Disparities with Hospital Case Volume Among Patients Undergoing Esophagectomy E. Gabriel,* S. Narayanan, E. Al-Sukhni, K. Attwood, M. Kukar, S. Hochwald, S. Nurkin. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Outcomes following esophagectomy in high volume centers have been shown to be superior to low volume centers. The purpose of this study was to determine the presence of disparities among centers stratified by case volume and their association with outcomes. Methods The National Cancer Data Base, 2004-2013, was queried for patients who had undergone esophagectomy. Centers were divided based on the total number of cases during this time period: group 1 = low volume (1-99), 2 = middle (100-200), and 3 = high (> 200). Multivariable analysis was performed to determine the association of patient characteristics stratified by center on overall survival (OS). Results A total of 17,547 patients were included; 73.5% were in group 1, 14.6% in group 2, and 11.9% in group 3. Comparing groups 1, 2 and 3, respectively, group 3 had superior short term outcomes: ≥ 15 lymph nodes examined (33.0%, 50.5%, 57.4%, p<0.001), lower rates of positive margins (7.3%, 5.3%, 3.9%, p=0.002), shorter median length of stay (10, 10, 9 days, p=0.004), lower unplanned readmission (1.7%, 1.0%, 0.7%, p=0.002) and lower 30-day mortality (4.2%, 2.6%, 2.4%, p<0.001). The median OS was 37.4, 48.4 and 56.9 months for groups 1-3, respectively (p<0.001). On multivariable analysis for group 1, statistically significant disparate factors associated with poorer OS included ethnicity, insurance status and education. Group 2 disparate factors included race, insurance status and hospital setting. Group 3 disparate factors included insurance status only. Table 1 shows the hazard ratios for each of these findings. Conclusions This study shows an increasing number of disparate patient factors associated with low and middle volume centers compared to high volume centers, which were associated with worse OS for esophageal cancer. We show for the first time that disparities differed among centers based on case volume. In addition to the improved short term outcomes and OS, this study further makes the case for performance of esophagectomy at high volume centers, where fewer disparities were observed.

Multivariable analysis of patient demographic factors on overall survival stratified by hospital case volume for esophagectomy

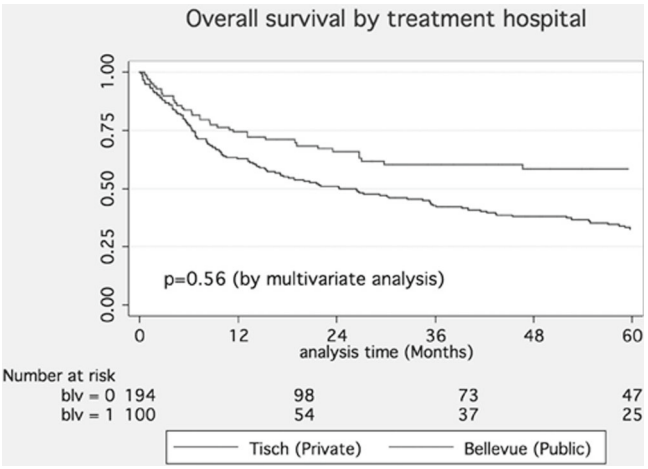
Characteristic	Comparison	Hazard Ratio	P-value
	Low Volume		
Ethnicity	Not Hispanic vs Hispanic	0.80 (0.64, 1.01)	0.05
Insurance	Private vs Not insured	0.84 (0.66, 1.08)	0.009
	Medicare vs Not insured	0.98 (0.76, 1.26)	
	Medicaid vs Not insured	1.01 (0.76, 1.35)	
	Other vs Not insured	0.99 (0.67, 1.46)	
Education*	<14% vs >29%	0.79 (0.70, 0.89)	<001
	14%-19.9% vs >29%	0.92 (0.82, 1.03)	
	20%-28.9% vs >29%	0.97 (0.86, 1.08)	
	Middle Volume		
Race	Black vs White	1.34 (0.88, 2.06)	0.03
	Asian vs White	0.49 (0.23, 1.05)	
	Other vs White	2.53 (0.92, 6.94)	
Insurance	Private vs Not insured	0.46 (0.26, 0.81)	0.002
	Medicare vs Not insured	0.55 (0.30, 0.99)	
	Medicaid vs Not insured	0.84 (0.44, 1.63)	
	Other vs Not insured	0.63 (0.28, 1.43)	
Hospital Setting	Rural vs Metro	0.70 (0.37, 1.33)	0.001
	Urban vs Metro	1.40 (1.15, 1.70)	
	High Volume		
Insurance	Private vs Not insured	0.37 (0.21, 0.67)	0.007
	Medicare vs Not insured	0.33 (0.18, 0.60)	
	Medicaid vs Not insured	0.48 (0.23, 1.01)	
	Other vs Not insured	0.36 (0.15, 0.87)	

* Education as reported by the NCDB is the percentage of adults in the area of residence of a given patient (based on zip code derived from the 2000 US Census) who did not graduate from high school.

PT408

Outcomes of Patients Undergoing Curative Intent Resection for Gastric Adenocarcinoma: Is there a Prognostic Difference Between Tertiary Referral Public and Private Hospitals? I. Hatzaras,* S. Rokosh, M. Melis, G. Miller, R. Berman, E. Newman, K. Rifkind, H.L. Pachter. *Surgery, NYU Langone Medical Center, Brooklyn, NY.*

Objective: We sought to assess our experience between a private (TH) and a public hospital (BH), both staffed by faculty and trainees of the same major university medical center. Methods: Our gastric cancer database was used to identify patients undergoing curative intent resection. Descriptive statistics were used to compare demographic data. Kaplan-Meier survival analysis was used to examine recurrence (RFS) and overall survival (OS). Multivariate proportional hazards regression was used to identify factors associated with RFS and OS. Data were risk – and disease stage- stratified. Results: There were 100 patients in the BH group and 242 in the TH group, with a median age 55 and 70.5 years respectively (p<0.001). The majority of BH patients were Asians (60, 60%), and Caucasians (172, 72.3%) in the TH group. The median number of days from diagnosis to surgical intervention at BH was 47.5 vs. 30 days in the TH (p=0.01). BH group had a smaller BMI and more frequently received distal or subtotal gastrectomy. Perioperative morbidity and mortality was equally distributed, as was 30-day readmission rate. Pathologic staging was similarly distributed. By multivariate analysis, hospital of treatment was not associated with RFS (p=0.48) nor OS (p=0.56). Conclusions: Patients receiving care for gastric cancer at major public hospitals have equally good clinical outcomes when compared to patients treated at private hospitals, if cared for by physicians within the same institution dedicated to disease specific entities.



PT409

Reducing Mortality in Gastric Cancer: Comparison of Multimodality Therapies Using the National Cancer Data Base S. Ahmad,* M. Seaton, A. Hanna, J. Terhune, C. Boutros, R.T. Williams, N. Hanna. *University of Maryland School of Medicine, Baltimore, MD.*

Introduction Adjuvant chemoradiation (ACR) or perioperative chemotherapy (PC) are considered standard of care in North America for resectable gastric cancer. Preliminary results of the CRITICS trial comparing neoadjuvant chemotherapy plus adjuvant chemoradiation (NC+ACR) versus perioperative chemotherapy alone (PC) showed no survival difference. No large population studies have compared outcomes between these multimodality treatments. Methods Data were obtained from the National Cancer Database for patients treated with gastrectomy for non-metastatic gastric cancer from 1998-2011. Patient variables from five treatment groups were retrospectively analyzed. Primary outcome was overall survival at 5 years. Cox regression was used to estimate age-adjusted risk of mortality for each treatment group versus surgery alone. Results Of the 32,707 patients who underwent surgery for stage I, II, and III gastric cancer, only PC significantly improved survival compared to surgery alone (HR 0.81, 95% CI 0.68-0.96, p=0.018). After exclusion of stage I disease, 15,741 patients remained, who underwent either A) surgery alone (n=10,529), or surgery with B) PC (n=292); C) ACR (n=4058); D) NC+ACR (n=153), or E) NC alone (n=709). 54% of Group A was treated prior to 2003. Five-year survival rates for Groups A-E were 18.55%, 59.59%, 46.87%, 49.67%, and 49.65%, respectively. Age-adjusted risk of mortality was lowest with PC (HR 0.48, 95% CI 0.40-0.58, p<0.001), followed by ACR (HR 0.58, 95% CI 0.55-0.61, p<0.001). There was no difference between NC (HR 0.62, 95% CI 0.55-0.69, p<0.001) and NC+ACR (HR 0.62, 95% CI 0.50-0.78, p<0.001) in their reduction of mortality compared to surgery alone. Compared to 1998-2003, mortality decreased over time: HR 0.87 (0.83-0.90, p<0.001) in 2004-2007 to HR 0.72 (0.69-0.76, p<0.001) in 2008-2011. Conclusion For stage II or III gastric cancer, NC with or without adjuvant therapy improved survival compared to surgery alone. Perioperative chemotherapy was associated with the strongest mortality risk reduction, suggesting that all patients with locoregional gastric cancer be evaluated for treatment by a multidisciplinary oncology team prior to surgery.

5-Year Risk of Death Per Treatment Group

Treatment	HR*	95% CI	p-value
Surgery alone	Reference	--	--
Perioperative chemotherapy	0.48	0.40-0.58	<0.001
Adjuvant therapy	0.58	0.55-0.61	<0.001
Neoadjuvant chemotherapy plus adjuvant chemoradiation	0.62	0.50-0.78	<0.001
Neoadjuvant chemotherapy	0.62	0.55-0.69	<0.001

*Age-adjusted hazards ratio estimated by Cox-proportional hazards regression

PT410

Correlation Between FOXP3$^+$ Regulatory T-Cells and Programmed Cell Death Ligand 1 as Prognostic Factor in Gastric Cancer

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Background: Immune escape plays an important role in tumor progression. Substantial evidence suggests that the up-regulation of regulatory T cells (Tregs) plays a important role in immunological evasion of tumors. Recent studies have demonstrated that a majority of tumor cells over-express Programmed cell death ligand 1 (PD-L1), and this overexpression is associated with poor disease prognosis. Although an increase of Tregs and PD-L1 has been revealed in several malignancies, there are few data on their clinical implication in gastric cancer. Methods: Immunohistochemistry was used to detect the expression of Tregs and PD-L1 in 87 gastric cancer tissues. The expression levels of these two molecules were statistically analyzed with clinicopathological factors involved in disease progression and prognosis. Results: In 87 gastric cancer patients, there are 69 (79.3%) patients that are over-expressed in FOXP3$^+$ Tregs and 44 (50.5%) patients in PD-L1. The correlation between the infiltration of FOXP3$^+$ Tregs and expression of PD-L1 was no statistical significance. (p=0.265). The over-expression of FOXP3$^+$ Tregs was associated with distal cancer (p=0.03), smaller tumor size (p=0.02), shallow tumor invasion (p=0.06), abscent lymph node metastasis (p=0.01), low TNM stage (p=0.00) and the absence of lymphatic invasion (p=0.02) and therefore exhibited better disease-free survival (p=0.05) and overall survival (p=0.05). There are no correlations between the expression of PD-L1 and the clinicopathological parameters and prognosis. Conclusions: FOXP3$^+$ Tregs and PD-L1 were over-expressed in gastric cancer. FOXP3$^+$ Tregs expression are favorable prognostic marker in gastric cancer.

PT412

Intraoperative Frozen Section Analysis of Margin Status as a Quality Indicator in Gastric Cancer Surgery

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Introduction: Positive pathologic margins following gastric cancer resection carries a poor prognosis. Intra-operative frozen section analysis may decrease positive margins, but the effect on survival is unclear. The primary objective of this study was to evaluate intra-operative frozen section analysis of resection margins as a quality indicator in gastric cancer surgery. Methods: A population-based cohort was constructed including all patients referred to a provincial cancer agency with non-metastatic gastric adenocarcinoma treated with curative-intent surgical resection between 2004-2012. Clinical, pathologic, and survival data were collected. Descriptive statistics were utilized to compare baseline characteristics. A multivariate logistic regression analysis was used to determine factors predictive of a positive surgical margin. Survival analysis was conducted with Kaplan-Meier curve estimation, log-rank test, and Cox proportional hazards modeling. Results: 377 patients were included in the analysis. Median age was 67 (range 22-88), 67.6% were male, and 49.9% were pathologic stage III. Pathologically positive surgical margins were noted in 16.2% of cases and were associated with worse overall survival (16.5 vs. 52.2 months, p<0.001). Intra-operative frozen section analysis of margins was done in 34.0% of cases. Performing frozen section analysis of margins was protective against a final positive surgical margin (OR 0.34, 95% CI 0.16-0.73, p=0.006), after adjusting for confounding factors. Frozen section analysis was also associated with improved OS (56.9 vs. 32.6 months, p=0.01). The OS benefit associated with frozen section (HR 0.72, 95% CI 0.54-0.98, p=0.04) persisted on multivariate analysis. Conclusions: Patients with intra-operative frozen section analysis of margins were more likely to have negative pathologic margins and had improved overall survival. These data support the importance of frozen section as a quality indicator for gastric cancer surgery.

PT413

Impact of Current "Insufficient" Clinical Nodal Staging on Treatment Decisions and Response to Neoadjuvant Chemoradiotherapy in Esophageal Cancer Patients

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Background: Although essential in treatment decision making, clinical nodal (cN) staging in esophageal cancer (EC) remains difficult. We assessed the rate of nodal up- and downstaging and its prognostic value on 5-year disease-free survival (DFS) in EC patients treated with surgery-alone or with neoadjuvant chemoradiotherapy (nCRT). Methods: For this retrospective study, we included 395 EC patients who underwent a curative esophagectomy with or without nCRT between 2000 and 2015. The surgery-alone and nCRT group were matched on clinical T-stage (cT), cN-stage, and histopathological type using propensity score matching (n=270). Staging consisted of PET with CT, or PET/CT, and endoscopic ultrasonography (n = 235). We compared cN and pathological N-stage (pN) and scored correct, down- and upstaging. The prognostic value of nodal up- and downstaging and localization of node metastases on 5-year DFS were assessed with multivariate Cox regression analysis (factors with a P-value <0.1 on univariate analysis). Results: Nodal upstaging (43.0% vs. 16.3%), correct staging (31.9% vs. 28.1%) and downstaging (25.2% vs. 55.6%) differed between the surgery-alone and nCRT group (P<0.001). Nodal upstaging was commonly present in adenocarcinoma and cT3-4a tumors. Independent prognostic factors for DFS were pN (P=0.002) and lymph-angioinvasion (P=0.016) in the surgery and cN metastasis under the diaphragm (P=0.012) and lymph node ratio (P=0.034) in the nCRT group. Conclusions: In esophageal cancer, clinical lymph node staging is still insufficient with >25% nodal downstaging. This inaccuracy might impede assessment of true nodal response to nCRT, affording dubious decisions for a 'wait-and-see' strategy.

PT414

Comparative Outcomes of Minimally Invasive and Robotic-Assisted Esophagectomy

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Objective: Minimally invasive esophagectomy(MIE) has demonstrated superior outcomes compared to open approaches. The myriad of techniques has precluded the recommendation of a standard approach. The addition of robotics has potential to further improve outcomes. We sought to compare the outcomes of existing techniques for MIE with robotic assisted approaches. Methods: Utilizing a prospective esophagectomy database we identified patients who underwent (MIE) via Ivor Lewis(TT), transhiatal(TH) or robotic assisted Ivor Lewis(RAIL). Patient demographics, tumor characteristics and complications were analyzed via ANOVA, Chi-Square, and Fisher Exact where appropriate. Results: We identified 302 patients who underwent MIE: TT 95(31.5%), TH 63(20.8%), and RAIL 144(47.7%) with a mean age of 65±9.6. The length of operation was longer in the RAIL: TT(299±87), TH(231±65), RAIL(409±104 minutes), p<0.001. However the EBL was lower in the RAIL patients: TT(189±188ml), TH(242±380ml), RAIL(155±107ml), p=0.03. Conversion to open was also lower in the RAIL group: TT 7(7.4%), TH 8(12.7%), RAIL 0, p<0.001. The R0 resection rate and lymph node (LN) harvest also favored the RAIL cohort :TT 86(93.5%), TH 60(96.8%), and RAIL 144(100%), p=0.01. LN:TT 14±7, TH 9±6, and RAIL 20±9, p<0.001. The overall morbidity was lower in RAIL patients: TT 29(30.5%), TH 39(61.9%), RAIL 34(23.6%), p<0.001. Mortality was lower in the TT and RAIL approaches compared to

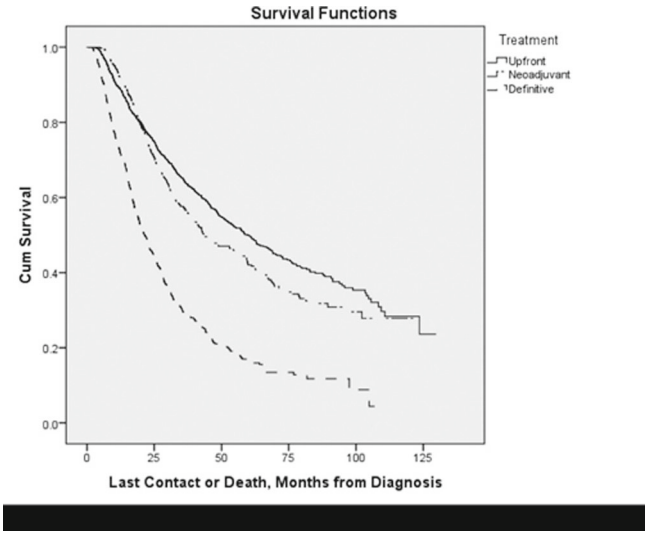
TH but was not significant: TT 2 (2.1%), TH 2 (3.2%), and RAIL 2 (1.4%), p=0.6. Conclusions: RAIL demonstrates lower EBL, conversion to open, and morbidity than other MIE techniques. Additionally the oncologic outcomes measured by R0 resections and LN harvest also favored the patients who underwent RAIL.

Surgical Complications	Transthoracic N=95 N (%)	RAIL N=144 N (%)	MIE Transhiatal N=63 N (%)	P Value
Anastomotic Leak	4 (4.2%)	4 (2.8%)	4 (6.3%)	.5
Anastomotic Stricture	3 (3.2%)	11 (7.6%)	16 (25.4%)	.001
Pneumonia	8 (8.4%)	10 (6.9%)	18 (28.6%)	.001
Aspiration	2 (2.1%)	3 (2.1%)	11 (17.5%)	.001
Wound Infection	6 (6.3%)	1 (0.7%)	10 (15.9%)	.001
Myocardial Infarction	3 (3.2%)	1 (0.7%)	0	.1
Cardiac Arrhythmias (includes A-fib)	17 (17.9%)	25 (17.4%)	10 (15.9%)	.9
Any Complication*	28 (29.5%)	34 (23.6%)	31 (49.2%)	.001
Pulmonary Complication**	18 (18.9%)	14 (9.7%)	24 (38.1%)	.001
Pulmonary Embolus	3 (3.2%)	3 (2.1%)	2 (3.2%)	.8
Pleural Effusion	9 (9.5%)	2 (1.4%)	7 (11.1%)	.005
Mortality	2 (2.1%)	2 (1.4%)	2 (3.2%)	.7

PT415

Comparative Outcomes of Upfront Surgery, Neoadjuvant Chemoradiation, and Definitive Chemoradiation for Clinical T2N0 Esophageal Adenocarcinoma: A National Cancer Data Base Analysis K. Meredith,[1]* J. Huston,[1] P. Briceno,[1] R. Shridhar.[2] *1. Gastrointestinal Oncology, Florida State University/Sarasota Memorial Health Care System, Sarasota, FL; 2. University of Central Florida, Orlando, FL.*

Purpose: To compare overall survival (OS) of T2N0 esophageal adenocarcinomas treated with either upfront surgery (US), neoadjuvant chemoradiation (NCR), or definitive chemoradiation (DCR) from the National Cancer Database (NCDB). Methods: The NCDB was accessed to identify patients with T2N0 esophageal adenocarcinoma treated between 2004-2013 with either US, NCR, or DCR. NCR and DCR patients were included if they were treated with a radiation dose between 45-50.4 Gy and received chemotherapy. Results: We identified 3371 patients (US 1707; NCR 825; DCR 839). Clinical staging in US patients was accurate pathologically in 31.4% of patients. Tumor and nodal upstaging were found in 21.2% and 28.9% of patients, respectively, while tumor downstaging was found in 35.8% of patients. Tumors >3 cm and poorly differentiated tumors predicted for higher tumor and nodal staging. DCR patients were significant older than US and NCR patients ($p<0.001$). Median OS for US, NCR, and DCR patients was 59.6 months, 43.8 months, and 21.4 months, respectively ($p<0.001$). NCR patients had significantly worse OS compared to upfront surgery in patients with tumors <3 cm ($p=0.01$) and/or well to moderately differentiated tumors ($p=0.001$). UVA and MVA of OS revealed that DCR and NCR patients achieving no pathologic response was associated with worse survival. Pathologic complete and partial response in NCR patients was not predictive of OS on UVA or MVA. Conclusion: Clinical staging for T2N0 esophageal adenocarcinoma continues to remain highly inaccurate. Upfront surgery yielded the highest OS, while NCR with no pathologic response and DCR was associated with inferior OS.



PF416

Does Faster Time to Surgery Impact Survival in Resectable Gasric Cancer? A U.S. Population-Based Study K.A. Mirkin,* C. Hollenbeak, J. Wong. *Department of Surgery, Penn State, Hershey, PA.*

Title: Does Faster Time to Surgery Impact Survival in Resectable Gastric Cancer: A U.S. Population Based Study Background: Convention suggests that faster time to initiation of care imparts a survival advantage. We sought to evaluate patient characteristics on access to surgical care for gastric cancer and to determine if delayed surgical resection was associated with survival. Methods: The U.S. National Cancer Data Base (2003-2011) was reviewed for patients with clinical stages I-III resected gastric cancer with time from diagnosis to surgery recorded. Patients who received neoadjuvant therapy (NAT) were excluded. Univariate, multivariate and landmark analyses were performed. Results: Of 6,240 patients who underwent initial surgery, 20.8% (N=1,300) were diagnosed at the time of surgery, 10.1% (N=631) underwent resection 1-2 weeks after diagnosis, 22.0% (N=1,373) 2-4 weeks, 33.3% (N=2,076) 4-8 weeks, and 13.8% (N=860) at 8-12 weeks following diagnosis. Multivariate analysis showed older patients (HR .84, p=0.013), Medicare (HR 0.90, p=0.027) or Medicaid coverage (HR 0.74, $p<0.001$), lack of insurance (HR .73, p=0.023), greater distance from treatment center (HR 0.81, p=0.0038) and treatment at an academic center (HR 0.77 p=0.001) were associated with shorter time to surgery. However, patients of other races (non-white/non-black/non-Hispanic), and those treated in the Midwest experienced longer time to surgery (HR 1.2 p=0.005, HR 1.2, p=0.002, respectively). In 3-, 6-, and 12-month landmark analyses, time to surgery did not significantly impact survival in any stage disease. On multivariate analysis, surgery at a later time was not associated with worse survival. Conclusions: For patients with resectable gastric cancer, there do not appear to be large disparities in access to surgery, with most undergoing surgery within one month of diagnosis. However, there appears to be no survival benefit to earlier surgical resection within 12 weeks from diagnosis. This suggests that allowing time for tissue confirmation and allowing for optimization in preparation for surgery may not negatively impact survival.

PF417

Using NSG Recipient Mice Improves Engraftment of Gastric Cancer Patient Derived Xenografts S.C. Wang,[1]* M. Zhu,[2] I. Nassour,[1] J. Shen,[3] J.C. Mansour,[1] D. Agarwal,[4] H. Zhu,[2] M.R. Porembka.[1] *1. Department of Surgery, The University of Texas Southwestern Medical Center, Dallas, TX; 2. Children's Research Institute, The University of Texas Medical Center, Dallas, TX; 3. Department of Pathology, The University of Texas Southwestern Medical Center, Dallas, TX; 4. Department of Internal Medicine, The University of Texas Southwestern Medical Center, Dallas, TX.*

Background: Previous gastric cancer (GC) patient derived xenograft (PDX) studies reported engraftment rates inversely proportional to the immunocompromised states of recipient mice (nudes 17%, scid 27%, and NOD/scid 34%). We tested highly immunocompromised NOD scid gamma (NSG) mice, which lack mature T cells, B cells, or functional natural killer cells, as recipients for low volume biopsies and post-treatment GC samples. Methods: Consent was obtained from GC patients who were scheduled to undergo esophagogastroduodenoscopy (EGD) and diagnostic laparoscopy as part of their disease management strategies. The following amounts of tumor were coated with Matrigel and inoculated into the flanks of NSG mice: EGD biopsies ~10 mg, post-treatment samples ~100 mm^3, and peritoneal metastasis biopsies ~100 mm^3. Tumors were serially measured and passaged when the greatest dimension reached 1.5 cm, or if there was overlying skin necrosis. Results: The engraftment rates were: EGD biopsies 48% (13 of 27 samples), post-resection samples 58% (7 of 12), and peritoneal metastases 11% (1 of 9). Median time to first passage was 10.1 weeks (range: 8.1 to 12.4) for EGD biopsies and 22.1 weeks (9.6 to 33.0) for post-treatment samples. Two (15%) engrafted EGD mice developed liver metastases, and one (7.7%) had axillary lymph node metastasis (AxLN). Three (47%) engrafted post-treatment mice had liver metastases and two (29%) had AxLN. Histology was generally maintained through passages and metastases. Mucinous components were lost over time, leaving only solid, poorly differentiated tumor. There were no associations between engraftment rate and any evaluated clinical or pathologic characteristics, including tumor response and patient overall survival. The tumor from the one patient who had a complete pathologic response after NAT did not engraft. Conclusions: Using highly immunocompromised NSG mice improved engraftment rates of GC PDX, even for challenging specimens such as endoscopic biopsies and post-treatment resection samples. Tumor histology was generally maintained through passages. Studies comparing the expression profiles of serially passaged tumors to the original clinical samples are ongoing.

PF418

Treatment Trends in Gastroesophageal and Gastric Cancers in the United States A.A. Mokdad,* A. Ali, I. Nassour, J.C. Mansour, S.C. Wang, M.R. Porembka. *Surgery, University of Texas Southwestern, Dallas, TX.*

Introduction: Randomized clinical trials reported in the last decade have helped define gastroesophageal junction (GEJ) and gastric cancer (GC) treatment. It is unclear, however, how practice patterns have evolved following these trials. This study explores the trends in treatment of GEJ and GC over the past decade in the United States. Methods: Patients with adenocarcinoma of the stomach and distal esophagus were identified in the National Cancer Database between 2006 and 2013. Tumor located in the distal esophagus and gastric cardia was denoted GEJ. Tumors distal to the cardia constituted GC. Tumors were categorized as early (Stage IA), locally advanced (IB-IIIC), and metastatic (IV). Detailed treatment was compared according to tumor stage and location. A time trend analysis was conducted. Results: A total of 120,729 patients (GEJ: 79,654 [66%], GC: 41,075 [34%]) were identified. Stage was similar in both groups (early: 12%, locally advanced: 55%, and metastatic: 33%). Overall, 73% of early GEJ and 74% of early GC underwent resection; of those, 43% and 12% were local excisions, respectively. Local excisions increased over time in both groups (annual odds ratio [OR]=1.2; P<0.01). In locally advanced GEJ, neoadjuvant chemoradiotherapy (CRT) increased among patients that received multimodality treatment (53% in 2006 to 73% in 2013; OR=1.1, P<0.01). In locally advanced GC, the use of neoadjuvant chemotherapy (CT) increased (5% to 20%; OR=1.2, P<0.01) as did perioperative CT (1% to 9%; OR=1.3, P<0.01) in lieu of adjuvant CRT (68% to 43%; OR=0.9, P<0.01) (Figure 1). Multimodality treatment use remained stable over the study period in both groups (GEJ: 42%, GC: 47%). Among patients with metastatic disease, only 61% of GEJ and 40% of GC patients received CT, with 32% and 40%, respectively, not receiving any therapy at all. Conclusions: Practice patterns for GEJ and GC changed in the last decade with increasing adoption of neoadjuvant therapy in locally advanced disease and local excision of early stage cancers. Treatment for metastatic disease remains markedly underutilized, particularly GC.

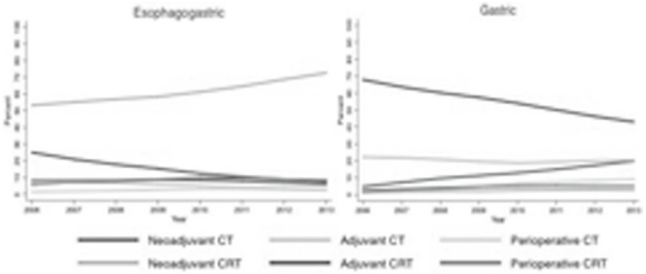


Figure 1. Treatment trends for advanced stage GEJ and GC that received multimodality treatment

PF419

Trends in Utilization of Chemotherapy and Radiation for Resectable Gastric Adenocarcinoma: An Analysis of the NCDB B.M. Motz,* P.D. Lorimer, K.K. Walsh, I.N. Perry, Y. Han, R.L. White, J.C. Salo, J. Hill. *Levine Cancer Institute, Charlotte, NC.*

Introduction: Locally advanced gastric adenocarcinoma (GACa) is optimally treated with a combination of surgery, chemotherapy (CHEMO) and radiation (RT). Utilization of therapies can vary with institutional practices and disparities in care. The National Cancer Database (NCDB) was used to evaluate trends in utilization of adjunctive therapy in patients (pts) with resectable GACa. Methods: The NCDB was queried for pts with GACa undergoing R0 resection (2006-2012). Pts with metastatic disease, incomplete pathologic staging, and incomplete CHEMO or RT sequencing data were excluded. Pts were divided into five groups defined by established treatment regimens: G1: perioperative CHEMO; G2: adjuvant CHEMO±RT; G3: neoadjuvant CHEMORT; G4: other adjunctive regimens; and G5: surgery alone. Pts who received neoadjuvant therapy were staged using clinical TNM, and those who did not or who did not have complete clinical staging were staged using pathologic TNM. Three subsets were created: LOCAL: T0-2N0, LOCALLY ADVANCED: T3-4N0, and REGIONAL: N+. Statistical analyses included Chi-square, univariate, multivariable with stepwise selection, and Cochran-Armitage time trend. Results: N=12946: G1=1099, G2=4771, G3=180, G4=244 and G5=6652. The percentage of pts receiving adjunctive therapy was determined for each subset: LOCAL=760/4430 (17.2%), LOCALLY ADVANCED=866/1448 (59.8%), and REGIONAL=4668/7068 (66.0%). Use of any adjunctive therapy increased from 2006: 44.4% to 2012: 53.0% (p<0.01), and use of perioperative CHEMO also increased from 2006: 4.3% to 2012: 17.8% (p<0.01). Other factors associated with use of adjunctive therapy on multivariable analysis are: age (p<0.0001), race (p<0.0001), median income (p=0.0002), insurance status (p<0.0001), Charlson-Deyo score (p<0.0001), and facility volume (p=0.01). Conclusions: Though utilization of adjunctive therapy is increasing, a large proportion of pts with locally advanced GACa did not receive recommended adjunctive therapy. This study highlights disparities in utilization of optimal multimodality care. National efforts to expand access to care are necessary to improve outcomes in locally advanced gastric adenocarcinoma.

Table 1: Adjunctive Treatment Group by Staging Subset

	Perioperative CHEMO N(row%)	Adjuvant CHEMO+/-RT N(row%)	Neoadjuvant CHEMORT N(row%)	Other Adjunctive Regimens N(row%)	Surgery Alone N(row%)	Total N(row%)
LOCAL	247 (5.6)	446 (10.1)	35 (0.8)	32 (0.7)	3670 (82.8)	4430 (100)
LOCALLY ADVANCED	264 (18.2)	509 (35.2)	43 (3.0)	50 (3.5)	582 (40.2)	1448 (100)
REGIONAL	588 (8.3)	3816 (54.0)	102 (1.4)	162 (2.3)	2400 (34.0)	7068 (100)
Total	1099 (8.5)	4771 (36.9)	180 (1.4)	244 (1.9)	6652 (51.4)	12946 (100)

PF421

Influence of Tumor Response and Treatment Schedule on the Distribution of Tumor Recurrence in Esophageal Cancer Patients Treated with Neoadjuvant Chemoradiotherapy K.M. Jipping,[1] J. Hulshoff,[1] E.A. Amerongen,[1] T.I. Bright,[2] D.I. Watson,[2] J.T.M. Plukker.[1]* *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. Flinders University, Flinders Medical Centre, Department of Surgical Oncology, Adelaide, SA, Australia.*

Background: Knowledge of pathologic complete tumor response (pCR) and the used neoadjuvant chemoradiotherapy (nCRT) schedule on the distribution of recurrent disease is important in the treatment of esophageal cancer (EC) patients. We assessed the effect of both pCR and different nCRT schedules on the pattern of first tumor recurrences in EC. Methods: The study was performed in two different centers in patients with T1N+/T2-4aN0-3/M0 EC. Patients were treated with nCRT according to the CROSS (carboplatin/paclitaxel/41.4Gy : n=134) and Cis/5FU schedule (Cisplatin/5-fluorouracil/45-50.4Gy : n=88) followed by surgery. First we determined the effect of pCR on tumor recurrence distribution (local, distant or combined) and site-specific recurrences in the CROSS group. After propensity matching on clinical T-stage, clinical N-stage and histology (n=63), we determined the effect of both nCRT schedules on the distribution of tumor recurrence and site specific recurrences. Results: The median follow-up after pCR (n=24) was significant longer (P=0.001) than in non-complete responders (pNCR); 45.5 (IQR 20.3-69.5) and 20.0 months (12.0-42.3), respectively. The pattern of recurrence also differed significantly (P=0.001), with 0 (0.0%) and 7 (6.4%) locoregional, 5 (20.8%) and 36 (32.7%) distant, and 0 (0.0%) and 21 (19.1%) local and distant recurrence between the pCR and pNCR group, respectively. Patients with a pCR had significant less local and distant recurrences. With equal median time to recurrence, the distribution of metastases in the matched groups differed only in the numbers of lung metastases (P=0.029), with 15 (23.8%) and 6 (9.5%), respectively. Conclusions: Patients with a pCR have less local and distant recurrences. With equal time to first recurrence, the nCRT schedule itself had only a minor influence on the distribution of recurrences.

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Difference in Complications and Survival Between the Sweet and the Mckeown Esophagectomy in Esophageal Cancer A. de Zanna, J. Hulshoff, B. van Etten, J.T.M. Plukker.* *University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands.*

Background: Transthoracic esophagectomy in distal esophageal and gastro-esophageal junction (GEJ) tumors can be performed through a right- or left-sided approach with a cervical (McKeown) or intrathoracic anastomosis (Sweet procedure). Evidence regarding the length of resection and the preference for these procedures are lacking. From a prospectively maintained database we analyzed complications and survival of both procedures. Methods: All patients with a transthoracic resection for potentially curable distal esophageal or GEJ cancer (T1-4a, N0-3, M0 ; n=306) between 2000 and 2014, were included. After propensity scored matching on histology, age (<70 years), clinical T- and N-stage, neoadjuvant chemoradiotherapy, tumor location, and tumor length, both the right- and left-sided group consisted of 130 patients. We assessed the amount of resected lymph nodes, tumor free resection margins (R0 : >0 mm), and difference in post-operative complications. Overall (OS) and disease-free survival (DFS) were determined with univariate and multivariate (factors with P<0.10) Cox regression analysis. Results: Patients with the right-sided procedure had significant more complications, including pneumonia (P=0.036), respiratory insufficiency (P=0.007), pleural effusion (P=0.031), chylothorax (P = 0.008), and vocal cord paralysis (P=0.018). Longitudinal resection margins were more frequently tumor free in right-sided procedures (P=0.046), while the number of resected lymph nodes (P=0.481) was equal. The surgical approach did not influence the 5-year OS (P=0.943) and DFS (P=0.965). Conclusions: Left-sided esophagectomy provided less post-operative complications with comparable survival outcomes and showed to be a good alternative in patients with distal esophageal or GEJ tumors.

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The Immediate Post-esophagectomy Chest X-ray Predicts Respiratory Failure and the Need for Tracheostomy E. Gabriel,* R. Shah, K. Attwood, M. Kukar, S. Hochwald. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Esophagectomy is a major surgical procedure associated with high rates of morbidity. The purpose of this study was to determine if the immediate first post-esophagectomy chest X-ray (CXR) is associated with morbidity or mortality. Methods This was a single institution analysis of patients undergoing esophagectomy, 2005-2015. A post-esophagectomy CXR (pCXR) was routinely performed. A pCXR score was developed based on the number of objective abnormal findings (i.e. atelectasis, effusion, pneumothorax). Statistical analysis was performed using patient/tumor variables and pCXR score to derive adjusted odds ratios (OR) on short-term outcomes. Results 182 patients had pCXRs available for analysis. Scores ranged from normal (0) to 4 depending on the number of abnormalities, with a mean score of 1.6. The mean patient age was 60.7 years. 92.9% had adenocarcinoma, 39.6% had T3/T4 tumors, and 48.4% were node positive. All patients received neoadjuvant chemoradiation. 51.6% of surgeries were open; 74.2% had chest anastomoses. The 30- and 90-day mortality rates were 2.2% and 3.9%, respectively. On univariable analysis, increasing pCXR scores were associated with increased risk of post-operative re-intubation (OR 1.67, 95% CI 1.21-2.36, p=0.002) and tracheostomy (OR 2.12, 95% CI 1.08-4.16, p=0.029). Multivariable analysis adjusting for age, comorbidities (ASA), performance status (ECOG), histology, pathologic stage, surgical approach and operative time confirmed a statistically significant association with pCXR score and respiratory failure with tracheostomy (OR 2.13, 95% CI 1.03-4.39, p=0.041). No significant associations were identified between pCXR score and LOS, other complications or mortality. Conclusions This is the first study to show an association between the first pCXR and respiratory failure requiring tracheostomy. Importantly, this increased risk for respiratory failure can be identified from the first pCXR and has implications for assigning the appropriate level of care for patients leaving the recovery room. Surgeons and anesthesiologists can use intraoperative strategies to minimize findings on the pCXR and reduce the risk of respiratory failure.

PF424

Impact of Central Lymph Node Examination in Gastric Cancer
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Introduction: We sought to determine the association between the identification of positive lymph nodes on D2 lymph node dissection (LND) with stage and outcomes, in the era of preoperative treatment for gastric cancer. Methods: We reviewed data from a prospectively maintained database of gastric cancer patients who underwent resection of gastric or gastroesophageal cancer at our institution from 2005-2016. Central lymph nodes (CnLN) were defined as common hepatic, celiac, and proximal splenic artery lymph nodes (stations #8, 9, and 11p). Risk factors for CnLN metastases, and overall survival (OS) were examined. Results: We identified 356 patients, median age was 64 years (IQR 54-71) and 59% were male. Preoperative therapy was given in 66% of patients. D2 LND was performed in 80% of patients, and the median number of LN examined was 25 (IQR 18-34). Most patients (N=244, 68%) had separately-examined CnLN in pathology, and the median number of examined LNs was higher in this group (27 vs 19; p<0.001). The CnLN positivity rate was 9.1% (22/244; #8: 4.8%, #9: 6.1%, and #11p: 4.8%), which was higher in advanced pT stage patients (pT0 - 3.1%, pT1 - 0%, pT2 - 5.6%, pT3 - 18%, pT4 - 13%; p=0.001). If we assume that D2 LND was not performed on these patients, a total of 7 (3%, 7/244) patients would have had pN stage down-migration (6 with N1 to N0, 1 with N2 to N1). Of the 22 CnLN-positive patients, 10 (45%) had pN1, 2 (9%) had pN2, and 10 (45%) had pN3 stages. On multivariate analysis, EUS N stage (positive) was associated with positive CnLNs (OR 2.86 [95%CI 1.08-7.58]). Among 342 patients who had R0 resection, the median follow-up was 3.6 years, and the median OS was 11.6 years. Among patients who received preoperative therapy, pT3/4 stage (HR 2.44 [1.27-4.69]; p=0.01) and positive CnLN (HR 5.44 [2.36-12.52]; p<0.001) had negative impact on OS by multivariate analysis. Conclusion: CnLN metastases are uncommon in gastric cancer, and are associated with an adverse impact on OS. However, long-term survival is still possible in patients with positive CnLN whom underwent a D2 lymph node dissection. Larger multi-institutional studies are needed to determine if CnLN positivity requires a separate staging category.

PF425

The Periesophageal Fascia, the Anatomic Border for an Adequate Nodal Dissection and Safety Surgical Circumferential Margin in Esophageal Cancer
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Background: Analogous to the mesorectal fascia in rectal cancer surgery, a peri-esophageal fascia (PEF) like fibrous envelope can be observed during en bloc esophagectomy with regional lymphadenectomy. In an explorative anatomic cadaver and in vivo study we identified the PEF envelope and assess its potential impact in achieving tumor free circumferential resection margins (CRM). Methods: According to the Institutional Ethical Board rules, the thoracic esophagus and gastro-esophageal junction were dissected meticulously in six human cadavers (two fixed in 3% phenol solution and four fresh frozen). After partial removal of the chest/sternum and cardiectomy, PEF was exposed in relation to the surrounding structures. We assessed the PEF in vivo and analyzed its role as a safe anatomical visible CRM in transthoracic esophagectomies. Results: Detailed anatomical dissection in the human cadavers (n=6) showed a thin PEF as a continuum of a fascial layer at the phrenoesophageal ligament/membrane within the GEJ complex running from the dorsolateral diaphragm, crossing the pulmonary vein laterally to end dorsally at the carina. PEF was observed as a semi-complete thin fascia like envelope, surrounding the distal and middle paraesophageal lymph nodes, implicating the clinical usefulness of PEF in achieving a radical tumor free (R0) procedure while facilitating a complete nodal dissection. Conclusions: A distinct thin peri-esophageal fascia enveloping adjacent distal and middle paraesophageal lymphatic tissues, might be a potential intraoperative guidance in achieving safe and tumor free CRM's during esophagectomy.

PF426

Short- and Long-term Outcomes with Robotic Assisted Esophagectomy
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Purpose: Surgical resection remains piviotal in the management of patients with esophageal cancer. Minimally invasive esophagectomy(MIE) has demonstrated superior operative outcomes compared to the open approaches. Robotic assistance has potential to further improve outcomes, however the long-term follow with this technique is lacking. Methods: Utilizing the National Cancer Database we identified patients who underwent esophagectomy and stratified by approach: open (OE), laparoscopic (LE) or robotic (RE). Baseline comparisons were made for continuous variables using both the Mann-Whitney U and Kruskal Wallis as appropriate. Pearson's Chi-square test was used to compare categorical variables. Survival analysis was performed using the Kaplan-Meier method comparing survival curves with the log-rank test. All statistical tests were two-sided and α (type I) error <0.05 was considered significant. Results: We identified 18,869 patients who underwent esophagectomy with a mean age of 65 ± 10 years. There were 10,882 (57.7%) OE, 7,102 (37.6%) LE, and 885 (4.6%) RE. There was no difference in T stage or N stage among groups. Thirty and 90-day mortality was 3.2% and 6.9% and was lower in the MIE groups compared to open 6.2% vs 7.9% p<0.001. Median length of hospitalization in RE, LE and OE was comparable at 9, 10, and 10 days respectively, p=0.06. Neoadjuvant therapy was administered in 9,118 (48.3%) patients and was more frequent in the RE 66.0% vs 57.5% OE vs LE 32% p<0.001. Oncologic quality as indicated by R0 resections and median lymph node harvested were improved in patients undergoing RE: 836 (94.9%) and 16, LE: 5,322 (86.7%) and 4, and OE: 9,631 (91.1%) and 12, p<0.001. The median and 5-year survival by approach: RE, LE and OE was 54.4 months and 47.7%, 55.6 months and 50.3%, and 47.4 months and 43.7%, p<0.001. MVA demonstrated that age, location, neoadjuvant therapy, T-stage, N-stage, hospital volume, MIE, and R0 resections were predictive of survival. Conclusions: Short and long-term outcomes with robotic assisted esophagectomy demonstrates low mortality with superior R0 resections and lymph node harvest. Overall survival is benefited in patients undergoing MIE.

PF427

Lymphadenectomy for Gastric Cancer is an Independent Predictor of 10-Year Overall Survival
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BACKGROUND: Lymphadenectomy for gastric adenocarcinoma (GA) seems to improve outcomes. However, its extension for curative-intent treatment (CIT) of GA remains on debate even after clinical trials. The main concern is if the inherent morbidity of the procedure could be justified based on benefits in oncologic outcomes. This study addressed the role of lymphadenectomy as predictor of overall survival (OS). METHODS: Consecutive patients who underwent gastrectomy for GA, by the same team, were identified in a prospective maintained database. Determinants of OS were assessed by univariate and Cox regression models. RESULTS: From 1994 to 2015, 656 consecutive patients who underwent gastrectomy were evaluated. Briefly, 455 patients (69.4%) were male, 397 patients (60.5%) underwent total gastrectomy, Roux-en-Y reconstruction was done in 483 patients (73.6%), and R0 resection was achieved in 632 patients (96.3). More clinicopathological and operative data are outlined in the Table. According to multivariate analysis, the risk of death was increased with older age (≥ 70-y), high-grade tumors, lesions ≥ 5 cm, positive nodes ≥ 3, and extra-gastric resections. On the opposite side, more extensive lymphadenectomy (D2) improved median OS (37 versus 16 months), 3-y (51.1 versus 32.2%), 5-y (43.2 versus 26), and 10-y OS (30.6 versus 9.4%). These results were corroborated by the cox model (HR 0.48, 95% CI 0.34 – 0.67, p < 0.001). The median OS for all patients was 31 months and 3-, 5-, and 10-y were 47.6, 40, and 27%, respectively. The median follow-up for all patients was 26 months, and for survivors it was 65 months. CONCLUSION: This study showed D2 lymphadenectomy for GA as independent good predictor of OS, even after 5-y and until 10-y. Our study suggests that D2 should be offered as local control for all patients with GA who are fit for CIT.

Univariate and multivariate analysis for overall survival.

	Total	Overall survival				Univariate analysis	Multivariate analysis ¶		
Characteristics	N (%)	Median (mo)	3-y	5-y	10-y	p value	HR	95% CI	p value
Overall	656	31	47.6	40	27				
Age						0.021	1.46	1.11 - 1.93	0.008
< 70	462 (70.4)	31	47.9	40.7	30.2				
≥ 70	194 (29.6)	30	46.9	38.6	17.8				
Tumor grade α						0.007	1.32	1.01 - 1.72	0.042
I and II	266 (42.4)	47	55.2	48.2	30.5				
III	361 (57.6)	26	41.7	34.6	24.7				
Tumor location						<0.001	1.12	0.85 - 1.47	0.433
Lower	326 (49.7)	41	54.7	45	30.3				
Upper	330 (50.3)	26	40.5	35.1	23.7				
Borrmann classification β						<0.001	1.04	0.7 - 1.55	0.83
0 - II	102 (16.8)	81	70.5	61.8	46.5				
III - IV	507 (83.2)	29	45.9	38	24.7				
Tumor size *						<0.001	1.36	1.01 - 1.83	0.04
< 5 cm	201 (33.3)	93	71.3	61.4	41.1				
≥ 5 cm	402 (66.7)	24	38.9	33.4	22.4				
Number of positive nodes μ						<0.001	2.34	1.74 - 3.13	<0.001
< 3	310 (47.4)	96	69.2	60.9	43.6				
≥ 3	344 (52.6)	17	28	21.3	12.1				
Combined resection						<0.001	1.61	1.12 - 2.31	0.01
Yes	93 (14.2)	38	51.2	43.5	29.5				
No	563 (85.8)	15	22.3	15.4	9.1				
D2 Lymphadenectomy						<0.001	0.48	0.34 - 0.67	<0.001
Yes	536 (81.7)	37	51.1	43.2	30.6				
No	120 (18.3)	16	32.2	26	9.4				
Adjuvant treatment Ω						<0.001	1.35	0.97	1.88
Yes	411 (64.5)	94.8	38.5	30.2	18.8				
No	226 (35.5)	24	67	60.3	44.3				

mo – months; α n = 627; β n = 609; * n= 603, μ n = 654; Ω n = 637; ¶ n= 461; HR – Hazard Ratio; CI – Confidence Interval.

PF428

Clinical and Epidemiological Features in 495 Gastroenteropancreatic Neuroendocrine Patients R. Guzman,* L. Garcia, L. Marisol. *Sarcomas and digestive tube, Oncology Hospital, Mexico City, Mexico.*

Background. Data, incidence and/or prevalence about gastroenteropancreatic neuroendocrine tumors remains unknown in Mexico. Also there is no evidence about any Mexican multicenter study reporting information such as clinical presentation, diagnostic approach and treatment. The biggest problem is the lack of clinical and therapeutic management results so physicians can validate the proper patient protocols. Objetive: To know the clinical, epidemiological and therapeutic characteristics of NET-GEP patients treated at the 5 biggest Concentration Mexican Medical Institutions. Methods: This paper was developed with the support of 5 Public Medical Institutions: Mexican Social Security Institute (IMSS), Institute for Social Security and Services for State Workers (ISSSTE), Secretary of the Mexican Navy, Petroleos Mexicanos (PEMEX), Ministry of Public Health and 1 Private Hospital. 495 Patients from 6 hospitals where included: Oncology Hospital, CMN XXI Century, Hospital No. 25 25, Monterrey IMSS, National Cancer Institute (INCAN), National Medical Center November 20, Naval General Hospital of High Specialty and Private Institutions. Results: Of 495 patients, 59.7% (296) were women and 40.32% (200) were men, 26% of them had around 50 years old. Diagnosis symptoms included: abdominal pain 47.27% (234), gastrointestinal bleeding 18.58% (92) no-predominant symptoms 28.88% (143). Around 32.25% (160) had Carcinoid syndrome and 67.74% (336) were nonfunctioning. The predominant location was pancreas 33.27% (165) and stomach 28.02% (139). 36% resulted circumscribed neoplasia (179), features polypoid 26% (129) and infiltrative 15% (73). The size was> 2cm in 49% (242)> 1-2cm: 36% (180) 0.5 to 1 cm 9% (45) <0.5 cm 6% (29). Grade: GI 64% (316), GII 13% (66), GIII 23% (114). Positive lymphnodes metastases (6%) (31), negative (94%) (465). Only seven cases extra nodal metastases (liver (3), lung (2), spleen (2)). All patients were treated surgically. Conclusions. This research reflects specific differences in the location of the NET. The trend is more sluggish than it reported worldwide and provides the basis for future clinical trials.

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Analysis of Tumor Immune Protein Expression and Clinical Outcomes in Gastric Adenocarcinoma A.M. Blakely, W. Young,* A. Matoso, T.J. Miner. *Rhode Island Hospital / Brown University, Providence, RI.*

Introduction: Up- and down-regulation of various immunomodulating proteins may reflect gastric tumor aggressiveness, possibly correlating with disease progression. Although a growing focus of investigation, literature is still lacking on which proteins may be predictors of patient outcomes. Methods: Retrospective review of a prospective database was performed of patients who underwent gastrectomy for adenocarcinoma with curative intent, 2003 to 2013. Patient demographics, operative details, pathology data, and outcomes were captured. Results: 86 of 105 gastrectomy patients had sufficient tissue for microarray analysis. Patients were mostly males (65.1%); median age was 74 years. 31 patients (36.0%) underwent total gastrectomy; the remainder underwent subtotal resection. 59 specimens (68.6%) had ≥15 lymph nodes harvested. Median tumor size was 4.9 cm; 55 (64.0%) were at least stage T3 and 63 (73.3%) had nodal involvement. 13 margins (15.1%) were positive, 50 had lymphovascular invasion (LVI, 58.1%), and 43 had perineural invasion (PNI, 50.0%). Median follow-up was 43 months; 28 patients (32.6%) died in follow-up. 9 patients (10.5%) developed local recurrence while 27 (31.4%) had regional/distant recurrence; median time to recurrence was 12 months. Recurrence was associated with LVI (50.0% vs. 25.0%, p=0.028) and PNI (53.5% vs. 30.2%, p=0.029). LVI was associated with microsatellite instability (MSI) (70.0% vs. 20.0%, p=0.021). PNI was associated with suppressed programmed death-ligand 1 (PD-L1) expression in epithelium (73.1% vs. 41.4%, p=0.0072) and lymphocytes (60.0% vs. 37.1%, p=0.038). PD-L1 positive lymphocytes were associated with positive margins (21% vs 2%, p=0.004). Epithelial indoleamine dioxygenase (IDO) expression was associated with lower recurrence (30.0% vs. 57.1%, p=0.012). Conclusions: Histopathologic analysis of gastric cancer specimens may help identify which patients are more likely to develop recurrent disease. Downregulation of immunosuppressive proteins such as PD-L1 and IDO and MSI suggest more aggressive tumor biology. Knowledge of tumor protein expression profiles could be used to tailor adjuvant therapy to improve long-term oncologic outcomes.

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Erratum: Abstracts Not Presented at SSO 70th Annual Cancer Symposium

PT170— Potential Utility of Cysteine Dioxygenase 1 Gene Promoter Methylation as a Marker of Tumor Diagnosis in Pancreatic Adenocarcinoma N. Nishizawa, K. Yamashita, S. Ishii, T. Tanaka, K. Yokoi, R. Nishiyama, H. Katoh, T. Kaizu, Y. Kumamoto, M. Watanabe

PT171— When to Wait: The Impact of Time from Completion of Neoadjuvant Radiation to Pancreaticoduodenectomy K.A. Mirkin, C. Hollenbeak, J. Wong

PT172— Greater Lymph Node Retrieval and Lymph Node Ratio Does Not Impact Survival in Non-Functional Pancreatic Neuroendocrine Tumors K.A. Mirkin, C. Hollenbeak, J. Wong

PF416— Does Faster Time to Surgery Impact Survival in Resectable Gastric Cancer? A U.S. Population-Based Study K.A. Mirkin, C. Hollenbeak, J. Wong

PF241— Length of Stay and Discharge to Skilled Nursing Facility are the Strongest Modifiable Risk Factors for Readmission Following Pancreaticoduodenectomy. K.A. Mirkin, N. Gusani, C. Hollenbeak, A.B. Cooper

PF231— Radioembolization for Hepatocellular Carcinoma: A Nation-wide 10-Year Experience of 1,222 Cases S. Tohme, A. Chidi, A. Tsung