Presentation #5 | Clinical Science | Surgical Oncology

## THE 70-GENE SIGNATURE TEST AS A PROGNOSTIC AND PREDICTIVE BIOMARKER IN PATIENTS WITH INVASIVE LOBULAR CARCINOMA

J. Asher Jenkins, B.Sc.; Schelomo Marmor, PhD; Jane YC Hui, MD; Heather Beckwith, MD; Anne H. Blads, MD; David Potter, MD PhD; Todd M. Tuttle, MD

**Presenter:** J. Asher Jenkins BS University of Minnesota

**Background:** Genomic expression assays provide prognostic information and guide adjuvant chemotherapy decisions for patients with estrogen receptor (ER)-positive breast cancer. Few studies have evaluated the utility of such assays for invasive lobular cancer (ILC).

**Objective:** The objectives of this study are to evaluate the 70-gene signature test (ST) as a prognostic factor and as predictive tool for ILC in a national cancer database.

**Method:** We identified patients diagnosed with stage I-III ER-positive ILC from 2004-2016 using the National Cancer Database. All patients underwent 70-gene ST testing. We used Kaplan-Meier and Cox proportional hazard analyses to determine overall survival based on genomic risk classification. We also determined the benefit of adjuvant chemotherapy for patients with high genomic risk ILC based on 70-gene ST testing.

**Results:** We identified 2,719 patients with ILC who underwent 70-gene ST testing; 300 (11%) were classified as high genomic risk. Five-year survival rates were significantly worse for patients classified as high risk (83%) as compared with those classified as low risk (94%, $p<0.05$). In Cox models, high genomic risk was independently associated with a significantly increased hazard of death. In our Cox models of patients who were genomic high-risk, adjuvant chemotherapy was not significantly associated with improved overall survival.

**Conclusion:** In this large database study, we found that the genomic risk category determined by the 70-gene ST was significantly associated with survival outcomes for patients with ILC. However, the 70-gene ST was not useful in predicting the benefit of adjuvant chemotherapy for patients with high genomic risk.

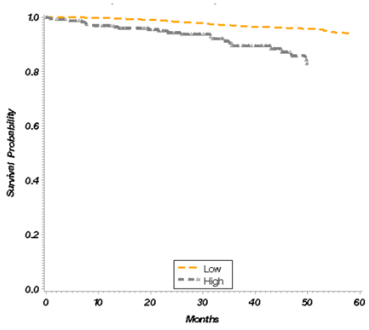



Figure 1: Kaplan-Meier Curve of Overall Survival of Patients with Invasive Lobular Carcinoma Classified as Low- or High-Risk by 70-gene ST ($p<0.05$).

Presentation #6 | Clinical Science | Surgical Oncology

## ONCOLOGIC OUTCOMES OF PATIENTS WITH LYMPH NODE POSITIVE MERKEL CELL CARCINOMA WITH UNKNOWN PRIMARY

Jane Yuet Ching Hui, MD, MS; Saranya Prathibha, MD; Christopher LaRocca, MD; Jacob Ankeny, MD; Evidio Domingo-Musibay, MD; Eric H. Jensen, MD; Todd M. Tuttle, MD, MS; Schelomo Marmor, PhD, MPH

**Presenter:** Saranya Prathibha MD University of Minnesota

**Background:** Merkel cell carcinoma (MCC) is a rare cutaneous neoplasm that can occasionally present with an unknown primary (MCCUP).

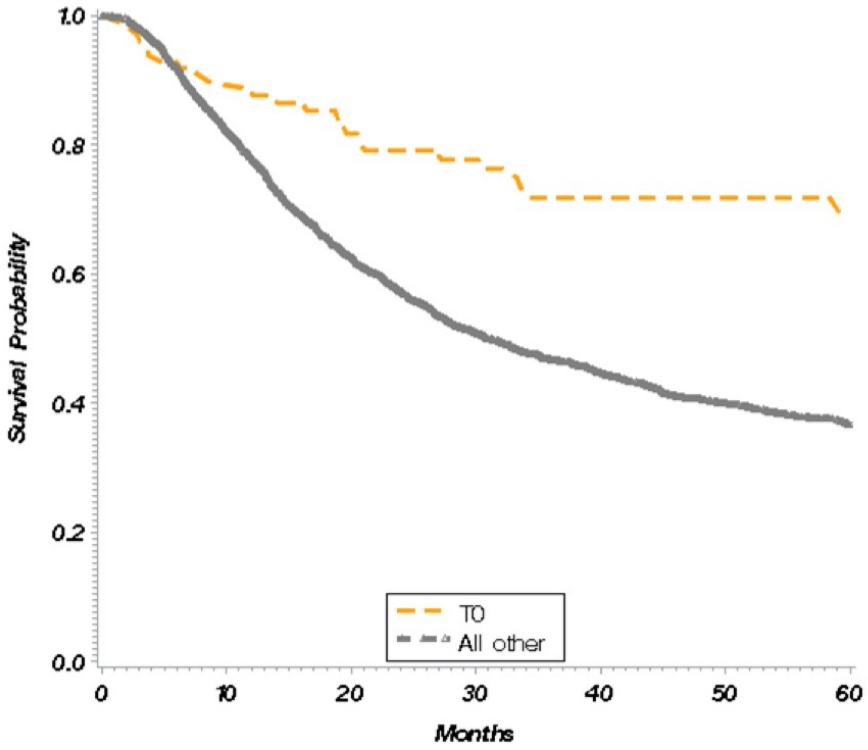
**Objective:** Our objective was to compare the survival rates of patients with MCCUP compared to those with known primaries, using a nationwide hospital-based dataset.

**Method:** We identified 3077 adults with lymph node positive MCC using 2004 to 2016 data from the National Cancer Database. Patients with known and unknown primary tumors were compared using Pearson's Chi-Squared test and logistic regression model. Overall survival was analyzed with the Kaplan-Meier method and a Cox proportional hazard model that included age, gender, race, year of diagnosis, tumor grade, lymph nodes evaluated, lymph node status, Charlson comorbidity score, academic or community treatment location.

**Results:** The majority of patients with lymph node positive MCC were older than 65 (79%), female (68%), and white (91%). The majority (92%) also had little to no comorbidities, with a Charlson comorbidity index of 0 or 1. Of these, 126 (4%) had MCCUP. Significant factors associated with unknown primary included younger age (OR 1.86, 95% CI 1.21 to 2.86) and more recent year of diagnosis (OR 2.5, 95% CI 1.5 to 4.2)). The 5-year overall survival rate for lymph node positive MCCUP patients was 69%, significantly higher than those with a known primary (37%, $p \leq 0.0001$, see Figure 1). This survival difference was not seen when MCCUP patients also had distant metastatic disease ($p=0.89$).

**Conclusion:** Lymph node positive MCCUP is an uncommon cancer presentation that portends an improved 5-year overall survival when compared to patients who present with lymph node positive MCC with an identifiable primary tumor. Further evaluation of these patients is warranted to determine the drivers of this phenomenon.

Figure 1. Kaplan Meier survival curve for patients with Merkel cell carcinoma of unknown primary (T0) versus known primary (T1 to T4, "all other" below) from the National Cancer Database (2004- 2016).



Presentation #7 | Clinical Science | Surgical Oncology

## DEFINING THE ROLE OF ADJUVANT THERAPY FOLLOWING INADEQUATE SURGERY FOR EARLY-STAGE GALLBLADDER CANCER

Jensen EH, Ankeny, JS, LaRocca CJ, Hui JYC, Tuttle TM, Akers M, Marmor S

**Presenter:** McKenzie Akers MD University of Minnesota

**Background:** Despite current guidelines, many patients do not undergo liver resection and portal lymph node (LN) dissection following cholecystectomy for T1b-T3 gallbladder cancer (GBC).

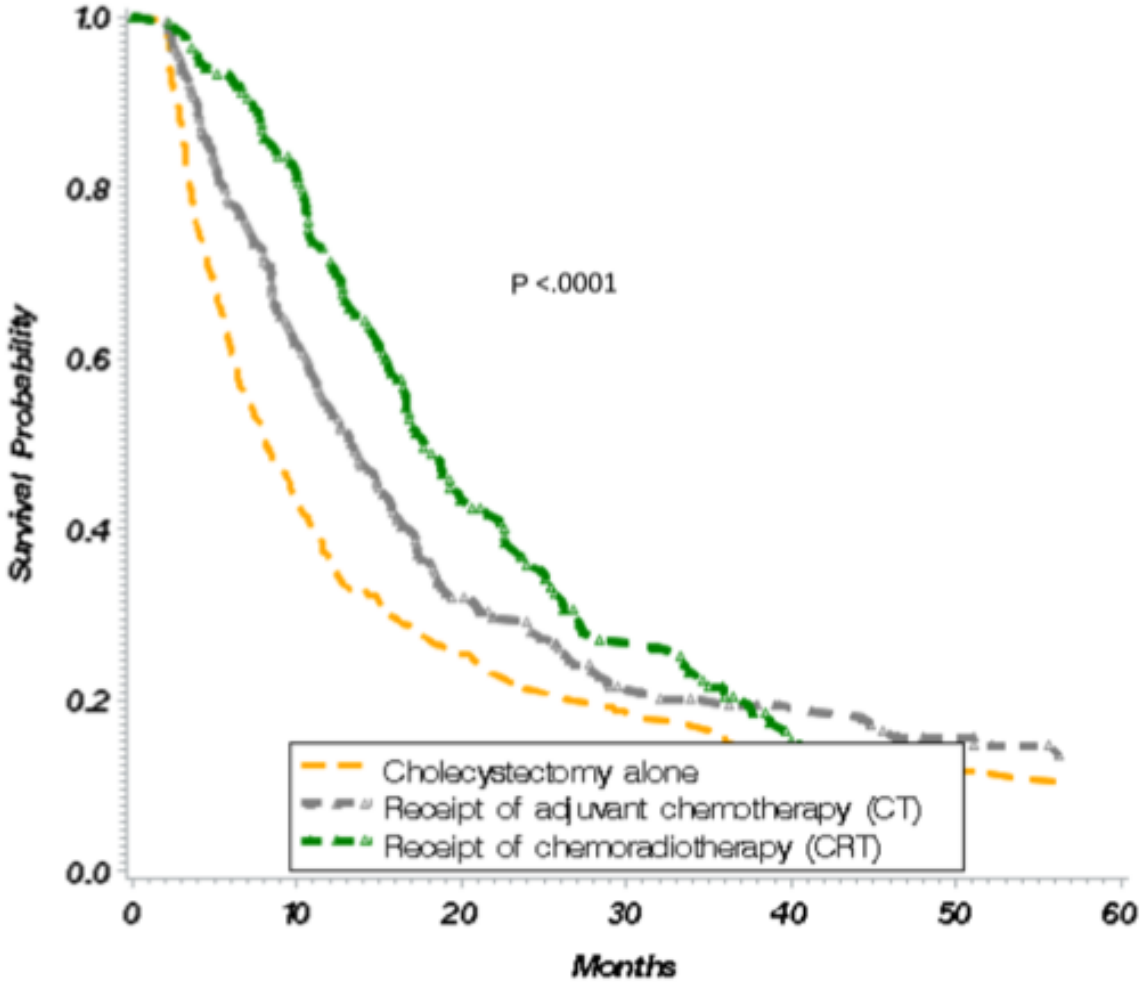
**Objective:** The purpose of this study is to evaluate the role of adjuvant therapy after "inadequate surgery" (cholecystectomy alone) for early stage GBC (T1b-T3).

**Method:** We used the National Cancer Database to identify individuals who had surgery for T1b-T3 GBC between 2004-2016. Patients were stratified by receipt of cholecystectomy alone, and receipt of adjuvant chemotherapy (CT) or chemoradiotherapy (CRT). Survival was evaluated using Kaplan-Meier and Cox proportional hazard models.

**Results:** We identified 3,151 patients who underwent surgery for T1b-T3 GBC, with 2115 (67%) receiving cholecystectomy alone. Median age was 70 (Standard Deviation (SD); 12.21), most were Non-Hispanic White (64%) and female (72%) while 31% had a Charlson comorbidity index score>1. The strongest predictors of receipt of inadequate surgery were older age (>65 years old), more recent year (2009-2016), margin positive, no LN examined ($p<0.05$). Following cholecystectomy, 1,278 (62%) had no further treatment, while 465 (26%) had CT and 317 (15%) had CRT. For patients with T1b and T2 tumors, CRT was significantly associated with improved survival over cholecystectomy alone (50 months versus 34 months, $p<0.05$). For T3 tumors, adjuvant CT and CRT were also significantly associated with improved survival compared to cholecystectomy alone (8 months versus 13 months versus 17 months, $p<0.001$). For all T-stages, CRT was significantly associated with improved survival for LN positive or margin positive disease over surgery alone. For all T stages, CRT was superior to CT after inadequate surgery ($p<0.001$).

**Conclusion:** Adjuvant CRT is associated with improved survival after cholecystectomy alone for T1b/T2 and T3 GBC. Although we continue to recommend liver resection and portal LN dissection for medically fit patients, those who do not undergo radical resection should be offered CRT in order to optimize survival outcomes.

***Overall survival for T3 GBC***




*Cholecystectomy alone median survival: 8 months*
*CT median survival: 13 months*
*CRT median survival: 17 months*

Presentation #8 | Clinical Science | Surgical Oncology

## DOWNSTAGING AFTER TOTAL NEOADJUVANT THERAPY VS CONVENTIONAL CHEMORADIOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER

Matthew Wheelwright, Joy Chen, Qi Wang, Robert Madoff

**Presenter:** Matthew Wheelwright MD University of Minnesota

**Background:** Total neoadjuvant therapy (TNT) is increasingly used to treat locally advanced rectal cancer. Compared with conventional neoadjuvant chemoradiotherapy (CRT), patients who receive TNT experience higher rates of pathologic complete response; however, mortality remains unchanged. Patients with partial response to TNT are at higher risk of local and distant recurrences. Little is known about the benefit of TNT over CRT in partial responders.

**Objective:** Our goal is to compare downstaging and complete response after TNT versus CRT for locally advanced rectal cancer. We hypothesize that TNT will lead to increased downstaging compared to CRT.

**Method:** A retrospective review of patients aged 18 and over with locally advanced rectal cancer treated at the University of Minnesota Medical Center between January 2010 and October 2019 was performed. Demographic and clinical variables were collected including chemotherapy regimens, operative data and final pathology. Magnitude of T and N downstaging was quantified. TNT cases and CRT controls were matched 1:2 based on age +/- 10, gender and T+N stage. Statistical analysis utilized t-test for comparison of continuous variables and Chi-square or Fisher's exact test for categorical variables.

**Results:** A total of 147 patients were included. Of these, 23 patients who received TNT were matched with 46 patients who received CRT. There were no differences in tumor size, tumor location or serum CEA between the 2 groups. Watch-and-Wait therapy was offered to 7 (32%) of patients who received TNT, versus none of the patients who received CRT. A trend towards an increased rate of complete response was seen with TNT compared to CRT (43% vs 24%, p=0.10). No significant difference was seen in the magnitude of T or N downstaging (delta-T, p=0.47; delta-N, p=0.71).

**Conclusion:** While the benefit of TNT seems to be an increased complete response in other studies, our institutional experience suggests that there is no significant difference in T or N downstaging. The mechanism linking tumor response to potential reduction in rates of local recurrence and distant metastasis remains to be defined. Future investigations to better understand pathologic or radiographic tumor response might help predict which patients will respond to TNT and potentially benefit from nonoperative therapy.

| T stage | | | |
|---|---|---|---|
| **Downstaging** | **TNT (N=23)** | **CRT (N=46)** | p=0.47 |
| No change | 9 (39%) | 14 (30%) | |
| -1 | 3 (13%) | 13 (28%) | |
| -2 | 1 (4%) | 3 (7%) | |
| -3 | 8 (35%) | 15 (33%) | |
| -4 | 2 (9%) | 1 (2%) | |

| N stage | | | |
|---|---|---|---|
| **Downstaging** | **TNT (N=23)** | **CRT (N=46)** | p=0.71 |
| No change | 8 (35%) | 11 (24%) | |
| -1 | 7 (30%) | 19 (41%) | |
| -2 | 8 (35%) | 13 (28%) | |
| -3 | 0 | 0 | |
| +1 | 0 | 2 (4%) | |

| | **TNT (N=23)** | **CRT (N=46)** | p=0.10 |
|---|---|---|---|
| pCR or cCR | 10 (43%) | 11 (24%) | |
| Incomplete response | 13 (57%) | 35 (76%) | |

Presentation #9 | Clinical Science | General Surgery

## DISPARITIES IN THE SURGICAL MANAGEMENT OF EARLY STAGE RECTAL CANCER

Luke A. Martin, Sonja M. Boatman, Sruthi Shankar, Ann C. Lowry, Christine C. Jensen

**Presenter:** Sonja Boatman MD University of Minnesota

**Background:** Identification of factors that contribute to appropriate versus inappropriate surgical treatment presents an important opportunity to improve outcomes of rectal cancer treatment. If differences in patient characteristics are apparent between these groups, this could represent a crucial opportunity to improve the quality of care for patients with rectal cancer.

**Objective:** We sought to identify factors associated with inappropriate surgical management of early rectal cancer.

**Method:** The NCDB (2006-2016) was retrospectively reviewed for rectal neoplasms (n=245,115). Patients were grouped based on procedure: TME, appropriate (apLE) and inappropriate local excision (inLE). LE qualified as inappropriate if pathology showed LVI, N+, or ≥T2 without subsequent TME.

**Results:** Univariate analyses showed associations: inLE vs TME with older age (71 vs 63 yrs, $p < 0.01$), female sex (43.5 vs 38.6%, $p < 0.01$), more comorbidities ($p < 0.01$), government insurance (68.6 vs 49.5%, $p < 0.01$); inLE vs apLE with older age (71 vs 66 yrs, $p < 0.01$), more comorbidities ($p < 0.01$), governmental insurance (68.6 vs 55.5%, $p < 0.01$), negatively with higher socioeconomic status (SES) (29.5 vs 35.1%, $p < 0.01$). Multivariate logistic regressions showed: inLE associated with older age (vs TME, OR 1.1, $p < 0.01$; vs apLE, OR 1.03, $p < 0.01$), female sex (vs TME, OR 1.15, $p < 0.01$), comorbidities (vs TME, OR 1.5, $p < 0.01$; vs apLE, OR 1.48, $p < 0.02$), black race (vs TME, OR 1.19, $p = 0.05$), treatment at academic centers (vs TME, OR 1.33, $p < 0.01$; vs apLE, OR 1.4, $p < 0.01$), higher SES (vs apLE, OR 0.82, $p = 0.05$).

**Conclusion:** We identified patient-level factors, including age, race, gender and SES, associated with nonstandard rectal cancer surgery that offer insights to improve outcomes of rectal cancer treatment.