

# Moderated Poster Session VI: Oncology

## Friday, October 8, 11:00 a.m. — noon

### P85

#### Temporal Stage and Grade Migration in Surgically-Treated Patients with Upper Urinary Tract Transitional Cell Carcinoma

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**Introduction and Objective:** Few population-based studies addressed contemporary cancer-control outcomes in patients with upper urinary tract transitional cell carcinoma (UT-TCC). We examined the temporal trends in stage and grade at presentation, as well as cancer-specific mortality (CSM) rates, in surgically-treated patients with UT-TCC.

**Materials and Methods:** Within the SEER database, we identified 4915 patients diagnosed with UT-TCC between 1983 and 2004, who underwent either a nephroureterectomy (NU) or a segmental ureterectomy (SU). Patients were divided into 4 groups according to the year of surgery quartiles. The chi-square test and the chi-square trend test were respectively used for comparison of proportions and trends over time. Kaplan-Meier plots were used to graphically depict CSM rates. Multivariable Cox regression models tested the effect of the year of surgery quartiles on CSM. Covariates consisted of SEER stage and region, tumor grade, age, race, primary tumor site.

**Results:** Of 4915 assessable patients, 1316, 1328, 1146, and 1125 were respectively treated between 1983-1998, 1989-1994, 1995-1999 and 2000-2004. Of those, 4430 had a NU and 485 had a SU. The rates of non-localized stage and of grade III/IV disease at surgery increased respectively from 49.8 to 69.5% ( $p < 0.001$ ) and 45.7 to 70.2% ( $p < 0.001$ ) during the study period. CSM rates at four years after surgery reflected the temporal stage and grade differences and also increased from 18.2 to 23.9% ( $p < 0.05$ ) between 1983-1988 and 2000-2004. In multivariable analyses, no differences in CSM rates were observed for the four examined time periods (HR: 1.0;  $p = 0.9$ ).

**Conclusion:** We report an important stage migration and grade shift at NU or SU towards more aggressive disease between 1983 and 2004. These trends indicate that the majority of patients who are treated with definitive surgery for UT-TCC harbor poor-risk disease.

### P86

#### An Assessment of the Prognostic Significance of Tumor Grade in Patients with Upper Urinary Tract Transitional Cell Carcinoma: a Population-Based Study

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**Introduction and Objective:** Tumor grade is considered as a reliable predictor of T stage in upper urinary tract transitional cell carcinoma (UT-TCC). We examined the correlation between tumor grade and pathological T stage, as well as the prognostic impact of tumor grade on cancer specific mortality (CSM) in a large population-based cohort of UT-TCC patients.

**Materials and Methods:** Within the SEER database, we identified patients diagnosed with UT-TCC, who underwent either a nephroureterectomy

or a segmental ureterectomy between 1988 and 2004, and for whom tumor stage and grade were available. Univariable and multivariable models tested the ability of tumor grade to predict pathologic stage as well as cancer-specific mortality (CSM). Covariates consisted of T-stage, primary tumor location (renal pelvis vs. ureter), gender, age.

**Results:** Of 2042 assessable patients, 6.2% had grade I vs. 36.6% grade II vs. 39.8% grade III vs. 17.4% grade IV tumors. The proportions of patients with grade III UT-TCC were 29.4 vs. 41.0 vs. 53.7 vs. 43.5% for respectively T1, T2, T3 and T4 tumors. Similarly, 9.9, 18.0, 26.7 and 20.7% of T1, T2, T3 and T4 patients had grade IV tumors. The 5-year CSM-free rates according to tumor grade were 95.0% for grade I vs. 89.0% for grade II vs. 75.3% for grade III vs. 72.9% for grade IV UT-TCC. Grade IV UT-TCC was 55.8% accurate in predicting advanced pathologic stage (T2-4) at surgery and 54.6% accurate in predicting CSM after surgery. Conversely, combined grades III and IV were 64.1 and 61.6% accurate.

**Conclusion:** High-grade UT-TCC, defined as grade either grade IV or grade III and IV combined, are not highly accurate predictors of T2 or higher stage, nor are they accurate predictors of CSM after surgery. In consequence, presence or absence of high grade UT-TCC should be used with caution in clinical decision-making.

### P87

#### Segmental Ureterectomy Can Safely Be Performed in Patients with Ureteral Upper Tract Transitional Cell Carcinoma

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**Introduction and Objective:** The efficacy of segmental ureterectomy (SU) relative to nephroureterectomy with bladder cuff removal (NUC) or without bladder cuff removal (NU) was examined in patients with ureteral transitional cell carcinoma (U-TCC). We compared the cancer-specific mortality (CSM) rates associated with the three different approaches in a large population-based cohort of patients with exclusive U-TCC. **Materials and Methods:** Our analyses relied on 805 patients with T1-T4 N0M0 U-TCC from a large multi-regional database. Survival plots and Cox regression models addressed the effect of SU vs. NU vs. NUC on CSM. Covariates consisted of pathological stage and grade, age, race, geographic location, gender, as well as of the year of surgery.

**Results:** The median follow-up of censored cases was 40 months. Overall, 207 (25.7%) patients underwent a SU vs. 498 (61.9%) NUC and 100 (12.4%) NU. At 5 years, CSM-free rates of SU vs. NUC vs. NU were respectively 86.5 vs. 82.6 vs. 83.3%, respectively (log rank test  $p = 0.5$ ). In stratified stage-specific and multivariable analyses, none of the three examined surgical approaches affected the rate of CSM.

**Conclusion:** In patients with U-TCC, NU or NUC offers no survival benefit relative to SU. In consequence, based on lesser invasiveness of SU, the latter can be safely offered when tumors can be removed with this approach, including pT3 tumors.

**P88****The Impact of Tumor Stage and Nodal Metastases on Cancer Specific Mortality in Patients with Upper Urinary Tract Transitional Cell Carcinoma: Results from a Population-Based Study**

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**Introduction and Objective:** The TNM staging system represents the cornerstone for classifying patients with upper urinary tract transitional cell carcinoma (UT-TCC). We tested the prognostic impact of T and N stage on cancer specific mortality (CSM) in a large population-based cohort of UT-TCC patients.

**Materials and Methods:** Our analyses relied on 2299 patients who were treated with nephroureterectomy or segmental ureterectomy for UT-TCC within 9 Surveillance, Epidemiology, and End Results (SEER) registries between 1988 to 2004. CSM rates after surgery were graphically explored using Kaplan-Meier plots in the overall population, as well as after stratification of patients according to primary tumor location (renal pelvis vs. ureter). Univariable and multivariable Cox regression models tested the effect of T and N stage on cancer-specific mortality (CSM).

**Results:** Statistically significant differences in CSM rates were recorded between all T stages ( $p < 0.001$ ), except for T3 and T4 tumors ( $p = 0.3$ ). Moreover, the CSM-free rates in patients with nodal metastases (N1-3) were significantly worse relative to TanyN0 patients ( $p < 0.001$ ). In patients with renal pelvic tumors ( $n = 1424$ ), no statistically significant differences in CSM rates were recorded between patients with T1 and T2 UT-TCC ( $p = 0.2$ ) and between patients with T3 and T4 UT-TCC ( $p = 0.5$ ). In patients with ureteral tumors ( $n = 875$ ), statistically significant differences in the CSM rates were observed between all T stages ( $p < 0.001$ ), except for patients with T3 and T4 tumors ( $p = 0.9$ ). Moreover, patients with TanyN1-3 ureteral tumors showed similar CSM rates relative to T3-4N0 patients ( $p = 0.3$ ). In multivariable Cox regression models predicting CSM rates after surgery, both T and N stage achieved independent predictor status ( $p < 0.05$ ).

**Conclusion:** The TNM staging system represents an effective prognostic stratification tool for patients with UT-TCC. The detrimental effect of N1-3 stages implies the need for better staging and for salvage treatment in this patients category.

**P89****Patients with Renal Pelvis Upper Tract Transitional Cell Carcinoma Have Significantly Worse Cancer-Specific Survival than Patients with Ureteral Primaries**

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**Introduction and Objective:** The biologic effect of ureteral vs. renal pelvis location of upper tract transitional cell carcinoma (TCC) is unknown. We assessed the impact of tumor location (ureteral vs. renal pelvis) on the cancer-specific mortality (CSM) in a large, population-based dataset of surgically treated upper tract TCC patients.

**Materials and Methods:** Our study population consisted of 5029 patients with upper tract TCC from a large population-based cohort. The effect of location of upper tract TCC (ureteral vs. renal pelvis) on CSM was tested in univariable and multivariable Cox regression models. Covariates consisted of age, stage (gender, region of residency, race, year of surgery, grade, and type of surgery (segmental vs. radical with bladder cuff vs. radical without bladder cuff)).

**Results:** The median follow up of censored patients was 53 months. In multivariable analysis, patients with upper tract TCC of the ureter had a 19% lower rate of CSM than patients with a primary in the renal pelvis (adjusted hazard ratio [HR] 0.81;  $p = 0.007$ ). In absolute terms, at 5 years

after surgery patients with ureteral TCC had a 17.8% CSM rate vs. 25.8% CSM rate for patients with upper tract TCC of the renal pelvis.

**Conclusion:** Our report is the first to suggest a difference in the CSM rates between patients with ureteral and renal pelvis TCC. A number of reasons may explain the more favorable prognosis of an ureteral primary tumor in this patient group. Unfortunately, the current database does not allow identifying these. Nonetheless, our findings suggest that the outcome of patients with renal pelvis upper tract TCC may be undermined by diagnoses and treatment delays.

**P90****A Population-Based Assessment of Perioperative Mortality After Nephroureterectomy for Upper-Tract Transitional Cell Carcinoma**

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**Introduction and Objective:** Nephroureterectomy (NU) represents the standard surgical treatment for patients with non-metastatic upper-tract transitional cell carcinoma (UT-TCC). Currently, the perioperative mortality (POM) rate after NU is unknown. To address this limitation, we tested several predictors of POM after NU and attempted to devise a model for individual predictions of POM.

**Materials and Methods:** We identified 2824 patients who were diagnosed with UT-TCC and were treated with NU between 1988 and 2004. We quantified 90-day POM rates according to age, gender, region, race, stage, nodal status, grade, type of surgery (NU with or without bladder cuff removal), primary tumor site (renal pelvis vs. ureter) and year of treatment. Based on a development sample of 1223 patients from four series of database, we devised a logistic regression nomogram predicting 90-day POM. External validation was then performed on the remaining of 1601 patients from five other series of database.

**Results:** At 90 days, the overall POM rate was 4.7%. Age represented a statistically significant and independent predictor of 90-day POM. The use of age and T stage resulted in the most accurate validation of the model (70.7%) for prediction of the individual probability of 90-day POM after NU. Model calibration revealed excellent correlation between predicted and observed probability of POM after NU.

**Conclusion:** This is the first large-scale analysis of POM after NU and our model represents the first standardized and validated tool for POM risk prediction. In consequence, we suggest the use of the current model in individual decision-making and in informed consent considerations.

**P91****Gender-Related Differences in Patients with Upper Urinary Tract Transitional Cell Carcinoma: Results from the Surveillance, Epidemiology and End Results Database**

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**Introduction and Objective:** Few studies addressed the presence or absence of gender-related differences in patients with upper urinary tract transitional cell carcinoma (UT-TCC). Therefore, we examined the association between gender and patterns of disease at surgery and we tested the prognostic impact of gender in a large population-based cohort of patients diagnosed with UT-TCC.

**Materials and Methods:** Our analyses relied on 3138 UT-TCC patients, who underwent either a nephroureterectomy or a segmental ureterectomy between 1988 to 2004, within 9 Surveillance, Epidemiology and End Results (SEER) registries. Kaplan-Meier plots graphically explored

cancer-specific mortality (CSM) rates in the overall population and after stratification according to gender. Univariable and multivariable Cox regression models tested the effect of gender on CSM. Covariates consisted of T stage, N stage, tumor grade, age, primary tumor location, type of surgery, race, year of surgery, and SEER regions.

**Results:** Females (n=1251) were more likely to have renal pelvic tumors (65.3 vs. 58.1%) ( $p < 0.001$ ) and high T stage (52.6 vs. 46.2% of T3-4 tumors) ( $p = 0.005$ ). Kaplan-Meier plots showed a statistically significant worse CSM survival free rate in females (HR: 1.29;  $p = 0.003$ ). However, in multivariable analyses addressing CSM rates after surgery, gender failed to achieve the independent predictor status (HR: 0.96; 0.8).

**Conclusion:** Females are more likely to present with advanced tumor stage at surgery. However, gender is not an independent predictor of CSM after surgery in patients with UT-TCC.

## P92

### Significance of Positive Bladder Cuff in Nephroureterectomy Specimen in Patients with Upper Urinary Tract Urothelial Tumors

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**Introduction and Objective:** To study impact of malignant bladder cuff in nephroureterectomy specimen in patients with upper urinary tract tumors-urothelial carcinoma (UUT-UC).

**Materials and Methods:** Records of 168 patients treated surgically for localized UUT-UC were reviewed retrospectively. We revised pathological results in nephroureterectomy specimens for positive bladder cuff that was defined as the presence of urothelial carcinoma in the excised cuff. Univariate and multivariate analyses using logistic regression and Cox proportional hazards model were applied.

**Results:** Positive bladder cuff was diagnosed in 6 patients (4.2%). Histopathology revealed CIS in 1, T1 in 4 and T2 in 1 patient. There was no significant correlation identified between patient age, past history or associated bladder tumors as well as UUT-UC grade, stage or multicentricity with post-operative malignant bladder cuff. On the other hand, female gender, left-sided tumors, and associated carcinoma in-situ (CIS) were significantly associated with malignant bladder cuff by univariate analysis ( $p = 0.002$ , 0.01, 0.004, respectively). On multivariate analysis only CIS and female gender sustained their significance. Malignant bladder cuff was not significantly associated with overall subsequent bladder tumor recurrence ( $p = 0.3$ ), nevertheless it was a significant predictor for subsequent development of invasive bladder tumor ( $p < 0.02$ ).

**Conclusion:** Patients with positive bladder cuff in nephroureterectomy specimen are to be anticipated in female patients and those with CIS, Strict follow up is highly indicated as they are more prone to develop invasive bladder cancer.

## P93

### Intravesical Recurrence Post-Nephroureterectomy for Upper Urinary Tract-Urothelial Carcinoma, Analysis of Risk Factors

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**Introduction and Objective:** To study risk factors of developing bladder tumor post nephroureterectomy (NU) for upper urinary tract- urothelial carcinoma (UUT-UC).

**Materials and Methods:** We analyzed 168 patients who were treated for clinically localized UUT-UC between 1983 and 2006, risk factors for developing recurrent bladder tumor were judged utilizing univariate and multivariate analyses using logistic regression and cox proportional hazards model.

**Results:** Recurrent bladder tumors occurred in 78 patients (46%). The mean time for recurrence after NU was 20 months  $\pm$  24 (range 2-114). History of prior superficial bladder tumors were found only in 15 (19%) of those patients. Sixteen patients underwent radical cystectomy after 21 months  $\pm$  31 (range 2-216). There was no significant impact identified between patient age, sex, past history of bladder tumor, presence

of concomitant bladder tumor at diagnosis, as well as UUT-UC site, grade, stage, multicentricity, associated CIS or post-operative malignant bladder cuff with overall intravesical recurrence.

**Conclusion:** Incidence of overall subsequent bladder tumor post nephroureterectomy for UUT-UC is high without definite predictor risk factors.

## P94

### Development and External Validation of a Highly Accurate Nomogram for the Prediction of Cancer-Specific Mortality After Nephroureterectomy for Upper Tract Transitional Cell Carcinoma

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**Introduction and Objective:** Nephroureterectomy (NU) represents the standard surgical treatment for patients with upper-tract transitional cell carcinoma (UT-TCC). Currently, there are no clinical tools to predict individual risk of death of disease after surgery. Our objectives were to identify risk factors related to cancer-specific mortality in patients treated with NU for UT-TCC and to develop a model that predicts individual risk of cancer-specific mortality after NU.

**Materials and Methods:** We identified 2824 patients who were diagnosed with UT-TCC and were treated with NU within a multi-regional database between 1988 and 2004. Development (n=1479) and external validation (n=1345) of multivariable Cox regression models predicting the individual probability of cancer-specific mortality after NU were used to develop the nomogram. Predictors consisted of age, stage, nodal status, gender, grade, race, type of surgery (NU with or without bladder cuff removal) and location of tumor (renal pelvis vs. ureter).

**Results:** Median follow-up in patients who did not die of UT-TCC-specific causes was 3.7 years and 3.5 years in the development and validation cohorts, respectively. The freedom from cancer-specific mortality rates in the nomogram development cohort were 85.8% [95% confidence intervals (CI)=83.9-87.8] at 2 years after NU and 78.7% (95% CI=76.3-81.3) at 5 years after NU. In multivariable analyses, age, stage, nodal status and grade achieved independent predictor status. In the external validation cohort the nomogram predictions were 77.4% accurate at 2 years, 78.2% accurate at 3 years, 81.1% accurate at 5 years, and 82.6% accurate at 7 years.

**Conclusion:** Age, stage, nodal status and grade are important determinants of cancer-specific mortality after NU. Our model provides individual probabilities of cancer-specific mortality after NU, and its use should be highly encouraged during informed consent prior to planned NU.

## P95

### Prognostic Value of Insulin-Like Growth Factor-I and Binding Proteins 2 and 3 in Patients Treated with Radical Prostatectomy

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**Introduction and Objective:** Several studies have examined the relationship between insulin-like growth factor I (IGF-I), and its binding proteins 2 (IGFBP-2) and 3 (IGFBP-3) with prostate cancer risk. A meta-analysis concluded that high IGF-I levels are associated with an increased risk, while IGFBP-2 and IGFBP-3 are not. Data about IGF family members and cancer recurrence is more controversial. Shariat showed that IGFBP-2 and IGFBP-3 are both associated with disease progression. However, Yu suggested that IGF-I, IGFBP-2 and IGFBP-3 had no predictive value in the prognosis of prostate cancer. Hong concluded in the same direction. Based on these conflicting results, we propose to study the levels of different members of the IGF family as predictors of clinical outcome in prostate cancer.

**Materials and Methods:** Preoperative plasma levels of IGF-I, IGFBP-2 and IGFBP-3 were measured in 131 patients who were diagnosed with clinically localized prostate cancer and underwent radical prostatectomy between 1999 and 2002. Of these, 11 had received neoadjuvant

hormonotherapy and were excluded from our analysis because of the reported role of IGFBP-2 as an androgen-dependent predictor of prostate cancer. Clinical data was collected retrospectively and a Student t-test was done for comparison of categorical variables while a Cox regression model was performed for multivariate analysis.

**Results:** Average age at surgery was 63.6 years, mean preoperative PSA was  $11.75 \pm 14.52$  ng/mL and median follow-up was 7.8 years. 37 patients experienced PSA failure. Average levels of IGF-I, IGFBP-2 and IGFBP-3 were  $140.5 \pm 36.2$  ng/mL,  $307.8 \pm 185$  ng/mL and  $2.023 \pm 0.554$  mg/mL respectively. Plasma IGF-I levels did not predict risk of biochemical recurrence ( $p=0.57$ ) nor did IGFBP-2 ( $p=0.35$ ) or IGFBP-3 ( $p=0.53$ ). They also did not correlate with clinical stage, PSA level or Gleason grade. We did notice a significant correlation between all three markers with the surgical margins status, but when controlling for other known prognostic factors, the correlation was no more significant. Furthermore, there was no correlation with extracapsular extension, seminal vesicle involvement or lymph node status, which suggested that the markers were not useful predictors of organ-confined disease.

**Conclusion:** Despite much interest in IGF family members association to prostate cancer, our study suggests that IGF-I, IGFBP-2 and IGFBP-3 might not be helpful independent predictors of recurrence or progression for patients with clinically localized prostate cancer.

## P96

### Cesium-131 vs. Iodine-125 Implants for Prostate Cancer: Evaluation of Early PSA Response

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**Introduction and Objective:** The isotope Cesium-131 (Cs-131) has recently been introduced for use in prostate brachytherapy, although due to its novelty, outcome data is lacking. The present study compares initial prostate specific antigen (PSA) outcomes in men undergoing Cs-131 prostate brachytherapy with men who underwent prostate brachytherapy with the isotope Iodine-125 (I-125).

**Materials and Methods:** Our retrospective study compares initial 3-6 month post-procedure PSA results in 100 patients undergoing I-125 prostate brachytherapy and the first 100 patients undergoing Cs-131 prostate brachytherapy at a single institution. Comparisons included the total cohort as well as low and intermediate risk patients.

**Results:** Mean pre-treatment PSA was 6.9 in the I-125 cohort, and 6.9 in the Cs-131 cohort. Mean initial PSA obtained after treatment was 0.9 (range  $<0.1 - 4.6$ ) in the I-125 cohort and 1.2 (range  $<0.1 - 23.5$ ) in the Cs-131 patients. For low risk patients, mean pre-treatment PSA was  $5.8 \pm 1.9$  in the I-125 cohort, and  $5.1 \pm 1.9$  in the Cs-131 cohort ( $p=0.06$ ). Initial mean PSA after the procedure for low risk patients was  $1.2 \pm 0.9$  (range  $<0.1 - 4.6$ ) in the I-125 group and  $1.0 \pm 0.7$  (range  $<0.1 - 2.9$ ) in the Cs-131 patients ( $p=0.37$ ). For intermediate risk patients, mean pre-treatment PSA was  $7.3 \pm 3.8$  in the I-125 cohort, and  $7.3 \pm 2.5$  in the Cs-131 cohort ( $p=0.98$ ). Mean initial PSA after the procedure in intermediate risk patients was  $1.5 \pm 1.1$  (range  $<0.1 - 2.9$ ) in the I-125 group and  $1.2 \pm 0.8$  (range  $<0.1 - 4.6$ ) in the Cs-131 patients ( $p=0.52$ ). No significant difference was found in the mean change between pre and post treatment PSA in the I-125 and Cs-131 patients when stratified by low and intermediate risk patients. There was no statistically significant difference in 3-month PSA levels between Cs-131 and I-125 for any of the treatment groups.

**Conclusion:** Initial post-treatment PSA levels obtained 3-6 months after the procedure were similar in men undergoing prostate brachytherapy with either Cs-131 or I-125. The present study serves as a guide for practitioners who are beginning to incorporate Cs-131 into their prostate brachytherapy program. This study can assist these practitioners in counseling their patients undergoing Cs-131 as to what to expect in terms of initial PSA outcomes. Obviously, long term data are needed to document cancer control achieved with Cs-131.

## P97

### Treatment and Outcomes of Bladder Cancer Following Solid Organ Transplantation

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**Introduction and Objective:** Optimal management strategies and clinical outcomes of transitional cell carcinoma (TCC) in transplant recipients are not well-defined. We present our single institution experience managing patients with bladder cancer following liver and renal transplantation.

**Materials and Methods:** We retrospectively reviewed the University of Pittsburgh Medical Center's transplant database to identify patients diagnosed with bladder cancer following solid organ transplantation between January 1992 and December 2007. Demographic information, immunosuppressive regimens, pathologic findings, and oncologic outcomes were reviewed.

**Results:** Of the 2925 renal and 2761 liver transplant recipients in our cohort, we identified eight patients following kidney transplant and three patients following liver transplant ( $n=11$ , 0.2%) diagnosed with bladder cancer at a mean duration of  $39 \pm 24$  months (range 3.5-76 months). Maintenance immunotherapy protocols included tacrolimus + prednisone and tacrolimus + mycophenolate mofetil + prednisone in 82% and 18% of patients respectively. There were no deleterious effects on graft survival following urologic intervention. Of these eleven patients (100% male, mean age of  $67 \pm 12$  years (range 44-82 years)), 10 presented with gross hematuria, and 1 was diagnosed incidentally by imaging. Two patients with low grade T1 TCC were managed by transurethral resection (TURBT). Three patients with CIS and one patient with T1 TCC were treated by TURBT and adjuvant intravesical bacille Calmette-Guerin (BCG) immunotherapy, and to date all four are alive and free of recurrence at a mean follow-up of  $68 \pm 51$  (36-144) months. One patient with T1 high grade TCC and a history of bilateral cutaneous ureterostomies underwent radical cystectomy and ureteroureterostomy and remains disease free with a follow-up of 98 months. Muscle invasive transitional cell carcinoma was diagnosed in four patients at a median of 3.2 years following transplantation. Two patients underwent uncomplicated radical cystectomy with urinary diversion and are recurrence free with a mean follow-up of 32 months. Ileal loop urinary conduit and palliative radiation were performed in one patient with un-resectable disease. One patient received palliative XRT and died of metastatic bladder cancer 12 months following treatment.

**Conclusion:** Although diagnosis of bladder cancer is uncommon following renal and liver transplantation, it can be successfully managed with standard urologic methods. We report encouraging oncologic outcomes in eleven patients undergoing definitive therapy without compromising allograft function. The use of intravesical BCG is possible in select immunosuppressed patients with CIS or non-muscle invasive disease. Aggressive extirpative surgery and orthotopic bladder substitution is technically feasible and should be considered in transplant recipients with muscle invasive disease.

## P98

### Toremifene 80 mg Phase 3 Trial in Men on ADT Demonstrates Improvement in Gynecomastia Compared to Placebo

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**Introduction and Objective:** Use of androgen deprivation therapy (ADT) has increased over the last decade. The increase in ADT utilization is likely due to more aggressive approaches to prostate cancer (PCa) treatment and improvements in survival. An estrogen deficiency related side effect of ADT in men with prostate cancer is the development of gynecomastia characterized by breast tenderness. This occurs as a result of the change in the estradiol to testosterone ratio. We conducted a double blind, randomized, placebo controlled trial to determine if toremifene 80 mg could prevent fractures in men on ADT. Because of the prevalence of gynecomastia in men on ADT we also assessed the effect of toremifene on the

incidence and severity of breast enlargement and tenderness.

**Materials and Methods:** 1389 men with PCa were randomized to receive 80 mg toremifene or placebo orally for up to 24 months. All subjects were on ADT for  $\geq 6$  months, had a serum PSA  $\leq 4$  ng/mL, were  $\geq 70$  years of age or were at, or below, WHO thresholds for spine and hip (BMD). The primary endpoint was new morphometric vertebral fractures (MVF). Key secondary endpoints included gynecomastia, hot flashes and changes in BMD and lipids. The modified intent to treat population (446 toremifene subjects, 467 placebo subjects) was defined as all subjects who received at least 1 dose of study medication and had at least 1 on-study radiograph. Breast tenderness was assessed on physical examination by a physician and was scored as 1<sup>st</sup> or 2<sup>nd</sup> degree worsening, unchanged, or 1<sup>st</sup> or 2<sup>nd</sup> degree improved. Each assessment was performed at baseline and months 3, 6, 12, 18, and 24.

**Results:** At the end of study, a positive effect of toremifene on breast tenderness was observed with more subjects scored as improved and fewer subjects scored as worsened in the toremifene treated group compared to placebo using last observation carried forward (LOCF) ( $p=0.0034$ ). In subjects with documented use of bicalutamide (toremifene=99, placebo=101) there was an equally impressive improvement in breast tenderness using LOCF ( $p=0.0008$ ). Effects on breast glandular size were not statistically significant.

**Conclusion:** Toremifene demonstrated a positive effect on the treatment of gynecomastia in men on ADT. Toremifene is a selective estrogen receptor modulator with partial agonist and antagonist activity. Specifically, it is estrogenic in bone in the hypothalamus, and anti-estrogenic in the breast and prostate. These results suggest that treatment with a SERM can reduce breast tenderness in this patient population.

## P99

### Retroperitoneal Lymph Node Dissection of Post-Chemotherapy Residual Masses for Metastatic Germ Cell Testicular Cancer

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**Introduction and Objective:** Testicular cancer has become the model for a curable neoplasm. Selecting the best initial modality of treatment and integration of surgery and chemotherapy is critical to optimizing cure and minimizing morbidity. Nearly 80% of the patients can be cured by surgery removing the residual masses after the cisplatin-based chemotherapy. Of the patients requiring resections of residual disease after primary chemotherapy, approximately 90% will have either necrosis or teratoma in their resected specimens. However, there is continued controversy regarding the optimal treatment of patients with nodal metastases. While some investigators have reported relapse rates as low as 6.3% in patients with low-volume nodal disease managed expectantly, others have reported rates as high as 45%.

**Materials and Methods:** We reviewed the data from a single center and three surgeons over retroperitoneal lymph node dissection (RPLND) post chemotherapy treatment for germ cell testicular cancer. Our aim is to analyze the indications, clinical features, patterns of recurrence, surgical complications and final pathology diagnosis in residual masses. We have included patients with nonseminomatous histology, clinical stage II or III and residual masses post chemotherapy treatment.

**Results:** in a period between 1994 and 2008, we had 71 cases of RPLND post chemotherapy, including 2 cases called "desperation" procedures when the markers were still raising instead the use of appropriate systemic treatment. The majority of our cases were between 20 and 40 years old. The initial retroperitoneal masses were bigger than 5cm in 47% of patients. Almost 80% of patients received BEP chemotherapy from 2 to 4 cycles. After chemotherapy, 42% of patients had masses lesser than 3cm. The overall surgical complication rate was 39% but only 3 patients (4%) had grade IV complications and no one died. Only 22% of patients had viable cancer on retroperitoneum in final pathology report. The follow-up varied between 2 and 156 months with a mean of 47 months. After RPLND, we had only 2% of recurrence in retroperitoneum site and 8% of overall recurrence rate. Five patients (7%) died

due to testicular cancer, one is alive but with recurrent disease and 65 (91%) of patients are alive without disease.

**Conclusion:** The RPLND is safety and a well justified treatment option of germ cell residual masses after chemotherapy.

## P100

### Comparison of the Costs of Active Surveillance vs. Radical Prostatectomy

**Anthony T. Corcoran**, Ronald M. Benoit  
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**Introduction and Objective:** In part due to the concern of overtreatment in men with prostate cancer, watchful waiting with active surveillance (WWAS) has been increasingly utilized in men diagnosed with low risk prostate cancer. The present study investigates the difference in costs between men with low risk prostate cancer treated with up front radical prostatectomy (RP) and men who undergo WWAS.

**Materials and Methods:** A model was constructed using data from centers which have published their results in men who were followed with WWAS. Two WWAS arms were created, in which the follow up protocol and conversion rate to RP were varied. The two WWAS arms were further stratified by the length of time men were assumed to undergo serial prostate biopsies with the potential to convert to active treatment. The costs of WWAS in these scenarios were compared to the cost of up front RP. Costs were calculated for 15 years from the time of diagnosis in all arms of the model.

**Results:** Costs of up front RP including costs of surgery, complications, and follow up for 15 years were \$15,235 per person. Costs of WWAS were estimated using annual conversion rates from WWAS to RP of both 5% and 7%. Costs per person in the WWAS arms ranged from \$6,924 to \$11,992 in the scenarios created, which represent a 21.3% - 54.5% reduction in costs when compared to treatment of these men with up front RP.

**Conclusion:** Watchful waiting with active surveillance is being increasingly practiced as a method to decrease potential overtreatment of prostate cancer in men with low risk disease. The present study demonstrates that WWAS is likely to markedly decrease costs when compared to active treatment with RP.

## P101

### Phase III Trial in Men on ADT Demonstrates a Reduction in Hot Flashes in Men on Toremifene 80 mg Compared to Placebo

**Jeff Gingrich**<sup>1</sup>, Philip Aliotta<sup>2</sup>, Ronald A. Morton<sup>3</sup>  
<sup>1</sup>Pittsburgh VA Health Care Center, Pittsburgh, PA, US, <sup>2</sup>Center for Urologic Research of WNY, LLC, Williamsville, NY, US, <sup>3</sup>GTX, Inc, Memphis, TN, US

**Introduction and Objective:** Use of androgen deprivation therapy (ADT) has increased over the last decade. ADT results in castrate levels of testosterone and estrogen that leads to estrogen deficiency side effects such as hot flashes. In a randomized, double blind, placebo-controlled trial to determine if toremifene 80 mg could prevent fractures in men on ADT, we also assessed the effect of toremifene on the incidence and severity of hot flashes

**Materials and Methods:** 1389 men with prostate cancer were randomized to receive 80 mg toremifene orally or placebo for up to 24 months. All subjects were on ADT for  $\geq 6$  months, had a serum PSA  $\leq 4$  ng/mL, were  $\geq 70$  years of age or were at or below WHO thresholds for spine and hip (BMD). Hot flashes were reported by patients using a 7 day diary at baseline and every 3 months on study. Severe hot flashes and flushing were recorded as adverse events and analyzed between treatment groups based on the ITT population.

**Results:** Only US subjects with at least 6 hot flashes/day at baseline and not on Megace<sup>®</sup> were included in the analysis (toremifene=18 subjects, placebo=19 subjects). In this subgroup, toremifene 80 mg reduced the incidence of hot flashes from baseline at 6 months by 42% compared to a 26% decrease in the placebo group with a trend in favor of toremifene ( $p=0.0597$ ). At 9 months, toremifene significantly reduced the incidence of hot flashes from baseline by 42% compared to an 18% decrease in

the placebo group ( $p=0.0457$ ). The effect was maintained through the end of the study. The incidence of hot flashes and flushing reported as adverse events (reported by the patient as severe) was lower in the toremifene group (3.9%) compared to the placebo group (5.8%). This incidence showed a statistical trend in favor of toremifene ( $p=0.1188$ ).

**Conclusion:** In this randomized placebo controlled trial toremifene 80

mg demonstrated the ability to reduce hot flashes in a subset population that experienced on average a higher number of hot flashes at baseline than that observed in the ITT population. Additionally, fewer subjects reported severe hot flashes and flushing as adverse events.

## Moderated Poster Session VII: General Urology

### Friday, October 9, 4:00 – 5:00 p.m.

#### P102

##### **Research in Urology: A National Survey on Attitudes and Experience of Research in Urology Residency**

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**Introduction and Objective:** Involvement in clinical or basic science research as one component of the scholar role is an important part of urologic residency training. The teaching and evaluation of this role is often observational, based on participation in research, and performance-related, with respect to production of research publications and attendance at conferences. We sought to access the experiences with and attitudes towards research endeavours in Urology residents across Canada.

**Materials and Methods:** An anonymous, self-report questionnaire was filled out by 26 chief residents in Canadian Urology programs in February 2009. The questionnaire was composed of 30 open and closed-ended questions set to evaluate the residents experience with and attitudes toward research, both prior to, and during residency. The closed-ended questions were based on a five-point Likert scale. Descriptive and correlative statistics were used to evaluate responses to the survey. For ease of reporting herein, an agreement score was given by combining two agreement points on the Likert scale.

**Results:** The response rate from the questionnaire was 100%. The vast majority of residents had some experience in research prior to residency and have published at least one paper (92.3% and 84.6% respectively), with the average resident publishing over 4 papers (mean=4.65, range 0 - 11). However less than half those surveyed believed that research during their residency was important to their overall training (42%). Over half (58%) admitted that their motives for doing research was mainly to increase their chances of obtaining their desired fellowship program. Thirty-eight percent of the respondents agreed that there was dedicated time set aside for research endeavours in their residency and 69% of those surveyed would be more inclined to take part in research. The greatest obstacle to participating in research in urology residency appeared to be dedicated time and available preceptors.

**Conclusion:** There is a wide range of medical research activity and opinion regarding research during a urologic residency-training program. A significant proportion of respondents feel research is unimportant in their training. Nonetheless, over two-thirds of residents believe that they would be more inclined to perform research if they were provided more protected research rotations and time constraints were identified as the most common and important self-reported limiting factor to participation in research during residency.

#### P103

##### **Suprasacral Spinal Cord Injury Patients Managed by Reflex Voiding: Characterization of our Cohort**

John M. Rutkowski, Kevan Pranikoff, Jan Capuana

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**Introduction and Objective:** Suprasacral spinal cord injury patients require frequent urologic attention to prevent morbidity and mortality. Urodynamic

studies can help the clinician formulate a safe management plan for bladder storage and emptying. We attempt to characterize our cohort of suprasacral spinal cord injury patients managed by reflex voiding.

**Materials and Methods:** The census of all patients studied in our urodynamics laboratory over the past twelve months was reviewed. The records of all patients (34) with suprasacral spinal cord injuries managed by reflex voiding for at least three years were chosen for retrospective review. Ten patients were excluded for incomplete data.

**Results:** Mean time from injury was 17.3 years. 23/24 patients were male. Location of injury: C1-C7 (14), T1-T12 (10), L1-L5 (0). 21/24 were complete spinal cord lesions, 3/24 were incomplete lesions. Eight patients had a transurethral sphincterotomy. Three required repeat transurethral sphincterotomy for persistent autonomic dysreflexia. Indications for initial sphincterotomy include autonomic dysreflexia (4/8), hydronephrosis with a poorly compliant bladder (3/8) and autonomic dysreflexia with poor compliance (1/8). Detrusor external sphincter dysnergia (DESD) was observed in 21/24 patients. Those with complete spinal cord lesions were more likely to have type II or type III DESD (16/20). Bladder capacity was 77-947mL. Intravesical storage pressures prior to flow were 10-58 cm H<sub>2</sub>O. Intravesical leak point pressures were 43-144 cm H<sub>2</sub>O. Patients with prior sphincterotomy had an average leak point pressure of 49 cm H<sub>2</sub>O. Patients without prior sphincterotomy had an average leak point pressure of 90 cm H<sub>2</sub>O. 8/8 patients managed with sphincterotomy had type II or type III DESD. Abnormal renal ultrasound was observed in 4/24 patients. One developed bilateral hydronephrosis and renal insufficiency from persistent high storage pressures and was refusing intervention, one presented with bilateral staghorn, ureteral and bladder calculi with renal insufficiency requiring rescue procedures, one had staghorn calculi and refused intervention and one had bilateral renal scarring from a history of chronic pyelonephritis.

**Conclusion:** Urodynamics are crucial to the routine follow-up of patients with suprasacral spinal cord injuries managed with reflex voiding. Sphincterotomy is an effective means of stabilizing those who develop complications from poor bladder compliance or autonomic dysreflexia.

#### P104

##### **Surgical Treatment of Bladder Outlet Obstruction Improves Outcome in Male Interstitial Cystitis**

Roger E. Vega

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**Introduction and Objective:** Male interstitial cystitis continues to be a formidable challenge for urologists and an interesting subject for clinical research. Since the principal manifestation of this ailment is pelvic pain, current treatment is directed towards relief of pain with analgesics, alpha blockers, and antibiotics with outcome not worth duplicating. There is therefore a stimulus to look for another etiology and devise another treatment.

**Materials and Methods:** The medical records of 3015 male patients were reviewed over a 29 year period with a view to discovering those with symptoms approximating interstitial cystitis. 346 of these were judged