Purpose: Prostate needle biopsy (PNB) may result in significant morbidity. Sepsis secondary to PNB has been extensively reported and most often associated with quinolone resistant E. coli. Other serious complications including hemorrhage have received less attention. We report a two year assessment of serious complications following PNB at Genesis Healthcare Partners (GHP), a Large Urology Group Practice (LUGP).

Materials and Methods: A 25 month retrospective study of all biopsies from April 1, 2011 to April 31, 2013 was conducted. Patient hospitalization records within 30 days of prostate biopsy at GHP were assessed for sepsis, urinary tract infection, prostatitis, urinary retention, hemorrhage and other serious complications. Billing records from an electronic medical record (EMR), Allscripts, were evaluated for CPT codes linked to the complications being screened. Software developed at GHP screened the EMR hospital records and ICD 9 codes for PNB complications. Manual analysis of each complication was performed to verify the complication as a result of PNB.

Results: 2142 biopsies were performed with 47 serious complications (2.194%): 37 (1.727%) associated with hospitalization, 10 (0.467%) managed as outpatients. The results were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Hospitalized</th>
<th>Outpatient</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis (Confirmed by blood culture)</td>
<td>10 (0.467%)</td>
<td>0</td>
<td>10 (0.467%)</td>
</tr>
<tr>
<td>Sepsis (fevers only/ no available blood culture for verification)</td>
<td>8 (0.373%)</td>
<td>0</td>
<td>8 (0.373%)</td>
</tr>
<tr>
<td>Febrile UTI</td>
<td>2 (0.093%)</td>
<td>1 (0.047%)</td>
<td>3 (0.140%)</td>
</tr>
<tr>
<td>Febrile Prostatitis</td>
<td>2 (0.093%)</td>
<td>2 (0.093%)</td>
<td>4 (0.187%)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>6 (0.280%)</td>
<td>0</td>
<td>6 (0.280%)</td>
</tr>
<tr>
<td>Infected Device</td>
<td>1 (0.047%)</td>
<td>0</td>
<td>1 (0.047%)</td>
</tr>
<tr>
<td>Urinary Retention (caused by biopsy)</td>
<td>5 (0.233%)</td>
<td>6 (0.280%)</td>
<td>11 (0.514%)</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>0</td>
<td>1 (0.047%)</td>
<td>1 (0.047%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>3 (0.140%)</td>
<td>0</td>
<td>3 (0.140%)</td>
</tr>
</tbody>
</table>

10 verified cases of sepsis included: 6 fluoroquinolone resistant bacteria, 2 ESBL E. coli, 2 gentamycin resistant bacteria. Infected Device: LVAD infected, biopsy cannot be ruled out as cause. Syncope: related to medication allergy (2).

Conclusion: Our study suggests a serious PNB complication rate of 1-2% requiring hospitalization. A best practice has been established at GHP in an attempt to mitigate PNB complications:

1) Routine IM administration of gentamicin to prevent quinolone resistant bacterial sepsis.
2) Time Out prior to PNB ensuring absence of anticoagulants, antiplatelet drugs, patient identification and specimen bottle labeling is now routine best practice at GHP.

Monitoring post biopsy complications may identify opportunities to improve quality. Source of Funding: None
REDUCING INFECTIONS FOLLOWING PROSTATE NEEDLE BIOPSY BY CHANGING ANTIBIOTIC PROPHYLAXIS REGIMEN

John M Corman, M.D., Claudio Jeldres, M.D., Nae-Hwa Kim, M.D., Christopher R. Porter, M.D.: Seattle, WA
(Presentation to be made by Dr. Corman)

Objective: In response to the rise in bacterial resistance to fluoroquinolones, we expanded our prostate needle biopsy prophylactic coverage to include a fluoroquinolone in combination with a secondary antibiotic. Here we evaluate whether administration of an additional antibiotic reduced the risk of postprocedural infections.

Materials and Methods: Infection risk was compared among patients following administration of one (single) or two (dual) prophylactic antibiotics for prostate needle biopsy in an observational study. Patients received antibiotic prophylaxis consisting of fluoroquinolone (Ciprofloxacin) alone, Ciprofloxacin plus a 3rd generation cephalosporin (Ceftriaxone), or, in the case of penicillin allergy, Ciprofloxacin plus an aminoglycoside (Gentamycin). They did not receive mechanical bowel prep or enema. Urine cultures and blood cultures were obtained post biopsy following clinical presentation: fever, dysuria, urinary retention, suprapubic pain. Risk of infection using dual was compared to single therapy by Chi-Square and summarized by a Risk Ratio (RR), and stratified by year using Mantel-Hansel.

Results: Infection outcomes and antibiotic exposures were recorded for 788 procedures by three providers from 2001 to 2013. The infection rate was significantly reduced from 5.7% to 2.2% following dual compared to single therapy (11/489 and 17/299, respectively; RR = 0.40; p=0.012). Importantly, it was the addition of Ceftriaxone (% n/n RR, p), not Gentamycin (% n/n RR, p), that resulted in the reduction in infection rate. No association was observed stratified by year from 2008 to 2010, during a period of policy transition (RR = 1.05; p=0.99). Excluding the period of overlap, infection risk was lower following the policy change (4/65 before versus 7/372 following; RR=0.31; p=0.043).

Conclusions: AUA guidelines recommend either fluoroquinolone or cephalosporin for antimicrobial prophylaxis for prostate needle biopsy. We were able to combat the rise in fluoroquinolone resistance seen at our own institution by administering these antibiotics in combination. Unfortunately, patients with a reported penicillin allergy remain at an increased risk of infection. Given that reactions to 3rd generation cephalosporins occur less frequently than to 1st generation cephalosporins in patients with a history of penicillin allergy, the potential benefits of Ceftriaxone may exceed the risks for these patients following prostate needle biopsy.

Source of Funding: None
DIAZEPAM BEFORE PROSTATE BIOPSY—A PROSPECTIVE, RANDOMIZED TRIAL

Jonathan D. Creech, B.S.*, David J. Culpepper, B.S., B.A.*, Caroline L. Wallner, M.D., Gene O. Huang, M.D., Steven R. Engbretsen, B.S.*, Gaudencio Olgin, M.D., Don C. Arnold II, M.D., Roger Li, M.D., Michelle A. Lightfoot, M.D., Herbert C. Ruckle, M.D., D. Duane Baldwin, M.D.: Loma Linda, CA
(Presentation to be made by Dr. Li)

Purpose: Patient anxiety and discomfort are common during ultrasound probe insertion and needle biopsy of the prostate. The efficacy of oral anxiolytics to decrease patient anxiety and pain perception has been demonstrated in endoscopy, bone marrow aspiration, and lumbar puncture, but has not been studied in the setting of prostate biopsy. The purpose of this study was to investigate the effect of diazepam on pain perception during and after prostate biopsy.

Materials and Methods: One hundred patients undergoing prostate biopsy at a single academic institution were enrolled in this prospective, randomized, double-blinded, placebo-controlled study. Between 13 and 28 core biopsies were performed in a standardized fashion with a periprostatic nerve block (20 mL of 1% plain lidocaine). Prior to the procedure, a questionnaire was administered to determine baseline discomfort and pain history. Patients were surveyed about pain associated with each step of the procedure immediately after biopsy and at one-week follow-up. Pain perception was analyzed using a Visual Analog Scale. Responses were compared between groups using Mann-Whitney U, Fisher’s exact, and multivariate linear regression analyses.

Results: A total of 60 patients (29 diazepam, 31 placebo) had completed pre- and post-biopsy surveys for analysis. Number of cores sampled during biopsy was controlled during analysis, and was found to have no correlation with total pain measured (p = 0.179). There were no differences between diazepam and placebo groups in age, pre-biopsy survey results, or immediate post-biopsy survey results. However, upon one-week recall of the same pain parameters, the diazepam group displayed significantly greater pain scores during probe insertion (p = 0.012).

Conclusions: This study demonstrates that diazepam does not improve patient perception of pain after prostate biopsy. Omitting diazepam simplifies the biopsy procedure and does not interfere with complicated patient tasks such as operating heavy equipment or driving. Based on our results, we cannot recommend routine use of diazepam for biopsy.

Source of Funding: None
SURGEON PERFORMANCE AND DISTRACTIONS IN THE OPERATING ROOM: A RANDOMIZED, CONTROLLED, CROSSOVER TRIAL
Ryan W. Speir, M.D., Richard N. Greene, M.D., Thomas S. Lendvay, M.D., Raywin R. Huang, Ph.D., Eric Bean, Ph.D., Timothy C. Brand, M.D.: Tacoma, WA
(Presentation to be made by Dr. Greene)

Purpose: Surgery is a complex interaction of cognitive and psychomotor skills that requires a great deal of concentration to perform safely. Cognitive overload (often the result of distraction and multi-attending) is frequently cited as a source of error in many fields and in daily life. The modern operating room is a complex environment with many distractions that may affect how resident and attending surgeons operate. This study examined how cognitive load affects actual surgeon performance.

Materials and Methods: We conducted a prospective randomized controlled trial with ten resident and ten attending surgeons. Participants were required to meet proficiency benchmarks on the Virtual Reality daVinci desktop simulator (dV Trainer, Mimic Technologies, Seattle WA) to minimize performance variability. Participants then performed four simulated surgical tasks with increasing complexity on the dV Trainer. Participants performed each task four times with cross-over; twice with distraction and twice as a control. Distraction was provided by 85 decibels of background operating room noise and non-related specialty based medical questions. Surgical performance was then determined from total procedure time, economy of motion, time instruments were out of view, and number of errors. Data were then analyzed using SPSS.

Results: Distraction had a detrimental effect on surgeon performance. There was a trend towards significance for increase in time for resident surgeons for time required to complete the most challenging task (rocking pegboard): 177 seconds vs. 185 seconds in the distraction group (4.5% difference, p=0.35). This percent difference in task time for task completion was similar across the tasks. Also, for the rocking pegboard, averaged across all subjects, economy of motion differed significantly at 722 cm vs 770 cm (p=0.02). The effect of distraction was greatest in resident surgeons. Distraction affected economy of motion more significantly for residents with an average economy of motion on pegboard level 1 with distraction of 485 cm vs 447 cm without distraction (p=0.03). Whereas attending surgeons on that exercise had no statistically significant difference in economy of motion: 446 cm without distraction vs 448 cm with distraction (p=0.86).

Conclusions: We have shown that distractions during VR robotic task performance such as background noise and questioning may adversely affect surgeon performance. This effect seems to be greatest in surgical trainees. These data inform us that the detrimental effect distractions have on surgical performance among trainees should be studied in the operating room.

Source of Funding: None
THE SHORT-TERM EFFECTS OF ROBOTIC PROSTATECtOMY ON LOWER URINARY TRACT SYMPTOMS: WHO BENEFITS AND WHEN?
(Presentation to be made by Ross Anderson, B.S.*)

Purpose: A limited number of prior reports suggest that men with moderate or severe lower urinary tract symptoms (LUTS) experience clinically significant improvement in LUTS after open radical prostatectomy. However, LUTS has been less well studied after robotic-assisted laparoscopic prostatectomy (RALP) and the time course for improvement in voiding symptoms, and who might benefit is less certain in this group. We evaluated the short-term (over 12 months postoperative) effect of RALP on LUTS with particular attention to determining who might benefit and at what time in the early postoperative period.

Materials and Methods: Over a three year period, (2010-2012) a total of 339 patients with prostate cancer underwent RALP and had preoperative data available to assess baseline LUTS. American Urological Association symptom score (AUASS) questionnaire was completed at baseline, 4 weeks following catheter removal, and at 3, 6 and 12 months postoperatively. Patients were grouped according to preoperative AUASS as having minimal (AUASS 0-8), moderate (AUASS 9-19) or severe (AUASS > 20) LUTS. Paired two sample t-tests were used to compare change in AUASS for each symptom group. Factors predicting change in LUTS were determined in univariate analysis, and the time course for improvement or worsening of symptoms was determined according to preoperative AUASS group.

Results: Of 339 patients with preoperative AUASS, LUTS was minimal, moderate or severe in 52%, 39% and 9%, respectively. Prostate weight was associated with preoperative AUASS grouping (p=0.01). There was no association between baseline AUASS and age, BMI or preoperative SHIM score. For patients in the minimal symptom group, AUASS was significantly worse at 3 months postoperatively (from 3.3 to 6.7, p<0.001). However, LUTS returned to near baseline (AUASS 4.2) by 12 months postoperatively (p=0.06). Patients with moderate LUTS had significant improvement in AUASS by 3 months (from 12.5 to 8.5, p<0.001) and continued to improve until 12 months postoperative (6.7, p<0.001). Men with severe voiding symptoms benefited the most with a significant improvement in LUTS even as early as 4 weeks after catheter removal (from 24.8 to 12.3, p<0.001) and continued to improve even further until 12 months after surgery (9.7, p<0.001).

Conclusions: In men with moderate or severe LUTS, robotic prostatectomy results in significant improvement in voiding symptoms as early as 4-12 weeks postoperatively. This infrequently discussed and less well-documented benefit of surgical therapy should be considered when patients are weighing the risks and benefits of the treatment options for localized prostate cancer.

Source of Funding: None
EVALUATION OF LENGTH, MAXIMUM GLEASON SCORE, AND EXTENSION OF DISEASE AT POSITIVE SURGICAL MARGINS DURING RADICAL PROSTATECTOMY
Hooman Djaladat, M.D., Mehrdad Alemozaffar, M.D., Christina Day, M.D., Manju Aron, M.D., Jie Cai, Tracy Campanelli, Gary Lieskovsky, M.D., Siamak Daneshmand, M.D.: Los Angeles, CA (Presentation to be made by Dr. Djaladat)

Introduction: A positive surgical margin (PSM) found following radical prostatectomy (RP) for prostate cancer is known to affect subsequent recurrence and survival. However, the extent of PSM in addition to other pathologic parameters, have been shown to have a significant impact on clinical outcomes. We examined the effect of length of PSM, extent of disease at PSM, and maximum Gleason score at PSM on oncologic outcomes.

Methods: A retrospective review of 3971 patients undergoing RP for prostate cancer at our institution between 1978 - 2009 revealed 1053 patients with PSM, out of whom 814 received no neoadjuvant or adjuvant hormone therapy. The initial 175 out of 814 patients were selected in order to maximize available follow-up time and data, and their pathology slides were re-reviewed to evaluate the following parameters: length of PSM (mm), maximum Gleason score at PSM, and maximal extension of PSM (intraprostatic incision vs. extracapsular extension). Data was available in 107 patients who are the subject of this study. Stepwise multivariable Cox regression models were used to evaluate the impact of the above PSM features as well as age, preoperative PSA, pathologic Gleason score, pathologic stage and adjuvant radiation therapy on biochemical and clinical recurrence-free survival (RFS), and overall survival (OS).

Results: Median follow-up for the cohort was 17.6 years. The maximum extension of PSM was limited to intraprostatic incision in 63 (58.9%) and extracapsular extension in 44(41.1%) patients. The median length of PSM was 4 mm (range 1-55 mm); 41 (38.3%) with <3mm and 66 (61.7%) with >≥4mm. The maximum Gleason score at PSM was ≤6 in 70 (66.0%) and >≥7 in 36 (34%) patients. 10-yr PSA RFS, clinical RFS, and OS were 60.2%, 80.7%, and 60.2%, respectively. Multivariable Cox regression modeling showed the length of PSM >≥4mm and extracapsular extension at PSM were independent predictors of PSA RFS and clinical RFS, while age and extracapsular extension at PSM were independent predictors of OS. Maximum Gleason score at PSM was not independently associated with worse clinical outcomes on multivariable analysis.

Conclusion: Patients with PSM after RP for prostate cancer with a length of PSM >≥4mm and extracapsular extension at PSM have a higher risk of PSA and clinical recurrence. These findings can help decision-making regarding adjuvant therapy in patients with PSM and should be reported by pathologists in addition to the presence of PSM.

Source of Funding: None

Table 1. Multivariable Cox regression modeling

<table>
<thead>
<tr>
<th></th>
<th>PSA RFS HR</th>
<th>p-value</th>
<th>Clinical RFS HR</th>
<th>p-value</th>
<th>Overall Survival HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.068</td>
<td>0.009</td>
</tr>
<tr>
<td>Length of PSM &gt;≥4mm</td>
<td>2.640</td>
<td>0.011</td>
<td>6.120</td>
<td>0.157</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Extracapsular Extension at PSM</td>
<td>2.842</td>
<td>0.002</td>
<td>7.544</td>
<td>&lt;0.001</td>
<td>2.666</td>
<td>0.002</td>
</tr>
</tbody>
</table>
FACTORS AFFECTING INCIDENCE OF INCISIONAL HERNIA AFTER ROBOTIC ASSISTED RADICAL LAPAROSCOPIC PROSTATECTOMY
Michael Nazmy, M.D., Nora Ruel, M.A. *, Clayton Lau, M.D.,
Timothy Wilson, M.D.: Duarte, CA
(Presentation to be made by Dr. Nazmy)

Introduction: Robotic assisted laparoscopic radical prostatectomy (RALP) is traditionally performed with a periumbilical camera port incision. Our aim was to compare incidence of post-operative incisional hernias with use of a transverse fascial incision versus a vertical fascial incision as well as examine other potential factors that may contribute to postoperative incisional hernia.

Methods: An IRB-approved database of robotic prostatectomy patients was queried for those having had no history of previous umbilical hernia diagnosis. A total of 1490 patients had a vertical fascial incision, and 427 had a transverse fascial incision. Closures were performed by the attending surgeon and assisting fellow. Uni- and multi-variable logistic regression analyses were performed to identify predictors of postoperative umbilical hernia.

Results: Median follow-up for the vertical incision group was 42 months, and 12 months for the transverse incision group. No difference was noted in age, Charlson Comorbidity Index scores, or specimen weight; however, BMI in the transverse incision group was significantly higher than in the vertical incision group (28.0 vs. 27.3, p=0.0004). The incidence of hernias at 12 months after surgery with transverse fascial incision was 1.17% vs. 3.02% with vertical fascial incision, p=0.07, and 1.64% vs. 3.83% at 24 months, p=0.03.

A multivariable logistic regression model was then used to determine whether type of incision would affect incidence of incisional hernias during the first 2 years post-RALP. Demographic predictors BMI (>30 vs <=30), specimen weight (>70g vs <=70), and surgical age were tested as predictors in the multivariate model. The results showed that a vertical fascial incision was associated with higher rate of hernias (OR=2.6, p=0.02), as was BMI>30 (OR=2.1, p=0.006), and specimen weight >70g (OR=1.9, p=0.03). Surgical age of patient was not a significant factor in predicting incidence of incisional hernias (p=0.7) in the multivariable model.

Conclusions: Our data suggests that vertical fascial incision is associated with a higher risk of postoperative umbilical hernias than transverse fascial incision. Specimen weight greater than 70g significantly increases the risk of postoperative umbilical hernia following robotic assisted radical prostatectomy.

Source of Funding: None
Objective: To evaluate the rates at which patients are offered, and receive local salvage therapy (LST) after failure of primary radiotherapy for localized prostate cancer as it is the only potentially curative treatment for localized recurrence, but appears to be underutilized when compared to androgen deprivation therapy or observation.

Materials and Methods: Patients with localized prostate cancer who received primary radiotherapy with curative intent between 1999-2000 were identified in the British Columbia Tumour Registry. Exclusion criteria included patient age > 72, PSA > 40 and clinical stage T4 at diagnosis. Data on clinicopathologic features, primary therapy, PSA kinetics, and salvage therapy were collected retrospectively. Radiation failure was defined as biochemical recurrence according to the Phoenix criteria or by initiation of salvage therapy.

Results: Out of 1782 patients treated in the study period, 1067 met inclusion criteria. Of these, 257 failed radiation. Radiation failure was managed with observation (>12 months) in 126 patients and androgen deprivation therapy (ADT) in 119. Of the observed patients, 66 subsequently received ADT. Five patients (1.8%) received LST (3 radical prostatectomy, 2 brachytherapy).

Conclusions: Only 2% of patients relapsing after radiation for localized prostate cancer received local salvage therapy. While the benefits of LST are unproven, these findings reveal a possible underutilization of LST, and indicate a need for enhanced collaboration between specialties to optimize care of this challenging cohort.

Source of Funding: Summer Student Research Program (UBC Faculty of Medicine) Vancouver Coastal Health Research Institute
Purpose: Patients with radiation-recurrent prostate cancer (RRPC) after primary radiation therapy have limited treatment options. Salvage treatment, including radical prostatectomy and cryotherapy, have historically resulted in higher complication rates than primary treatment. Advancements in cryotherapy technology offer patients with RRPC a potentially curative therapeutic option with reduced morbidity. The purpose of this study is to report outcomes of salvage cryotherapy (SC) at our institution, with particular interest in those treated with proton radiation.

Materials and Methods: A retrospective review of 62 SC patients at a single academic institution between 2004 and 2012 was completed. All patients had biopsy-proven RRPC after receiving primary radiation therapy. Patient demographics in addition to prostate cancer characteristics before primary radiation and SC were collected. Outcomes evaluated were post-operative prostate specific antigen (PSA) and complications. Biochemical failure and recurrence-free survival was defined using the Phoenix criteria.

Results: Of the 62 patients with RRPC, 67.7% received proton beam therapy (PBT), 24.2% external beam radiotherapy (EBRT), and 8.1% brachytherapy (BT) as primary radiation therapy. Survival curves demonstrated no difference in biochemical recurrence-free survival (bRFS) between those treated with PBT or EBRT (p = 0.567). Overall bRFS was 62.9% at an average of 22.5 months follow-up. Multivariate analysis revealed PSA nadir of >0.1 as an independent predictor of treatment failure (p = 0.023). Complications included acute urinary retention (31%), lower urinary tract symptoms (33%), hematuria (16%), urinary tract infection (14%), incontinence (23%), fistula (5%), erectile dysfunction (85%), and prolonged perineal pain (5%).

Conclusions: SC is a reasonable treatment with comparable oncologic control and acceptable morbidity when compared to other local salvage therapies. To date, this cohort represents the largest group of SC patients with primary PBT failure. As expected with similar radiation doses, primary treatment with PBT versus EBRT does not affect overall bRFS or observed complication rate after SC in the short-term.

Source of Funding: None
Background: Local recurrence of prostate cancer after non-surgical treatment presents a challenge for both patients and physicians. Salvage therapy can be curative though side effects may be considerable. We sought to determine the outcomes and complications of robotic salvage prostatectomy (RSP).

Methods: 51 consecutive patients underwent RSP after previous failed local therapy. Biochemical recurrence was defined as two post-operative PSAs ≥ 0.2 ng/mL. Complications at any time postoperatively were recorded by a modified Clavien system prospectively. The Kaplan-Meier method was used for survival estimation. Regression models were used to identify predictors of biochemical recurrence free survival (BCRFS) and complications.

Results: Median age at RSP was 68 years with a median of 68 months elapsed from time of primary treatment. Median follow-up was 34 months. Median operative time was 179 minutes with estimated blood loss of 175 ml. 50% of patients were pathologic stage 3 and positive surgical margins were seen in 31%. Overall complication rate was 47% with 35% major complication (Grade III-V) rate. Potency was maintained in 23% of pre-operatively potent men and 33% of all patients regained urinary control. Estimated 3-year BCRFS was 70%. No clinical variables were predictive of major complications or biochemical recurrence. Positive surgical margins were significantly associated with biochemical recurrence (p=0.04). Limitations are small population size and lack of a control group.

Conclusions: Robotic salvage prostatectomy provides oncologic control with potential avoidance of systemic non-curative therapy. Complication, incontinence, and erectile dysfunction rates are significant but frequently correctable. This reinforces the need for proper patient counseling and selection.

Source of Funding: None
Purpose: Gleason score, PSA and tumor stage are the most common tools used by physicians to guide clinical decisions in regards to prostate cancer treatment at diagnosis. However, these diagnostic markers have limited utility. Recently, studies have shown an association between a cell cycle progression (CCP) gene assay and biochemical recurrence (BCR). The aim of this study was to evaluate the ability of the CCP score, derived from the diagnostic biopsy, to predict BCR after radical prostatectomy (RP) in a community cohort.

Materials and Methods: The study population consisted of prostate cancer patients who had been diagnosed by needle biopsy and treated by RP at Intermountain Medical Center from 1999-2002 (n=151). Cases were men who had BCR within 10 years of surgery. Controls were sampled, in a case to control ratio of 1:2, from the study population and were free of BCR as of September 2011. All biopsy samples were processed at Myriad Genetic Laboratories, Inc. Results were reported as a CCP score. The primary end point for the study was time to BCR with metastatic disease as a secondary end point.

Results: In our study, 123/151 samples yielded passing CCP scores and could be included in the analysis. In the univariate analysis, the CCP score was strongly associated with a 10-year risk of BCR (HR=1.86, 95% CI for HR (1.25, 2.78), p = 0.0028). In the multivariate analysis, the CCP score remained significantly predictive of BCR risk (HR = 1.63, 95% CI for HR (1.05, 2.53), p = 0.029). The CCP score also significantly predicted metastatic status where the odds ratio for metastatic cancer was 3.73 (95% CI (1.32, 12.23) p = 0.023) for a one-unit increase in the CCP score.

Conclusions: The CCP score provided additional prognostic information beyond that of the usual clinical prostate cancer diagnostics. The CCP score was also found to be a significant risk indicator for metastatic cancer. This study provides additional evidence that the CCP score can be used at diagnosis to support treatment decisions and demonstrates that the score has utility in a community-based patient cohort.

Source of Funding: Myriad Genetics, Inc.
Background and Objective: Enzalutamide (formerly MDV-3100) is a recently approved androgen-receptor-signaling inhibitor that blocks nuclear translocation of the androgen receptor, DNA binding, and coactivator recruitment. Clinical trials show superior survival for enzalutamide compared to placebo for castration resistant prostate cancer (CaP). We sought to establish enzalutamide response rates in established CaP cell lines with differing androgen receptor (AR) expression levels and identify pre-treatment markers that predicted response.

Methods: We have collected 20 different CaP cell lines for use in drug screening studies. Enzalutamide drug screens were performed using nine 5-fold serial dilutions of enzalutamide in triplicate, with a maximum concentration of 50 uM. The concentration of drug where 50% of growth was inhibited was calculated and cell responses were binarized into sensitive and resistant pools. RNA was isolated from untreated cells using Trizol and submitted for Illumina RNAseq analysis. RNA gene clustering was performed to identify Androgen Receptor (AR) and Ets Regulated Gene (ERG) expression and subtype clustering. Associations between enzalutamide drug screen response and gene expression were calculated using Significance Analysis for Microarrays (SAM).

Results: Hierarchical clustering of 741 transcripts that showed the highest variability separated the CaP lines into two main clusters. Clustering appeared to be driven by AR status, with high expressing lines found in one branch while AR negative cells were found in a separate branch. High levels of ERG expression was observed in two cell lines (DuCaP and VCaP). We observed 7 sensitive and 10 resistant lines from the enzalutamide treatment (3 cell lines are still pending treatment). Preliminary analysis revealed 92 transcripts that are differentially expressed between responsive and non-responsive cell lines at a level of at least 10-fold difference, including KRT75, CDH11, and ETV4.

Conclusions: We have identified a panel of genes that are associated with response to enzalutamide in prostate cancer cell lines. This gene set represents a starting point for biomarker development to determine if the genes are predictive of response in patient samples, and also represent a pool of genes that can be interrogated using functional studies and siRNA knockdown approaches for their effect on enzalutamide sensitivity.

Source of Funding: None
DISPARITIES IN DISEASE CHARACTERISTICS BETWEEN CAUCASIANS AND AFRICAN AMERICANS RECEIVING SIPULEUCEL-T: DATA FROM PROCEED

Chiledum Ahaghotu, M.D., Ph.D., Sara Horton, M.D.;
Celestia S. Higano, M.D., Oliver Sartor, M.D., Matthew R. Cooperberg, M.D.,
M.P.H.; Raoul Concepcion, M.D., F.A.C.S., Manish Dhawan, M.D.,
Sanjay Goel, M.D., Simon J. Hall, M.D.; Andrew J. Armstrong, M.D., M.Sc.;
David Penson, M.D., M.P.H., Andrew Sandler, M.D., Candice McCoy, M.D.,
James Whitmore, Ph.D., Robert Tyler, Ph.D., Nadeem Sheikh, Ph.D.,
Chadi Nabhan, M.D.: Washington DC

(Presentation to be made by Dr. Ahaghotu)

Background: PROCEED is an ongoing, multicenter, phase 4 registry enrolling patients with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer receiving sipuleucel-T in community and academic practices. Information on patient demographics, disease characteristics, and prior treatments is being collected. One objective of the registry is to accrue African American (AA) men in order to gain insight into treatment patterns and exposure to investigational therapies in different ethnic cohorts.

Methods: Patients who were treated with sipuleucel-T within the prior 6-months were eligible to participate in PROCEED. All signed written informed consent and data were collected with a cutoff date of November 2012.

Results: Of 934 pts enrolled, 87.5% were Caucasian (CAU), 10.3% AA, and 1.9% other. Baseline demographics showed median age was similar between ethnic groups (CAU 72.0 yrs, AA 71.0 yrs); however the distribution of age appeared different with 20.6% CAU ≥80 yrs-old vs. 10.4% AA. The median age at prostate cancer diagnosis was the same in both groups (65 yrs), and the period from diagnosis to first infusion of sipuleucel-T was 5.6 yrs AA vs. 5.1 yrs CAU; \( P = 0.522 \). AA had higher ECOG-PS scores than CAU (ECOG-PS ≥ 1, 39.6% AA vs. 29.4% CAU; \( P = 0.047 \)) and higher median PSA (AA 33.0 ng/mL vs. CAU 18.3 ng/mL; \( P = 0.070 \)). The extent of metastatic bone disease was similar between the ethnic groups but AA appeared to have a higher rate of visceral metastases (AA 8.3% vs. CAU 5.4%; \( P = 0.243 \)). Notably, prior treatment with an investigational therapy was more frequent in CAU vs. AA (CAU 4% vs. AA 0%; \( P = 0.041 \)), and this difference appeared unrelated to co-morbidities (≥ 1 co-morbidity, AA 81.3% vs. CAU 77.8 %; \( P = 0.514 \)).

Conclusions: AA men in PROCEED appear to present for sipuleucel-T therapy at a younger age but with poorer performance status, higher PSA, and a higher rate of visceral metastases compared to the CAU group. The AA group was also less likely to receive investigational agents prior to sipuleucel-T.

Source of Funding: Dendreon Corporation
THE SURVIVAL BENEFIT OF PROSTATECTOMY IN METASTATIC PROSTATE CANCER

Mike M. Nguyen, M.D., M.P.H., Mihir Desai, M.D., Inderbir S. Gill, M.D.: Los Angeles, CA
(Presentation to be made by Dr. Nguyen)

Purpose: We determine whether men with prostate cancer metastatic to bone, tissue, or non-regional nodes at time of diagnosis derive a survival benefit from localized treatment with prostatectomy.

Materials and Methods: The SEER database between 2004-2009 was used to identify men who were diagnosed with prostate cancer metastatic at diagnosis. The primary outcome evaluated was overall survival in men who did or did not undergo radical prostatectomy. To insure accuracy, surgery cases were reviewed for correct coding for staging and treatment by each SEER registry. Only audited cases were included in the analysis. Student’s t test and Fisher’s exact test were used to compare baseline demographic and tumor data between the two groups. Kaplan-Meier curves and log-rank tests were used to compare survival. Cox proportional hazards regression was used to compare overall survival while controlling for available demographic and tumor characteristics.

Results: 8,473 men with metastatic prostate cancer who did not undergo surgery and 147 who did undergo surgery were included. Mean age, Gleason score, and PSA were significantly higher in the no-surgery group. The majority of cases were metastatic to bone for both groups (65.5% and 71.4% for no surgery and surgery respectively; p=0.299). Men who underwent surgery had a significant survival benefit (median survival not reached for surgery, median survival of 26 months for no surgery; log rank <0.0001). On cox proportional hazards analysis controlling for Gleason score, type of metastasis, race, PSA, and age, men who underwent prostatectomy retained a significant survival benefit over those who did not have surgery (HR 0.58, 95% CI 0.38-0.89; p=0.012). In contrast, men who underwent radiation or radiation with surgery did not demonstrate a survival advantage.

Conclusions: In a retrospective analysis, men with metastatic prostate cancer who undergo prostatectomy did significantly better than men who did not have surgery. Further research is needed to determine the true benefit of prostatectomy in this clinical scenario.

Source of Funding: None