IMPROVING HOLMIUM LASER ENUCLEATION OF THE PROSTATE EFFICIENCY: THE LUMENIS PULSE™ 120H LASER PLATFORM


(Presentation to be made by Dr. Karen Stern)

Objectives: Benign prostatic hyperplasia (BPH) affects approximately 50% of men over the age of 50 and 88% of men in their 80s, often leading to a decrease in quality of life and ultimately requiring treatment. Holmium laser enucleation of the prostate (HoLEP) has been suggested as the gold standard for surgical treatment for BPH. Multiple technological advances have been made over the last several years to improve the efficacy and efficiency of the procedure including the recent delivery of a new Lumenis Pulse™ 120H laser platform. The new platform allows for preset energy modes and a dual pedal footswitch to allow the surgeon to switch between two laser settings easily. Typically, lower energy settings are used for hemostasis and near the prostatic apex, compared to higher energy settings used for the majority of the enucleation. Theoretically, the dual foot pedal should allow the enucleation portion of the procedure to proceed more efficiently. The dual foot pedal should also allow for better hemostasis during the case secondary to ease of switching the laser to hemostatic settings with a quick switch using the foot pedal instead using a required laser trained technician to input the settings. This study compares the enucleation efficiency of HoLEP performed with the new Lumenis Pulse™ 120H laser platform with the older Lumenis 100 Watt VersaPulse.

Methods: Patients at a single institution who underwent HoLEP for lower urinary tract symptoms or urinary retention from BPH using the new Lumenis Pulse™ 120H laser platform were identified from a prospectively maintained database. Based on propensity score matching using a logistic model fitted by preoperative transrectal ultrasound (TRUS) prostate volume and age, each patient was matched with 2 patients who underwent HoLEP with the older 100 Watt laser. All HoLEPs were performed by or under the supervision of a single Endourology fellowship trained surgeon (M.R.H.). HoLEPs done in both groups were performed with similar laser settings, adjusting the power (Joules) and frequency (Hertz) for hemostasis and dissection. The standard 3 lobe technique previously described in detail was used for patients with trilobar hyperplasia, adjusting to a 2 lobe technique for patients with bilobar hyperplasia. The primary outcome for this study is evaluating the enucleation efficiency of each platform, utilizing the weight of prostate tissue (grams) resected for this calculation. Secondary outcomes include complications, need for blood transfusion, and total case time. Basic statistics, i.e. frequency (% percentage) for categorical data and mean ± standard deviation (SD) for continuous data, were used to summarize the data. McNemar test and conditional logistic model were used to associate predictors and cases. A p-value of 0.5 was considered statistically significant. All statistical analyses were performed by SAS 9.4 software (SAS institute Inc. Cary NC.)

Results: A total number of 29 patients who underwent HoLEP with the Lumenis Pulse™ 120H platform were matched with 58 patients who underwent HoLEP with the 100 watt platform. Mean age was 69.48 years in the control group and 69.52 in the Lumenis Pulse™ 120H group (p = 0.82). TRUS prostate volume was 87.81 cm³ in the control group versus 93.99 cm³ (p = 0.59) in the experimental group. Both groups of patients were similar after matching for propensity score. There was no significant difference in age, TRUS prostate volume, ASA, BMI, prostate anatomy (bilobar, trilobar, regrowth, etc), prior BPH surgery, prior BPH medication or final pathology. There were statistically significant differences in operating room total time, operating time, and enucleation time. Mean total OR time in the control group was 133.2 minutes. The Lumenis Pulse™ 120H group had a mean total OR time of 165.8 minutes (p = 0.005). Mean operating time was 102.2 minutes in the control group versus 124.5 in the experimental group (p = 0.04). Mean enucleation time was 54.98 minutes in the control group and 68.79 minutes in the experimental group (p = 0.03). Other outcome variables showed no statistically significant differences. Mean resected weight was 46.44 grams in the control group versus 58.48 grams in the Lumenis Pulse™ 120H group (p = 0.25). Enucleation efficiency, the primary outcome, was similar between the two laser platforms noting .89 grams per minutes in the control group versus .84 grams per minutes in the Lumenis Pulse™ 120H group (p = 0.72). Postoperative outcomes were also similar between both groups.

Conclusions: The efficiency of the new Lumenis Pulse™ 120H laser platform is comparable to the 100 Watt VersaPulse Holmium laser platform in HoLEP tissue enucleation.

Source of Funding: None
THE SAFETY AND EFFICACY OF TRANSURETHRAL MICROWAVE THERAPY IN HIGH-RISK CATHETER DEPENDENT MEN AT A SINGLE VETERANS AFFAIRS CENTER

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Introduction: Catheter dependence for benign prostatic hypertrophy impairs quality of life and increases risk of urinary tract infection (UTI). Previous studies funded by manufacturers have demonstrated high efficacy of Transurethral Microwave Therapy (TUMT). Our primary goal was to assess the safety and efficacy of TUMT in a population of high-risk catheter dependent men.

Methods: A retrospective analysis of 157 patients who underwent TUMT at a single Veterans Affairs facility for treatment of benign prostatic hyperplasia was completed. The primary efficacy variable was success in catheter removal. We recorded time of follow up, types of anticoagulation, prostate size, time to patient death, and number of UTIs a year prior and a year post procedure. We also analyzed post-procedural complications to include bleeding events.

Results: 105 men were in urinary retention (requiring an indwelling urethral catheter or clean intermittent catheterization) prior to treatment. Mean age was 76.9 (95% CI 74.9 - 78.8) and median ASA-score was 3. Median follow up was 26 months (range 1 - 65). 63.7% were catheter free at their last follow up visit. Of the treated patients 38% (40/105) died due to unrelated causes during the follow up period and postoperative retention was not associated with increased risk of death on Kaplan-Meier Survival Estimate (figure). Surprisingly, prostate size was inversely associated with postoperative retention (mean prostate volume 60.6 ml vs 42.9 ml, p<0.04). No significant predictor of success was found in a multivariable analysis. The mean number of UTIs decreased from 1.98 to 1.22 after treatment. Despite 86% taking some type of anticoagulant perioperatively (including 25% on warfarin) only 2 men had hematuria requiring any type of treatment postoperatively. The 30-day postoperative complication rate was low, with readmission required in only 2 patients (1.9%).

Conclusions: Our results demonstrate that although not as efficacious as previously published, TUMT remains a safe therapeutic option to relieve high-risk catheter dependent men and may potentially decrease rates of UTI. The inverse relationship of prostate volume with catheter independance suggests non-obstructive causes of retention in TUMT failures.

Source of Funding: None
1 YEAR RESULTS OF A PROSPECTIVE STUDY TO CHARACTERIZE PATIENT EXPERIENCE AFTER PROSTATIC URETHRAL LIFT

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(Presentation to be made by Dr. Gange)

Introduction/Objectives: Prostatic Urethral Lift (PUL) has been offered to patients as a minimally invasive alternative to medical and surgical therapy for lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). Key advantages of this treatment option are rapid recovery and ability to be performed with local anesthesia in the office setting. We present for the first time the 1 year outcomes of a multicenter, prospective, non-randomized study that sought to characterize PUL patient experience.

Methods: 51 men were treated with PUL at 7 US centers. Enrollment criteria included AUASI (American Urological Association Symptom Index) >12, peak urinary flow rate (Qmax) ≤ 12 mL/s, and prostate volume ≤ 80cc. During the PUL procedure, small permanent transprostatic implants are placed to hold encroaching lobes in a retracted position and open the prostatic urethra. Patient experience was measured via validated instruments such as a pain VAS, the Quality of Recovery VAS (QoR VAS), AUASI, QoL, BPH Impact Index (BPHII), and Qmax.

Results: All procedures were successfully completed with local anesthesia. Visual analog scale (VAS) average pain was 4.8 ± 2.9 with rigid cystoscopy and 5.0 ± 3.0 during the PUL implantation. Adverse events related to PUL were typically mild to moderate and resolved by 2 weeks. There were no reported occurrences of new onset, sustained ejaculatory or erectile dysfunction. By 1 month, 86% of subjects were recovered (>80% QoR VAS) and 96% had returned to pre-operative activity. In addition, subjects experienced significant improvement in lower urinary tract symptoms, as demonstrated by AUASI, QoL, BPHII, and Qmax changes through 1 year.

Conclusions: The PUL procedure can provide rapid and significant improvements in symptoms, flow rate, and quality of life for men suffering from LUTS. PUL is well tolerated under local anesthesia with pain VAS comparable to rigid cystoscopy alone. Patients can quickly return to pre-operative activity and avoid new onset sexual problems. The results indicate that average AUASI improvement is over 11 points at 1 year, which is comparable to other published studies.

Source of Funding: NeoTract, Inc.
EVALUATING MRI FUSION BIOPSY VS SYSTEMATIC ULTRASOUND GUIDED BIOPSY IN PREDICTING HIGH GRADE CANCER AT TIME OF RADICAL PROSTATECTOMY

Background: There is much enthusiasm for multi-parametric MRI (mpMRI)-ultrasound fusion biopsy in those with an elevated PSA, a prior negative biopsy or those on active surveillance. However, the predictive value of MRI – targeted biopsy in predicting final cancer grade has not been well addressed. The uncertainties of both over staging and under staging using MRI fusion targeted biopsy have not been well addressed.

Objective: We aimed to evaluate the accuracy of cancer risk estimation with MRI fusion biopsy; traditional sextant and anterior (14 cores) ultrasound guided biopsy or the combination, using whole-mount histopathology at time of prostatectomy.

Methods: We retrospectively analyzed 98 patients who had radical prostatectomy in 2014-2016. All patients had undergone systematic ultrasound guided biopsy and mpMRI fusion biopsy. We compared Gleason Score (GS) upgrading or downgrading between MRI fusion and systematic ultrasound guided biopsy to that of the final Gleason score evaluated by whole-mount histopathological analysis. Logistic regression was used to evaluate association to adverse pathological outcome for each biopsy approach.

Results: Of 98 patients, cancer grade found on MRI fusion biopsy matched final pathology in 41% of the cases while it was overestimated in 20% of patients and underestimated in 39%. Cancer grade found on traditional systematic biopsy matched final pathology in 47% of patients while it overestimated grade in 36% and underestimated grade in 17% of patients with GS≥7. The highest Gleason score from combined MRI fusion and systematic biopsy only underestimated 10% of patients but overestimated grade in 39% of patients who had GS≥7 on their final pathology. In the logistic regression model, having a GS ≥ 3+4 detected on MRI fusion biopsy was associated with higher odds (OR: 3.5 95% CI 1.3-9.3, p <0.01) of higher stage cancer (≥pT3a) at RP. The association persisted when the model was adjusted for clinical CAPRA score. This study was limited by its retrospective nature.

Conclusion: Risk of over - staging using MRI fusion biopsy is low compared to systematic biopsy. However, MRI fusion biopsy alone could significantly underestimate those with clinically significant. Using MRI fusion biopsy alone to detect high grade cancer may not be adequate in this contemporary cohort. This data may have important implications for guiding treatment decisions.

*Equal contributions
UPDATE TWO YEARS LATER: COMPARATIVE EFFECTIVENESS OF TARGETED VS EMPIRICAL ANTIBIOTIC PROPHYLAXIS TO PREVENT SEPSIS FROM TRANSRECTAL PROSTATE BIOPSY: A RETROSPECTIVE ANALYSIS
Richard J Szabo MD Irvine, CA
To be presented by Dr. Szabo

Objective: This is an update of a retrospective review of a large multi-clinic quality improvement study comparing the incidence of post-biopsy sepsis in targeted and empiric prophylaxis groups.

Methods: Urologists of Southern California Kaiser Permanente chose either targeted antibiotic prophylaxis or empiric antibiotic prophylaxis for transrectal prostate biopsy and rates of post biopsy sepsis were studied over a three year period.
For targeted prophylaxis, a rectal culture was performed in the office not more than two weeks prior to prostate biopsy and the cultures were analyzed at a Central Microbiology Laboratory using CLSI definitions for ciprofloxacin resistance. In the targeted prophylaxis group, ciprofloxacin was used if the rectal flora was sensitive to ciprofloxacin. If the rectal flora was resistant to ciprofloxacin, physicians changed the prophylaxis to specific dosages of one of the following antibiotics based on the sensitivities of the rectal culture results and patient allergies: Oral Trimethoprim-Sulfamethoxazole, IM Ceftriaxone, IM Gentamycin, IM Amikacin, IM Aztreonam or IM Imipenem. In the empiric prophylaxis group, physicians followed their usual protocol of prophylaxis with one or more antibiotics, oral and/or parenteral. Outcomes were identified through the Epic electronic medical record common to all of the clinics, using the Epic “Clarity Report” to collate and filter data. The primary outcome analyzed was post-prostate biopsy sepsis defined by ICD9 code 995.91 or 995.92, confirmed by direct chart review. Retrospective data was analyzed using the chi-squared test.

Results: Between 5/1/2013 and 1/31/2016, a total of 13,913 transrectal prostate biopsy procedures were performed. The incidence of sepsis among all procedures was 0.53% (74/13913). There was no statistical difference in the incidence of sepsis between the targeted prophylaxis group (0.42%, 19/4497) and the empiric prophylaxis group (0.58%, 55/9416); (chi squared: p = 0.22). The incidence of sepsis did not increase over the almost 3 years studied.

Conclusions: We still detect no statistically significant difference in post transrectal prostate biopsy sepsis using a pre-biopsy rectal culture targeted prophylaxis protocol compared to empiric prophylaxis and over the last three years the sepsis rates in our large multi-clinic study have leveled off at about 0.5%. However, although these post biopsy sepsis rates are among the lowest in the literature, the failure of antibiotic prophylaxis to decrease the rate of sepsis to less than 1 in 200 has led some urologists to look for other methods to further decrease and even eliminate post biopsy sepsis altogether.
STANDARDIZED PROCESS MEASURES IMPROVE ANTIBIOTIC SELECTION FOR PROSTATE NEEDLE BIOPSY
Franklin Gaylis MD, Paul Dato MD, Renee Calabrese LVN, Hilary Prime, Jason Woo MD, Christopher Kane MD

**Purpose:** The use of dual or tailored antibiotics (according to prior rectal culture) decreases Prostate Needle Biopsy (PNB) septic complications and hospitalization. We compare adherence to a standardized process measure, Biopsy Timeout Template (BTT), and its impact on dual antibiotic selection at Genesis Healthcare Partners (GHP) an integrated urology practice.

**Methods:** Baseline dual antibiotic (DA) selection was measured for the year 2011 prior to implementing a standardized BTT and educating GHP physicians as to the benefits of dual antibiotics (2012). DA selection was measured, according to CPT injection (Gentamicin, Rocephin) claims based data following implementation of the first version of BTT (BTT v1) which called for antibiotic documentation without antibiotic specification. A second version of BTT (BTT v2) was introduced on April 18 of 2016, a collaborative effort between GHP and the Department of Urology, University of California, San Diego (UCSD), requiring specific documentation of DAs. In addition, a system of report cards representing adherence to the best practice and comparative physician reporting was introduced. Data was abstracted from the electronic medical record (AllscriptsTM).

**Results:** GHP physicians were surveyed as to their preference of DA or Tailored Antibiotics. 100% of responding physicians only use DA.

<table>
<thead>
<tr>
<th>Year of Study</th>
<th>PNB Volume</th>
<th>Timeout Completed</th>
<th>Injection Administered</th>
<th>Both Injection Billed and Template Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011 (pre Template)</td>
<td>717</td>
<td>0 (0%)</td>
<td>97 (13.53%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>2012 (BTT v1)</td>
<td>978</td>
<td>536 (54.81%)</td>
<td>(12.99%)</td>
<td>55 (5.62%)</td>
</tr>
<tr>
<td>2013 (BTT v1)</td>
<td>913</td>
<td>668 (73.17%)</td>
<td>346 (37.9%)</td>
<td>270 (29.57%)</td>
</tr>
<tr>
<td>2014 (BTT v1)</td>
<td>817</td>
<td>688 (84.21%)</td>
<td>647 (76.66%)</td>
<td>546 (64.69%)</td>
</tr>
<tr>
<td>2015 (BTT v1)</td>
<td>844</td>
<td>676 (80.09%)</td>
<td>212 (64.62%)</td>
<td></td>
</tr>
<tr>
<td>2016 (BTT v1)</td>
<td>260</td>
<td>206 (79.23%)</td>
<td>168 (64.62%)</td>
<td></td>
</tr>
<tr>
<td>2016 (BTT v2)</td>
<td>102</td>
<td>76 (74.51%)</td>
<td>94 (92.16%)</td>
<td>70 (68.63%)</td>
</tr>
</tbody>
</table>

"BTT v1" = Biopsy Timeout Template version 1; "BTT v2" = Biopsy Timeout Template version 2; “Injection Administered” denotes Gentamicin or Rocephin CPT billed codes.

**Conclusion:** Our findings demonstrate improvement in the use of a parenteral antibiotic (Gentamicin or Rocephin) since introduction of a best practice and standardized evidence based Biopsy Timeout Template. This practice change is likely to reduce the incidence of sepsis and the need for hospitalization which will be prospectively measured in the future. Adherence to the best practice is a standard urology quality measure for the UCSD/GHP Clinically Integrated Network in San Diego.
THE IMPACT OF GENETIC VARIATION IN SOLUTE CARRIER ORGANIC ANION (SLCO) ENCODED MEMBRANE TRANSPORTERS ON PROSTATE CANCER RECURRENCE POST RADICAL PROSTATECTOMY

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(Presentation to be made by Dr. Mazen Alsinnawi)

Objectives: Androgens play a major role in prostate cancer (PCa). Solute carrier organic anion (SLCO) encoded membrane transporters may facilitate androgen uptake into PCa cells. Genetic variation in SLCO genes has been linked to clinical outcomes. There is a need for novel biomarkers to identify patients at a higher risk for PCa recurrence post radical prostatectomy (RP). We hypothesized that genetic variants in SLCO genes associated with more efficient transporter uptake of intracellular androgens in residual cancer cells may be associated with a higher risk of relapse in men with localized / locally advanced PCa undergoing RP.

Methods: Twelve single nucleotide polymorphisms (SNPs) in 7 SLCO genes (including 1B1, 1B3, 2B1, 2A1, 4A1, 5A1, 6A1) were genotyped using TaqMan SNP assays. We also evaluated 5 SNPs in steroid-5α reductase genes (SRD5A1 & A2) with a previously published role in PCa. Binary recurrence within 10 years was compared across different genotypes using Fisher’s Exact Test. Unadjusted Kaplan-Meier curves for time to recurrence within 10 years were produced. Cox proportional hazards models were used to compare time to recurrence within 10 years by genotype, adjusted for Tumor Volume, Staging, Pre-RP PSA, Gleason grade, and whether surgical margins were positive.

Results: Genomic DNA was obtained from 147 patients with PCa who had RP (1995-2010) at the University of Washington. Longitudinal clinical follow up (median 60 months) yielded 67 patients with and 80 without evidence of BCR. We found a significant lower BCR risk in carriers of minor allele A versus major allele G homogenous carriers in SLCO2B1, SNP rs949069 (HR 0.46, 95% CI 0.21-0.99; p= 0.021), and in major allele A versus homogenous minor allele G in SRD5A1, SNP rs166050 (HR 0.34, 95% CI 0.17-0.69; p=0.008).

Conclusions: SLCO2B1 rs949069 (GG vs A allele) and SLCO6A1 rs10055840 (C allele vs. GG) were associated with risk of BCR post RP. We did not observe associations with the SLCO1B3 or SLCO2B1 SNPs associated with time to CRPC on ADT including the SLCO1B3 SNP associated with testosterone transport (rs4149117), or the SLCO2B1 SNPs associated with DHEAS uptake or 2B1 expression (rs12422149, rs1077858, respectively). SLCO-mediated androgen uptake may be more significant in determining progression in the castrate state, and may not necessarily impact relapse in the eugonadal state. This is consistent with the observation that testosterone inhibits DHEAS uptake by SLCO2B1, which would abrogate a clinical impact of this transporter on tissue androgen uptake in eugonadal men1.

INHIBITION OF ERG ACTIVITY IN PATIENT DERIVED PROSTATE CANCER XENOGRAFTS USING THE SMALL MOLECULE INHIBITOR YK-4-279

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Introduction: ERG is expressed in TMPRSS2-ERG fusion positive prostate cancer (PCA). We studied the effects of the ERG small molecule inhibitor YK-4-279 on ERG+ LuCaP PCa patient derived xenograft (PDX) lines.

Methods: We blocked ERG activity using YK-4-279 in three subcutaneously implanted ERG+ (LuCaP 23.1, 86.2, and 35) and one ERG- (LuCaP 96) PDX. Tumor volume (TV), body weight (BW), prostate specific antigen (PSA), and overall survival (OS) were compared to vehicle treated controls using unpaired t-tests. Changes in gene expression were assessed by RNASeq and tissue microarrays were constructed to assess necrosis, proliferation, apoptosis, microvessel density, and ERG expression.

Results: LuCaP 23.1 PDX displayed significant decreases in TV (p=0.026) and PSA (p=0.022). LuCaP 86.2 PDX showed a trend towards decreased TV (p=0.056) while changes in PSA were not significant. LuCaP 35 and LuCaP 96 showed no significant changes in TV, or PSA. Overall survival (OS) was significantly decreased in LuCaP 96 ERG- treated animals (p=0.025) whereas the ERG+ PDX lines showed no increases in OS. RNASeq determined mineralocorticoid receptor (MR) and direct target genes of the MR were upregulated in the treatment resistant LuCaP 35 and LuCaP 86.2 PDX lines.

Conclusions: YK-4-279 treatment decreased tumor growth in one of three ERG+ LuCaP PDX models. Decreased survival in the ERG-LuCaP 96 PDX suggests there was treatment associated toxicity, likely explaining the lack of survival benefit in the LuCaP 23.1 PDX. This study suggests that while blocking ERG can impact ERG+ tumors not all ERG+ tumors will respond to treatment.

Source of Funding: DOD Grant W81XWH-12-1-0399
INTRAPARENCHYMAL THERAPY DELIVERY IN THE PROSTATE: THE ROLE OF IMAGING AND DEVICE DESIGN

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(Presentation to be made by Dr. Hoang-Kim Le)

Introduction/Objectives: New protein toxin therapies directly injected into the prostate are in clinical trials for prostatic diseases. Other directly injectable treatments are envisaged as well. Due to the cytoarchitecture of the prostate, particularly in the presence of pathology, the infusates injected may have limited and variable distribution. We aim to elucidate the distribution of injected therapies as a function of prostate anatomy and physiology, and of device design.

Methods: Magnetic resonance (MR) contrast reagents were infused into ex vivo human prostates after surgical excision in standard of care therapy for invasive bladder cancer patients. MR images were acquired using sequences that permitted the quantification of tracer concentration. Further, a needle that uses a porous customizable length was tested and compared with that of a standard needle. The amount delivered, volume distribution, and backflow were compared.

Results: Analysis of MR images revealed considerable heterogeneity with infusion into the ex vivo specimens. There was likely very low resistance to flow along ductal pathways and very high resistance to flow at areas such as the interface of nodules and smooth muscle/fibrous parenchyma. The data confirms infusion loss via urethra and ductal channels. The porous needle yielded greater delivery of tracer, with the fraction of dose in the tissue significantly higher compared to standard needle (p=.03). The volume of distribution divided by the amount infused (Vd/Vi) increased by 80% with the porous needle, but that was not significant with the small sample size. Backflow was more common with the standard needle. The bridging of heterogeneity was apparent in the porous needle, but both methods failed to infuse across boundaries into cystic nodules.

Conclusions: This imaging study demonstrates that prostatic tissue is heterogeneous in its anatomy. This indicates that preoperative imaging and pre-infusion treatment planning to manage prostate fluid flow heterogeneity for consistent therapeutic results will be of increasing potential value. Diversity of paths of efflux away from prostatic tissue suggests porous needles may more efficiently distribute infusate to targeted regions than the standard needle.

Source of Funding: National Institutes of Health, the Institute of Diabetes and Digestive and Kidney Diseases (NIH/NIDDK).
RESULTS OF SERIAL TESTING OF A 17-GENE GENOMIC PROSTATE SCORE IN PROSTATE CANCER PATIENTS ON ACTIVE SURVEILLANCE

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(Presentation to be made by Dr. Samuel L. Washington III)

Introduction: Molecular assays are increasingly used to improve risk stratification in men with prostate cancer. There is no published data on how molecular test results change upon serial testing in men on active surveillance (AS), or whether changes in genomic profiling scores may be used to predict disease progression. Using pathologic specimens from 111 patients, we analyzed serial results for the Genomic Prostate Score (GPS), a biopsy based 17-gene expression RT-PCR assay, which is an independent predictor of the likelihood of favorable pathology (low grade, organ-confined disease) at surgery.

Methods: In a pilot study, retrospective GPS testing (scale 0-100) was performed on diagnostic (dBX) and first surveillance biopsies (sBX) from 40 men on AS and whose sBX showed no increase in Gleason score (GS). GPS test results were also analyzed from 71 patients who had repeat GPS testing done prospectively in the commercial laboratory. All analyses were pre-specified in a statistical analysis plan. Summary statistics with 95% confidence interval (CI) were reported. Survival analysis was performed with the outcome of undergoing active treatment defined as radical prostatectomy, radiation therapy or androgen deprivation therapy, with reporting of hazard ratios (HR) and 95% CI.

Results: Valid GPS results were obtained specimens in this combined study cohort (77 GS 3+3, 28 3+4 on dBX). More than half of patients had at least 18 months between biopsies (68%). The mean GPS was 24.4 at dBX and 27.4 at sBX resulting in a mean change of 3.03 (95% CI: 0.85-5.20). 39 patients (35%) had GPS increase of ≥6 GPS units; 19 (17%) had GPS increase of ≥12. An increase in NCCN clinical risk group between the 2 biopsies was noted in 79 patients (71%) while 32 (29%) did not reclassify. The mean GPS change was 2.29 (95% CI:-0.22-4.80) for the 79 men with increased NCCN, and 4.84 (95% CI: 0.39-9.30) for the 32 men without. On multivariate analysis adjusted for age at diagnosis, GPS score at second biopsy was associated with increased risk of undergoing active treatment such as radical prostatectomy, radiation or androgen deprivation therapy, with reporting of hazard ratios (HR 1.07, 95% CI 1.02-1.11, p<0.01), though magnitude of GPS change from baseline was not significantly associated with treatment.

Conclusions: Among patients with prostate cancer managed with AS, genomic profile scores, as assessed with a 17-gene RT-PCR assay, remained stable in the majority of patients. Scores appeared to be largely stable on serial biopsies with minimal change between the first and second biopsy. The last GPS appeared to predict a transition from AS to active treatment. Larger changes were observed in a proportion of patients, seen in both men with clinical reclassification and otherwise clinically stable disease. Further investigation is warranted to determine whether changes in genomic profiles may better precede the occurrence of disease progression and serve as an improved endpoint during surveillance.

Source of Funding: Genomic Health, Inc.
DEVELOPMENT AND VALIDATION OF AN ACTIVE SURVEILLANCE THRESHOLD BASED ON THE CCP SCORE AND CAPRA TO PREDICT RISK OF AGGRESSIVE DISEASE

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“Presentation to be made by Dr. Daniel W. Lin”

Objectives: Active surveillance (AS) is an appropriate and increasingly utilized treatment modality for men with localized prostate cancer. However, better risk stratification is needed to appropriately select men for AS. The cell cycle progression score (CCP score, based on measuring the expression levels of CCP genes) has proven to be a robust predictor of prostate cancer outcomes in various clinical settings, including in conservatively managed cohorts. Here, we present development and validation of potential AS thresholds based on a risk estimate that combines the CCP score with CAPRA (defined as the combined clinical-cell-cycle risk (CCR) score) to predict prostate cancer mortality (PCM) in men who are considering deferred treatment.

Methods: We evaluated two thresholds based on the CCR score. The first was developed using men who might typically be considered for AS based on AUA criteria (Gleason score ≤ 3+3, PSA < 10 ng/ml, < 25% cores positive, and clinical stage ≤ T2a); and the second was based on more liberal criteria described by NCCN guidelines which uses similar clinical characteristics as above but also includes Gleason score = 3+4. A CCR threshold score was selected such that 90% of the men in the training cohort had scores below the threshold (CCR = 0.6 for AUA criteria or CCR = 0.8 for modified NCCN criteria). The performance of both thresholds was evaluated in a validation cohort of men with prostate cancer who were initially conservatively managed (N=765), and in a consecutive series of 7,881 men who were submitted for commercial testing at Myriad Genetic Laboratories, Inc. Survival data were censored at 10 years.

Results: Both thresholds validated in the conservatively managed cohort, in that they dichotomized the cohort into high and low risk groups (log rank p-value = 0.012 and 0.00048 respectively). There were no deaths in patients below either threshold, and the Cox proportional hazard estimates of 10-year PCM associated with the CCR thresholds of 0.6 and 0.8 were 2.7% and 3.3%, respectively. Using the more liberal NCCN criteria for AS to evaluate the commercial cohort, 36% of the patients qualified based on clinical parameters alone. When applying the threshold of 0.8 to this cohort, 60% had CCR scores below the AS threshold and, therefore, had estimated risks of aggressive disease that were consistent with typical AS patients.

Conclusions: The thresholds presented here are based on an integrated risk assessment that combines both clinicopathologic and molecular features for a better prediction of disease outcome, and as such, could enable more appropriate selection of patients for AS.

Financial Disclosure: Study funded by Myriad Genetic Laboratories, Inc.
PROLARIS AND ONCOTYPE DX ARE VALUABLE PROGNOSTIC TESTS FOR RISK STRATIFICATION OF PROSTATE CANCER PATIENTS: A COMPARISON OF THESE TWO NEW TESTS

Michael A Maccini, MD; Priya N Werahera, PhD; Paul Arangua; Wendy Poage; Clifford Jones; E David Crawford MD

Introduction and Objective: The Prolaris and Oncotype Dx tests are new commercially available genetic tissue-based tests designed to aid in decision-making in patients with newly diagnosed prostate cancer. While the prognostic information provided by the two tests is different, the overall goal of both is the same: to provide additional information to allow the physician and patient to make more informed decisions and help identify and reduce overtreatment of low risk disease. The main objective of our study was to determine whether these two tests correlate well with each other in terms of clinical decision-making information provided.

Methods: We examined the medical records of 20 patients with prostate cancer who had undergone both Prolaris and Oncotype Dx tests. Both tests were performed in men who wanted confirmation from one of the tests. Patient PSA, TRUS biopsy results, AUA and NCCN risk levels, and genetic test results were collected. We compared test results and clinical outcomes for this cohort of patients. We used the worst prognosis when there were multiple indications depending on which biopsy cores were tested.

Results: The decision-making information provided by two tests was the same in 17 of 20 patients examined (85% concordance). In one patient the Prolaris test predicted a significantly more aggressive cancer than the Oncotype Dx test, while in the other two patients the reverse was observed. 14 patients elected intervention (surgery or radiation) based on their results, including 5 who underwent targeted focal cryotherapy. Men felt reassured by the confirmatory results of each test and the different outcomes defined.

Conclusions: The clinical utility of Prolaris and Oncotype Dx test results correlate well in the majority of cases. Either test can provide additional information for clinical-decision making in newly-diagnosed prostate cancer. Men requesting both tests felt reassured with their decisions for treatment.
DECIPHER TEST IMPACTS TREATMENT DECISION-MAKING AMONG PATIENTS WITH BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY: RESULTS FROM THE MULTICENTER PROSPECTIVE PRO-IMPACT STUDY


Introduction and Objective: Patients and providers have tremendous uncertainty as they decide on the appropriate timing for intervention with salvage radiation therapy (SRT) for suspected local recurrence after radical prostatectomy (RP). We prospectively evaluated the impact of the Decipher® test (GenomeDx Biosciences Inc., Vancouver), which predicts metastases after RP, on patient and provider decision quality.

Subjects and Methods: 115 salvage patients were enrolled by 43 urologists from 19 community and academic practices. We included patients with rising PSA after RP. Participating physicians provided a management recommendation before and after exposure to Decipher test results. Patients completed validated surveys on health-related quality of life, decisional conflict, and prostate cancer-related anxiety.

Results: Median patient age at enrollment was 63 years; 43% had pathologic T3 stage classification and 49% had positive surgical margins at RP. Decipher classified 33%, 25%, and 42% as low-, intermediate-, and high-risk, respectively. Pre-Decipher, 58.3%, 32.2% and 9.6% of patients were recommended for observation, SRT, and other treatments, respectively. 32% (95% CI 24-42%) of management recommendations changed post-Decipher, including 18% of Decipher low-risk patients and 50% of Decipher high-risk patients. Patients’ Decisional Conflict Scale (DCS) scores decreased (indicating higher decision quality) after exposure to Decipher test results (median DCS pre-Decipher 27 [IQR 16-41], post-Decipher DCS 23 [IQR 4-30], p<0.001), with greatest decreases in the subdomains of decision uncertainty and decision support. Patients with low-risk Decipher results experienced a significant reduction in prostate cancer anxiety (p=0.05). Among physicians, median DCS scores decreased from 33 [IQR 26-36] to 29 [IQR 22-34] (p<0.001). Decipher results were associated with the decision to pursue SRT and other treatments in multivariable logistic regression (OR 1.41; 95% CI 1.09-1.81, p=0.01).

Conclusions: Knowledge of Decipher results was associated with treatment decision-making among patients with recurrence after RP. Patients found to be low risk for metastases by Decipher had higher rates of observation recommendations and patients at high risk had higher rates of additional treatment recommendations including SRT. Decision quality was improved and prostate cancer-specific anxiety was decreased among patients considering SRT after RP exposed to Decipher results.

Funding Source: GenomeDx Biosciences Inc.
FAT INTAKE AFTER PROSTATE CANCER DIAGNOSIS AND RISK OF PROSTATE CANCER PROGRESSION: DATA FROM CAPSURE™


(Presentation to be made by Dr. Erin Van Blarigan)

Objectives: Recent studies suggest that men who consume high levels of saturated fat after prostate cancer diagnosis have higher risk of disease progression, while men who consume more fat from vegetable sources after diagnosis have lower risk of disease progression.

Methods: We prospectively examined saturated, monounsaturated, and polyunsaturated, as well as animal and vegetable fat, intakes after diagnosis in relation to risk of prostate cancer progression among 1,414 men initially diagnosed with non-metastatic prostate cancer in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™). Disease progression was defined as prostate cancer death, bone metastases from prostate cancer, biochemical recurrence, or initiation of secondary treatment. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using multivariate Cox Proportional Hazards regression adjusted for age, calories, time from diagnosis to the questionnaire, CAPRA score, smoking, body mass index, treatment, and walking pace.

Results: We observed 314 events of prostate cancer progression during a median follow-up of nine years. Men in the highest quartile of post-diagnostic saturated fat intake had a 92% increased risk of prostate cancer progression compared to men in the lowest quartile (HR: 1.92; 95% CI: 1.14, 3.25; p-trend: <0.01), independent of clinical, sociodemographic, and other lifestyle factors. The median saturated fat intake for men in the highest quartile was 35 g/d (range: 29-82 g/d); men in the lowest quartile consumed 13 g/d (range: 4-17 g/d). None of the other fats examined were statistically significantly associated with risk of prostate cancer progression.

Conclusion: Among men initially diagnosed with non-metastatic prostate cancer, higher intake of saturated fat may increase risk of prostate cancer progression.

Source of Funding: This work was supported by the US Department of Defense Prostate Cancer Research Program (W81XWH-13-2-0074, W81XWH-04-1-0850) and the NIH National Center for Advancing Translational Sciences (KL2TR000143).
OUTCOMES OF ACTIVE SURVEILLANCE FOR PROSTATE CANCER: UPDATES FROM EXTENDED FOLLOW-UP

Selma Masic, Michael S. Leapman, Janet E. Cowan, Peter R. Carroll

Purpose: Active surveillance (AS) is an increasingly utilized clinical management strategy for men with low-grade prostate cancer (PCa). Given the necessity to describe the long-term safety and efficacy of this approach, we report treatment-free rates and risk factors for disease reclassification in a large cohort of patients managed with AS at our institution.

Methods: We identified men enrolled in a prospectively followed AS cohort at our institution between 1990 and 2016. Patients were included based on a strict definition of low-risk disease (PSA<10 ng/ml, biopsy Gleason 3+3, cT stage 1/2, <=33% positive cores and <=50% of a single core) as well as a proportion of carefully selected men outside of these criteria. Kaplan-Meier plots were used to estimate reclassification-free (defined as any upgrade >=3+4 and as major upgrade >=4+3), treatment-free, and overall survival, and multivariable Cox proportional hazards regression was used to determine risk factors associated with outcomes. Among men who underwent delayed radical prostatectomy (RP), we evaluated risk of adverse surgical pathology (Gleason>=3+4, >=pT3a, pN1 or positive margins) with logistic regression.

Results: A total of 1,507 men were enrolled in our AS cohort, 929 were diagnosed with Gleason 3+3 or 3+4, underwent multiple biopsies or RP and were included in this analysis, with 653 (70%) meeting strict AS criteria. In our cohort, mean age was 61.37 ± 7.20 years, 86% of patients were white, 78% partnered, 70% clinical T-stage 1, with median PSA at diagnosis 5.40 ng/ml and median PSA density (PSAD) at diagnosis 0.13 ng/ml/cc. Median follow up was 59 months, and median time between biopsies 15 months. Median time to any upgrade was 26.4 months and median time to treatment was 73 months. At 5 years, any upgrade-free survival was 53%, major upgrade-free survival 83%, and treatment-free survival 61%. The 5-year overall survival was >99%. Factors associated with risk of any upgrade were age (HR 1.02 95%CI 1.01-1.04) and PSAD (log HR 2.09 95%CI 1.7-2.5), both p<0.01. Additionally, secondary Gleason pattern 4 (HR 2.8 95%CI 1.7-4.67) was associated with risk of major upgrade (p<0.01). PSAD was associated with risk of treatment (log HR 2.28 95% CI 1.91-2.72), p< 0.01. Factors associated with adverse pathology at radical prostatectomy were PSAD (log OR 2.2 95%CI 1.2-4.0) and total number of biopsies (OR 1.8 95%CI 1.3-2.6), both p< 0.01. One patient died from a non-PCa related cause (<1%), and none died from PCa. Three patients (<1%) had bone metastases at 5 years.

Conclusions: In the appropriately selected patient, AS is a safe and effective clinical management strategy with rare metastatic events and disease-specific deaths. Age and PSAD are risk factors for disease reclassification, and PSAD is a risk factor for treatment. Secondary Gleason 4 and number of biopsies play a role in reclassification and adverse pathology, respectively.
PATIENT-REPORTED PERIOPERATIVE SYMPTOMS FROM PLACEMENT OF POLYETHYLENE GLYCOL HYDROGEL SPAKER AND CARBON FIDUCIAL MARKER IMPLANTATION IN ANTICIPATION TO PROTON BEAM THERAPY FOR PROSTATE CANCER

Rafael Nuñez-Nateras M.D., Nicholas Jacob B.S.*, Sean Mc Adams M.D. and Mitchell R Humphreys M.D. (Presentation to be given by Dr. Nuñez-Nateras)

Objectives: Proton beam therapy is one of the treatment options for localized prostate cancer. It is known that its success in cancer control comes with a cost in rectal toxicity. The use of polyethylene glycol hydrogel (PEG) spacer has shown to be an effective method to spare the rectum from radiation toxicity. Here we report our initial experience in patient symptomatology after injection of PEG spacer at the time of carbon fiducial marker implantation in anticipation to proton beam therapy for prostate cancer.

Methods: We performed a retrospective review of our prospectively maintained prostate cancer database. All patients with localized prostate cancer who have undergone injection of PEG spacer at the time of carbon fiducial marker implantation were included. All patients have completed a survey that included AUA SI, EPIC and SHIM questionnaires, and 5 investigator generated questions at two time points: before the procedure and at 1 month after the procedure or right before the initiation of radiotherapy. Results are presented as medians with minimum and maximum values. All variables were analyzed with non-parametric tests using commercially available software (SPSS vs, 21, Chicago, Illinois).

Results: A total of 11 patients were analyzed. Median patient age was 74 years old (62 – 81) and BMI was 29 mg/kg² (22 – 42.6 mg/kg²). Two patients required a double injection of the PEG spacer: one due to a failure of the PEG gel to create a symmetric space, and in the second patient due to a very large prostate that required a higher volume to create an adequate plane. No rectal perforations occurred. Two patients developed hematuria that resolved 3 days after the procedure. In terms of reported outcomes, patients experienced no significant change with AUA SI, Bother score, or with SHIM (detailed results in table below). Additionally, no patient experienced a change in their bowel symptom score.

Conclusion: Transrectal ultrasound-guided placement of PEG spacer at the time of carbon fiducial marker implantation fiducial marker insertion is well tolerated. The sample size analyzed limits the power of the observations, however findings are encouraging.

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PATIENT REPORTED COMPARATIVE EFFECTIVENESS OF CONTEMPORARY INTENSITY MODULATED RADIOTHERAPY VERSUS EXTERNAL BEAM RADIOTHERAPY OF THE MID-1990’S

Brock O’Neil MD, Karen E. Hoffman MD MPH, Matthew J. Resnick MD MPH, David F. Penson MD MPH and Daniel A. Barocas MD MPH

Salt Lake City, UT; b. Houston, TX; c. Nashville, TN;

Presentation to be made by Dr. O’Neil

Objective: Little is known about differences in patient reported outcomes between contemporary external beam radiotherapy (EBRT) that delivers higher doses of conformal radiation and older techniques. This study examined sexual, urinary, and bowel function between men undergoing contemporary intensity modulated radiotherapy (IMRT) versus those undergoing EBRT in the mid-1990s.

Methods: Subjects treated with EBRT for prostate cancer were selected from two large population-based prospective cohort studies. Subjects completed baseline, 6, and 12 month standardized patient-reported outcome measures. Main outcomes were between-group differences in scores at 6 and 12 months after adjusting for baseline differences. Secondary analyses examined adjusted odds ratios comparing groups reporting a clinically significant decline in each domain of interest.

Results: The cohort consisted of 943 men, 467 diagnosed in 2011-2012 and 476 diagnosed in 1994-1995. Men undergoing contemporary IMRT reported better bowel function at 6 months (mean difference 4.3 points, 95% CI 1.6 to 7.0) but not at 12 months. Contemporary IMRT subjects reported statistically worse, but probably not clinically meaningful different urinary function at 12 months (2.7; 0.5 to 4.8 points lower), and no difference at 6 months. No between-group differences in sexual function at 6 or 12 months were found. Secondary analyses confirmed better outcomes for contemporary IMRT with lower odds of reporting clinically meaningful declines in bowel function at 6 and 12 months and sexual function at 12 months. However, IMRT subjects had higher odds of reporting clinically meaningful declines in urinary continence at 12 months.

Conclusion: Despite delivery of higher doses with contemporary IMRT, men treated with contemporary IMRT reported fewer gastrointestinal, and possibly fewer sexual side effects than men treated with EBRT in the mid-1990s. However, delivery of dose-escalated IMRT may cause more urinary side effects.

Funding: This study was supported by the US Agency for Healthcare Research and Quality (grants 1R01HS019356 and 1R01HS022640-01); the National Cancer Institute, National Institutes of Health (grant R01-CA114524) and through a contract from the Patient-Centered Outcomes Research Institute.
INTRODUCTION: The presence of accessory pudendal arteries (APAs) is well-documented; however the need for their preservation remains unsettled. Due to stapling of the DVC in our technique, all APAs were transected. We prospectively evaluated potency outcomes in men undergoing RARP with and without APAs.

METHODS: 878 men undergoing RARP (2007-2014) had intraoperative mapping of all APAs. Excluded men: SHIM <15 (n= 157), adjuvant therapies, etc. (n=140) leaving 581 for analysis. Self-reported sexual function was assessed 3 ways: 1. Potency (Yes/Yes): "Yes- to erections firm enough for penetration" and "Yes-Are they satisfactory" 2. SHIM score, and 3. % Erection Firmness compared to pre-op. Results between groups were evaluated with t-tests, ANOVA and unadjusted odds ratios.

RESULTS: Of the 193 (33.2%) men with APAs, had either one APA, 22.6% or ≥2 APAs, 10.6%. The no-APA to APA groups were equivalent for demographics and follow-up time, see Table 1. Odds ratios for recovery of potency using all 3 methods of assessment showed no reduction in sexual function among men with 1, 2, or no APAs, see Table 2. By ANOVA, there were no differences between men with no APAs, 1 APA, or 2 APAs in pre or post-operative demographics, potency, SHIM scores, or fullness of erections (P value >0.10). Men who had bilateral APAs resected had no difference compared to no-APA for any of the 3 potency parameters (all p≥0.86). We further assessed the influence of advancing age and SHIM conjunctively through subgroup analysis (<65 + 15-21, <65 22-25, >65 + 15-21, and >65 + 22-25), and again found no differences in baseline demographics or postoperative recovery of potency, SHIM scores, or fullness of erections.

CONCLUSIONS: We prospectively assessed men undergoing RARP without APAs and with transected APAs demonstrating no difference in potency recovery. This held true for advancing age, number of arteries and ED. Our experience strongly supports that recovery of potency is not negatively impacted by the sacrifice of APAs during RARP.
EXTENDED PELVIC LYMPHADENECTOMY IN PATIENTS UNDERGOING RADICAL PROSTATECTOMY: A RETROSPECTIVE ANALYSIS OF INTRAOPERATIVE AND POSTOPERATIVE COMPLICATIONS

Section of Urology, Department of Surgery, University of Manitoba, Winnipeg, Manitoba, Canada

Background: Extended pelvic lymphadenectomy is considered the gold standard for the detection of occult lymph node metastases in patients undergoing radical prostatectomy. Current literature suggests that due to higher complication rates, this procedure should be reserved for men with medium to high-risk disease. Common complications generally associated with extended pelvic lymphadenectomy include neurovascular injury, ureteral injury, thromboembolic events and lymphocele formation.

Objective: To assess whether certain operative and pathological staging variables are independent risk factors for intraoperative and postoperative complications in patients undergoing extended pelvic lymphadenectomy.

Methods: 470 men having undergone radical prostatectomy with extended pelvic lymphadenectomy were considered from January 2003 to March 2014. Of all 470 subjects, 440 had complete pathological and perioperative data available for analysis. Preoperative clinical variables (PSA, Gleason sum), pathological variables (pathological stage, node positivity, margin positivity, total core length) and intraoperative variables (operator, number of lymph nodes sent for pathology) were collected. Intraoperative and postoperative complications were collected and organized according to Clavien-Dindo recorded. Univariate and multivariate analyses were conducted using SAS software.

Results: Of all subjects analyzed, the rate of intraoperative and postoperative complication was 28.2% (124 of 440). When stratified by Clavien-Dindo classification, our series demonstrated 11 (8.9%) Clavien I, 84 (67.7%) Clavien II, 42 (33.9%) Clavien IIIA, 5 (4.0%) Clavien IIIB and 2 (1.6%) Clavien IVA complications in total. There were no Clavien IVB or Clavien V complications encountered. The incidence of lymphocele formation, neurovascular injury, thromboembolic events, and ureteral injury was 0.68% (3), 0.23% (1), 1.14% (5) and 0.45% (2) respectively (2.27% total). These are complications traditionally associated with extended pelvic lymphadenectomy. Univariate and multivariate analyses determined that operator/surgeon (p<0.0001) was the only statistically significant variable in terms of predicting complications. Univariate and multivariate analysis of the total number of intraoperative lymph nodes harvested is still pending.

Conclusion: With the exception of surgeon/operator, our data suggests there are no preoperative, pathological, or intraoperative variables that can reliably predict complication rates in patients undergoing RP with extended BPLNLD. However, the majority of reported complications were ≤ Clavien II, and dependent on the degree of follow-up and documentation. There were no statistically significant differences observed for complications ≥ Clavien III. Analysis including the total number of intraoperative lymph nodes harvested is still pending.
THE IMPACT OF OF LYMPH NODES COUNT AND ADJUVANT THERAPY ON ONCOLOGIC OUTCOMES IN MEN WITH LYMPH NODE METASTASIS AT THE TIME OF RADICAL PROSTATECTOMY

Hao G. Nguyen MD, PhD, Janet E. Cowan MS, Michael Leapman MD, and Peter R. Carroll MD, MPH

1Department of Urology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, California, USA

Background: While pelvic lymph node dissection (PLND) offers prognostic value at time of diagnosis for patients with intermediate and high risk prostate cancer, the survival benefit of PLND at radical prostatectomy (RP) is still unclear. In addition, data is limited regarding the value of adding adjuvant radiotherapy in the setting of positive lymph node metastasis.

Objective: To evaluate associations between oncologic outcomes and nodal count in patients with positive nodes at RP (pN1). Secondary objective is to determine any association between adding adjuvant therapy in patients with lymph node metastasis (pN1+) and improved oncologic outcomes.

Method: We analyzed 10,733 men who underwent RP between 1990-2015 at multiple institutions (43 CAPSURE study sites and UCSF Department of Urology), 6,789 of whom had PLND. Median follow up after RP was 56 months. Outcomes after RP were biochemical recurrence-free survival (RFS), bone metastasis-free survival (MFS) and cancer-specific survival (CSS). The associations between adjuvant treatment (none, radiation, ADT), number of nodes dissected, and surgical CAPRA risk score and oncologic outcomes were analyzed using Cox regression models. Analyses were repeated for the subgroup of 254 patients with pN1+.

Results and limitations: Among the 6,789 men who had PLND, men with positive nodes had worse pathological staging, cancer grade (Gleason score) and oncological outcomes at 5 years after RP compared to those with pN0 (BCR: 96% vs 80%, MFS: 99% vs 90%, CSS: 99% vs 97%, all log rank p<0.01). Of the 254 men (4%) who had positive lymph node at RP, the median number of LN removed was 12 (interquartile range (IQR) 7-18) and the median number of positive LN was 1 (IQR 1-2). The nodal count as a continuous variable or with cutoff of less or more than 14 did not show any significant association with oncologic outcomes in node positive men. BCR, MFS and CSS for pN1+ patients who received adjuvant therapy in the forms of ADT, XRT or combination did not differ significantly from patients without adjuvant therapy. Main limitation was the small sample size of pN1 patients and retrospective nature of the analysis.

Conclusions: In a multi-institutional analysis, we found that patients with positive lymph nodes had worse outcomes. In patients with lymph node metastasis, neither nodal count nor adjuvant therapy was associated with better outcomes.
INTENSE EXERCISE FOR SURVIVAL AMONG MEN WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER (INTERVAL-MCRPC): A MOVEMBER FUNDED MULTICENTER, RANDOMIZED, CONTROLLED PHASE III STUDY


Montreal, QC; San Francisco, California; Perth, Melbourne, and Canberra Australia; Edmonton, AB; Sheffield, UK; Dublin, Ireland; Bristol, UK; San Antonio, TX; Boston, MA; Seattle, WA | Presentation to be made by Dr. Kenfield

Objective: Provocative evidence supports the beneficial role of physical activity on prostate cancer survivorship. Evaluating exercise as a low-toxicity adjuvant intervention that can be combined with standard therapy to improve outcomes in men with prostate cancer could reduce the clinical and public health burden of the disease. Exercise may affect prostate cancer survival via inflammation, hormonal, and energy metabolism pathways. Our goal is to compare overall survival (OS) among men with MCRPC randomly assigned to psychosocial support +/- high intensity aerobic and resistance training for 96 weeks. Secondary outcomes include: time to disease progression, occurrence of a skeletal-related event, or progression of pain; and degree of pain, opiate use, and physical and emotional quality of life.

Methods: We will assess if inflammation, dysregulation of insulin and energy metabolism, and androgen biomarkers are associated with OS, and if they mediate the primary association between exercise and OS. The study will establish a biobank for future biomarker discovery or validation. This multi-site global trial will include MCRPC patients who are treatment naïve or on abiraterone and/or enzalutamide without evidence of progression at enrolment. Patients will be randomized (1:1) to psychosocial support +/- high intensity aerobic and resistance training. The first 48 weeks of training will include a structured period of tapered supervised exercise with increasing self-managed exercise and behavioral support with text messages, to support self-management for an additional 48 weeks. Exercise prescriptions will be tailored to participant's fitness and cancer/treatment morbidities.

Results: Assuming a median OS of 33.5 months in the controls, the sample size to detect a hazard ratio of 0.78 with 80% power at significance level of 0.05 is 824; assuming missing data on OS for 5%, we aim to enroll 866 men. To date, 18 sites in 7 countries are participating. Currently, our pilot site in Perth, Australia is IRB-approved and 2 patients have been randomized. We are seeking additional sites for this trial.

Conclusions: This is the first prospective randomized trial to examine exercise and survival in men with prostate cancer; and is designed to elucidate the mechanisms by which exercise delays cancer progression.

Funding Source: Movember Foundation
IMAAGEN TRIAL SAFETY AND EFFICACY UPDATE: EFFECT OF ABIRATERONE ACETATE AND LOW-DOSE PREDNISONE ON PROSTATE-SPECIFIC ANTIGEN AND RADIOGRAPHIC DISEASE PROGRESSION IN PATIENTS WITH NONMETASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Charles J. Ryan*, MD, E. David Crawford, MD, Neal D. Shore, MD, Willie Underwood III, MD, MPH, MSci, Mary-Ellen Taplin*, MD, Anil Londhe*, PhD, Peter St. John Francis*, MD, MBA, Jennifer Phillips*, PhD, Tracy McGowan*, MD, Philip W. Kantoff*, MD; San Francisco, CA; Aurora, CO; Myrtle Beach, SC; Buffalo, NY; Boston, MA; Horsham, PA; Horsham, PA; New York, NY (Presentation to be made by Dr. Tracy McGowan)

Objectives: IMAAGEN is a phase-2, multicenter study evaluating abiraterone acetate (AA) 1000mg plus prednisone 5mg (AA+P5) for the treatment of patients with nonmetastatic castration-resistant prostate cancer (nmCRPC). The primary endpoint was proportion of patients with ≥50% decrease in prostate-specific antigen (PSA) levels after 6 treatment cycles. Herein, we report updated results on secondary endpoints and safety from the IMAAGEN study (database cutoff: Oct. 2015).

Methods: All enrolled patients had high-risk nmCRPC: PSA ≥10ng/mL or PSA doubling time ≤10 months at screening. Patients received AA+P5 daily; treatment cycles were 28 days. Secondary endpoints included time to PSA progression, time to radiographic progressive disease, and safety.

Results: At the time of database cutoff, 44 (33.6%) of the 131 enrolled patients remained on study treatment, and Kaplan-Meier estimate of median follow-up was 40.0 months. Mean age was 72 (48-90) years. Median time to PSA progression was 28.7 months (95% CI 21.2, 38.2). With 31 confirmed progression events, the median time to radiographic progressive disease was not reached; however, in a sensitivity analysis including 15 additional unconfirmed progressions that led to initiation of new therapy, the median time to radiographic progressive disease was 41.4 months (95% CI 27.6, NE). 96.2% of patients had an adverse event (AE) (61.1% had a Grade ≥3 AE) and 43.5% had a serious AE (SAE) (41.2% had a Grade ≥3 SAE). 15.3% of patients had AEs resulting in study treatment discontinuation. Seven patients had AEs resulting in death.

Conclusions: Treatment of high-risk nmCRPC patients with AA+P5 resulted in a median time to PSA progression of 28.7 months and a median time to radiographic progressive disease of 41.4 months. The safety profile of AA+P5 reported in this update is consistent with the safety profile from previously reported studies of AA 1000mg in combination with either 5 or 10mg prednisone.

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ANALYSIS OF OVERALL SURVIVAL BY NUMBER OF RADIUM-223 INJECTIONS RECEIVED IN AN INTERNATIONAL EXPANDED ACCESS PROGRAM (IEAP)

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(Presentation to be made by Dr. S. Malone)

Background: In ALSYMPCA, 6 injections (inj) of radium-223 (Ra-223) at 50 kBq/kg v placebo, improved overall survival (OS) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). Early identification of pts likely to receive the planned 6 inj of radium-223 is important. Here are OS analyses by number of Ra-223 inj from iEAP and ALSYMPCA, including prognostic factors associated with 1-4 v 5-6 inj, respectively.

Materials and Methods: The open-label, single-arm, phase 3b iEAP provided Ra-223 to bone-predominant mCRPC pts. OS was analyzed post hoc by number of Ra-223 inj (1-4 v 5-6) and compared with ALSYMPCA data. Stepwise logistic and stepwise Cox regression analyses of number of inj and OS, respectively, were done.

Results: Baseline characteristics for iEAP v ALSYMPCA pts are presented (Table). In iEAP, median (med) OS was 6.3 mo in pts with 1-4 inj and not reached with 5-6 inj. In ALSYMPCA, med OS was 6.2 mo in pts with 1-4 inj and 17.9 mo with 5-6 inj. In a logistic regression analysis from iEAP, receipt of 5-6 inj was associated with less pain (none-mild v moderate-severe; P<.0001), lower ECOG score (0-1 v ≥2; P=.0081), lower PSA level (med <141 µg/L v ≥141 µg/L; P<.0001), and higher Hgb (≥10 g/dL v <10 g/dL; P=.0227) at baseline. Stepwise Cox regression analysis showed that 5-6 inj was associated with longer OS (P<.0001).

Conclusions: These exploratory analyses suggest that pts with less pain, lower ECOG score, lower PSA level, and higher Hgb level at baseline are more likely to receive 5-6 Ra-223 inj. A prospective randomized trial is needed to confirm a causal relationship between number of inj and OS.

Source of Funding: None
IMMUNOGENICITY OF SIPULEUCEL-T (SIP-T) IN ABIRATERONE (ABI)/ENZALUTAMIDE (ENZ) SENSITIVE AND RESISTANT METASTATIC CASTRATE-RESISTANT PROSTATE CANCER (MCRPC)

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(Presentation to be made by Lawrence Karsh)

Objective: Immune responses to Sip-T in mCRPC patients (pts) correlate with survival (NEJM 2010;363:411). Adding Abi or Enz to Sip-T does not blunt Sip-T immune responses (CCR 2015;21:3862; JCO 2015;33 suppl:abs 5040). It is unknown if pts with primary resistance (1°res) to Abi or Enz have impaired Sip-T immune responses.

Methods: STAMP (NCT01487863) and STRIDE (NCT01981122) are similar randomized phase 2 studies. mCRPC pts received Abi (n=69) or Enz (n=52) concurrently (Con) with or sequentially (Seq) after Sip-T. In vitro immune activation was assessed by antigen presenting cell (APC) activation in each Sip-T product. In vivo immune responses were assessed by cellular (ELISPOT and proliferation assays) and humoral (ELISA) immune responses to target antigens PA2024 and PAP. Pts with a PSA decline from baseline (BL) of ≥50% were defined as Abi/Enz sensitive (sens); those with <50% PSA decline had 1° res. Immune responses in Abi/Enz sens and 1° res pts were retrospectively analyzed, in each trial, in pooled Con vs Seq arms across trials, and for all pooled data.

Results: The % of pts with Abi/Enz sens was similar across pooled arms (Con: 72%; Seq 68%). No differences were seen in in vitro or in vivo immune responses for Abi/Enz sens vs 1° res pts at any time point (see Table).

<table>
<thead>
<tr>
<th>All pooled data</th>
<th>Abi/Enz sens (n=82)</th>
<th>Abi/Enz 1° res (n=35)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69 (43–88)</td>
<td>74 (57–91)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gleason sum ≥8, n (%)</td>
<td>51 (64)</td>
<td>19 (56)</td>
<td>NS</td>
</tr>
<tr>
<td>BL PSA, ng/mL</td>
<td>13 (5–49)</td>
<td>31 (10–66)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BL LDH, U/L</td>
<td>187 (161–214)</td>
<td>199 (164–218)</td>
<td>NS</td>
</tr>
<tr>
<td>Cumulative APC activation*</td>
<td>35.5 (26.7–43.5)</td>
<td>34.5 (28.6–43.9)</td>
<td>NS</td>
</tr>
<tr>
<td>T cell ELISPOT count*</td>
<td>16.3 (3.7–94.7)</td>
<td>13.8 (0.7–46)</td>
<td>NS</td>
</tr>
<tr>
<td>T cell proliferation stimulation index*</td>
<td>10.9 (3.8–24.2)</td>
<td>8.7 (4.0–21.8)</td>
<td>NS*</td>
</tr>
<tr>
<td>Antibody titers (ELISA)*, x10³</td>
<td>51.2 (12.8–102.4)</td>
<td>25.6 (6.4–102.4)</td>
<td></td>
</tr>
</tbody>
</table>

Median (range/IQR); (%); ⁶wk 6 for PA2024; ⁷NS = not statistically significant at any time point, i.e. BL, wks 2, 4, 6, 10, 14, 20, 26, 40, 52, 56 for PA2024 and PAP (data not shown)

Conclusions: The magnitude of in vitro and in vivo immune responses after Sip-T appear to be independent of androgen sensitivity (i.e. PSA decline) to Abi or Enz, suggesting that Sip T therapy may have a role in pts with primary Abi or Enz resistance.

Source of Funding: Dendreon Pharmaceuticals, Inc.

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