Prostate Cancer

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GOALS

- Epidemiology, Screening and Prevention
- Risk Stratification
- Treatment of Early and High Risk Disease
- Hormonal Therapy
- Treatment of Advanced Disease
Percent of New Cases by Age Group: Prostate Cancer

Prostate cancer is most frequently diagnosed among men aged 65-74.

Median Age At Diagnosis

66

SEER 18 2008-2012, All Races, Males
The percent of prostate cancer deaths is highest among men aged 75-84.

Median Age At Death

80

U.S. 2008-2012, All Races, Males
Chemoprevention

5 ARIs reduce risk of prostate cancer but long term effects are not yet known.

- FDA has chosen not to approve
- Long term effect on survival and toxicity?
Does PSA based Screening Reduce Mortality?

• PLCO
• ERSPC study
• Göteborg study
Randomized Screening Studies for Prostate Cancer

- **PLCO (NEJM 2009)**
  - 150,000 men
  - 52% contamination
  - Median follow-up of 7 years
  - No difference in prostate cancer mortality

- **European Screening Study (NEJM 2009)**
  - 162,243 men
  - Median follow up of 9 years
  - 20% reduction in prostate cancer mortality $p=0.04$
  - NNT- 48 needed to be treated to prevent 1 death

- **Göteborg screening trial (Lancet Oncology 2010)**
  - 20,000 men
  - Median follow-up of 14 years
  - 44% reduction in prostate cancer mortality ($p=0.0002$).
  - NNT-12 needed to be treated to prevent 1 death
Conclusions

• Low mortality of prostate cancer in first 10 years (few events)

• PSA screening probably reduces mortality but longer follow-up needed

• Apparent large amount of over-diagnosis and overtreatment (at least as seen in first 10 years)
Impact of USPTF on Screening

National Prostate Cancer Screening Rates After the 2012 US Preventive Services Task Force Recommendation Discouraging Prostate-Specific Antigen–Based Screening

Michael W. Drazer, Dezheng Huo, and Scott E. Eggener
Diagnosis Suspected

- Abnormal PSA
- Abnormal DRE
- CaP detected on TURP
Gleason's Pattern

1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation

Well differentiated

Moderately differentiated

Poorly diff./Anaplastic
Risk Groups

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>PSA Range</th>
<th>Gleason Range</th>
<th>Stage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>PSA &lt; 10</td>
<td>Gleason &lt; 7</td>
<td>T1c or T2a</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>PSA 10-20</td>
<td>Gleason 7</td>
<td>T2b</td>
</tr>
<tr>
<td>Poor Risk</td>
<td>PSA &gt; 20</td>
<td>Gleason &gt; 7</td>
<td>T2c</td>
</tr>
</tbody>
</table>
• Bone scan and CT scan
  – Only required in intermediate and poor risk patients
ONCOTYPE DX

- Genomic Health
- 17 gene signature
- Stratifying Low risk and Intermediate risk disease
Treatment Choices

- No treatment-Active surveillance
- Radical prostatectomy
- Radiation
  - External beam-conformal
  - Brachytherapy-seeds
  - Neutrons
  - Protons
- Hormonal therapy
- Combination therapies
Outcome of Surgically Treated Patients

- **The cohort**: 24,441 patients who underwent RP between 1987-2005 at:
  - Cleveland Clinic
  - MSKCC
  - Baylor College of Medicine
  - University of Michigan
  - JHH

- All pathological specimens reviewed by genitourinary pathologists at each institution

- Endpoint: Prostate cancer mortality

Stephenson et al. *J. Clin Onc* 2009
- **Gleason 8-10**: 10% of all cases
  - 49% 15-year PCSM
  - 45% of all cancer deaths
- **Gleason 7**: 40% of all cases
  - 8% 15-year PCSM
  - 50% of all cancer deaths
- **Gleason 6**: 50% of all cases
  - <1% 15-year PCSM
  - 1 of 3756 patients with organ-confined, Gleason 6 cancer has died of prostate cancer
Long-term outcome of AS

Long-Term Follow-Up of a Large Active Surveillance Cohort of Patients With Prostate Cancer

Laurence Klotz, Danny Vesprini, Perakaa Sethukavalan, Vibhuti Jethava, Liying Zhang, Suneil Jain, Toshihiro Yamamoto, Alexandre Mamedov, and Andrew Loblaw
Remaining on AS  

CS survival

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**Graphs showing survival rates over time:**

- **Remaining Alive and on Surveillance (probability):**
  - Time (years): 0, 2, 4, 6, 8, 10, 12, 14, 16
  - No. at risk: 993, 804, 564, 375, 219, 120, 69, 38, 11

- **Cause-Specific Survival (probability):**
  - Time (years): 0, 2, 4, 6, 8, 10, 12, 14, 16
  - No. at risk: 993, 889, 712, 532, 353, 206, 132, 70, 22

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Presented By Fred Saad at Genitourinary Cancers Symposium 2016
Conclusions

- Active surveillance for favorable-risk prostate cancer is feasible and seems safe in the 15-year time frame.
- 2.8% developed metastatic disease, 1.5% died of PCa.
- Mortality rate is consistent with expected mortality in favorable-risk patients managed with initial definitive intervention.
Multimodality Treatment: High Risk Disease
EBRT vs EBRT + 3 Years HT: EORTC Trial 2002

Overall Survival (%)

Log-rank test $P<.0001$
Hazard ratio 0.51
(95% CI, 0.36–0.73)

Time Since Randomization (Years)

Summary-Locally Advanced Tumors: XRT + ADT

- Overall survival
  3 years or longer provides benefit

- Prolonged duration needs to be balanced with side effects
Multimodality Therapy: What about Patients with Intermediate and High Risk but Localized Disease (T1-2)
XRT vs. XRT + ADT for Intermediate and High Risk Patients

- 205 patients with PSA > 10 or Gleason > 6
- Randomized to XRT or XRT + 6 months of ADT
- Median follow-up 7.6 years
- Overall survival HR = 1.8 (p = 0.01)
- PCSM HR = 4.1 (p = 0.01)

D’Amico et al JAMA 2008
Overall Survival

D’Amico et al JAMA 2008
Adjuvant Therapy

• Adjuvant radiation i.e. radiation post radical prostatectomy in high risk patients
  – Two studies demonstrating OS benefit
  – ? Should be considered standard of care

• Adjuvant chemotherapy
  – No proven benefit
  – Several randomized trials underway (docetaxel)

• Adjuvant ADT
  – No proven benefit
Immediate hormonal therapy improves survival in node positive patients

Randomized trial
98 patients
Nodal metastases

**Messing EM, et al. Lancet Oncol. 2006**
Adjuvant Hormone Ablation
ECOG 3886: Results at 10 Years

Prostate Cancer-specific Survival

Log Rank Test $P < .001$

Survival Probability

Survival Time (months)

Immediate Hormones

Delayed Hormones

<table>
<thead>
<tr>
<th></th>
<th>TOTAL</th>
<th>DEAD</th>
<th>ALIVE</th>
<th>MEDIAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Hormones</td>
<td>47</td>
<td>7</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Delayed Hormones</td>
<td>51</td>
<td>24</td>
<td>27</td>
<td>136.1</td>
</tr>
</tbody>
</table>
Natural History of Prostate Cancer

Under the care of ONCOLOGIST

Castrate Sensitive
Asymptomatic
Non Metastatic

Castrate Resistant
Symptomatic
Metastatic

Local Therapy
Androgen Deprivation
Therapies After LHRH Agonists
Chemotherapy

12 mths
12 to 48 mths
15 to 20 + years

Death
Postchemo

Castrate Sensitive
Castrate Resistant
Natural History Of Rising PSA

- 304 men relapsed after surgery
- No hormones until (+) bone scan
- Time to PSA rise, Gleason, PSADT were predictors of survival

Pound JAMA 1999
Patients with a Rising PSA - Importance of PSADT

Freedland SJ, et al. JAMA. 2005
Does local control matter in locally advanced prostate cancer?


Conclusion

- Role of radiation therapy clearly established for high risk and locally advanced prostate cancer
- Evidence mounting for metastatic patients
- Mounting evidence for surgery but RCT’s not available
Androgen-deprivation therapy (ADT) is any treatment that blocks interaction of androgen with the androgen receptor

- Orchiectomy
- LHRH agonists
- LHRH antagonists
- Estrogens
- Combined androgen blockade
- Antiandrogen monotherapy

Existing therapies do not adequately suppress adrenal or intratumoral production of androgen

LHRH = luteinizing hormone-releasing hormone.
ADT: Indications

• Indications
  – Newly diagnosed metastatic disease
  – Adjuvant therapy of node positive disease discovered at prostatectomy
  – Combined with radiotherapy in patients with intermediate/high-risk disease

• Use of ADT in patients with biochemical progression is controversial
Metastatic Prostate Cancer
M1 Prostate Cancer *Then & NOW*

**Metastatic PCa patients are living longer**

Racial Gap has decreased

What is a good response to ADT?

- SWOG 9346 Intermittent ADT Trial
- 1345 eligible patients
- Level of PSA after 8 months of ADT

Hussain et al J.Clin Onc 2007
S9346: “A PSA of $\leq 4$ and $< 0.2$ ng/mL after 7 Months of ADT is A Strong Predictor of Overall Survival”

Presented By Maha Hussain at Genitourinary Cancers Symposium 2016
E3805: CHAARTED: ChemoHormonal Therapy vs Androgen Ablation Randomized Trial

**STRATIFICATION**

- Extent of Mets
  - High vs Low
- Age
  - ≥70 vs < 70yo
- ECOG PS
  - 0-1 vs 2
- CAB > 30 days
- Yes vs No
- SRE Prevention
  - Yes vs No
- Prior Adjuvant ADT
  - ≤12 vs > 12 months

**RANDOMIZE**

**ARM A:**
ADT + Docetaxel 75mg/m2 every 21 days for maximum 6 cycles

**Evaluate every 3 weeks while receiving docetaxel and at week 24 then every 12 weeks**

**ARM B:**
ADT (androgen deprivation therapy alone)

**Evaluate every 12 weeks**

- ADT allowed up to 120 days prior to randomization.
- Intermittent ADT dosing was not allowed.
- Standard dexamethasone premedication but no daily prednisone

**Follow for time to progression and overall survival**

- Chemotherapy at investigator’s discretion at progression

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**Presented By Maha Hussain at Genitourinary Cancers Symposium 2016**

**Sweeney C, et al ASCO 2014 – NEJM 2015**

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**PRESENTED AT:** 2016 Genitourinary Cancers Symposium

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Overall Survival: All Patients & by Metastatic Disease Extent

A All Patients

- Hazard ratio for death with ADT+docetaxel, 0.61 (95% CI, 0.47–0.80) P<0.001
- ADT+docetaxel (median overall survival, 57.6 mo)
- ADT alone (median overall survival, 44.0 mo)

N=790
Median OS:
ADT + D: 57.6 months
ADT alone: 44.0 months
HR=0.61 (0.47-0.80)
p=0.0003

B Patients with High-Volume Disease

- Hazard ratio for death with ADT+docetaxel, 0.60 (95% CI, 0.45–0.81) P<0.001
- ADT+docetaxel (median overall survival, 49.2 mo)
- ADT alone (median overall survival, 32.2 mo)

N=514
Median OS:
ADT + D: 49.2 months
ADT alone: 32.2 months
HR=0.60 (0.45-0.81)
p=0.0006

C Patients with Low-Volume Disease

- Hazard ratio for death with ADT+docetaxel, 0.60 (95% CI, 0.32–1.13) P=0.11
- ADT+docetaxel (median overall survival, NR)
- ADT alone (median overall survival, NR)

N=276
Median OS:
ADT + D: Not reached
ADT alone: Not reached
HR=0.63 (0.34-1.17)
p=0.1398
Table 2. Secondary End Points.

<table>
<thead>
<tr>
<th>End Point</th>
<th>ADT plus Docetaxel (N=397)</th>
<th>ADT Alone (N=393)</th>
<th>P Value</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA level &lt;0.2 ng/ml at 6 mo — no. (%)</td>
<td>127 (32.0)</td>
<td>77 (19.6)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>PSA level &lt;0.2 ng/ml at 12 mo — no. (%)</td>
<td>110 (27.7)</td>
<td>66 (16.8)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Time to castration-resistant prostate cancer — mo*</td>
<td></td>
<td></td>
<td></td>
<td>0.61 (0.51–0.72)</td>
</tr>
<tr>
<td>Median</td>
<td>20.2</td>
<td>11.7</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>17.2–23.6</td>
<td>10.8–14.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to clinical progression — mo†</td>
<td></td>
<td></td>
<td></td>
<td>0.61 (0.50–0.75)</td>
</tr>
<tr>
<td>Median</td>
<td>33.0</td>
<td>19.8</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>27.3–41.2</td>
<td>17.9–22.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The time to castration-resistant prostate cancer was the time until documented clinical or serologic progression with a testosterone level of less than 50 ng per deciliter (or source documentation of medical castration or surgical castration).
† Clinical progression was defined by increasing symptoms of bone metastases; progression according to the Response Evaluation Criteria in Solid Tumors, version 1.0; or clinical deterioration due to cancer according to the investigator’s opinion.
What are the Side Effects of ADT?
## Side-Effects of ADT

<table>
<thead>
<tr>
<th>“Big Three”</th>
<th>What you see</th>
<th>What you don’t see</th>
<th>What you feel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of libido</td>
<td>Weight gain</td>
<td>Loss of BMD</td>
<td>Fatigue, Lack of energy, Lack of initiative</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>Gynecomastia</td>
<td>Anemia</td>
<td>Depression</td>
</tr>
<tr>
<td>Hot flashes</td>
<td>Loss muscle mass, strength</td>
<td>Onset/worsening of lipids, HTN, diabetes, CVD</td>
<td>Emotional lability</td>
</tr>
<tr>
<td></td>
<td>Decr size penis and testes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hair changes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention of Fractures from ADT

- Replete Vitamin D
- Adequate calcium intake
- Risk of fracture assessment based on health profile
- Baseline and yearly BMD
**Table 3.** Propensity Score–Matched Cox Regression Analysis for the Association of ADT Use With Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Exposure</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propensity score–matched analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ADT use</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>ADT use</td>
<td>1.88 (1.10 to 3.20)</td>
<td>.021</td>
</tr>
<tr>
<td>Traditional multivariable-adjusted analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ADT use</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>ADT use</td>
<td>1.66 (1.05 to 2.64)</td>
<td>.031</td>
</tr>
</tbody>
</table>

**Table 4.** Propensity Score–Matched Cox Regression Analysis for the Association of ADT Use With Alzheimer’s Disease by Therapy Duration

<table>
<thead>
<tr>
<th>Duration of ADT Use (Months)</th>
<th>HR (95% CI)</th>
<th>P</th>
<th>P for Trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ADT use</td>
<td>Ref</td>
<td>Ref</td>
<td>.016</td>
</tr>
<tr>
<td>ADT users</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months ADT use</td>
<td>1.62 (0.82 to 3.21)</td>
<td>.165</td>
<td></td>
</tr>
<tr>
<td>≥ 12 months ADT use</td>
<td>2.12 (1.11 to 4.03)</td>
<td>.011</td>
<td></td>
</tr>
</tbody>
</table>

**Nead KT, et al. J Clin Oncol. 2015 Dec 7**
Castrate Resistant Prostate Cancer (CRPC)

• Definition: Rising PSA or objective progression (bone +/- soft tissue) despite castrate testosterone levels
  – Serum Testosterone < 50ng/dl or < 1.7nM/dl

• CRPC will develop in all patients who receive Androgen Deprivation Therapy

• Androgen Receptor (AR) is still present and functional
Castrate Resistant Prostate Cancer

• Increased Androgen Biosynthesis
  – Persistent androgens in primary tumors\textsuperscript{1,2}
  – Persistent androgens in metastasis\textsuperscript{3}
  – Upregulated enzymes of steroidogenesis\textsuperscript{3}

• Persistent Androgen Receptor Signaling
  – AR amplification
  – AR splice variants
  – AR signaling via alternate ligands (steroid receptor superfamily)
  – AR signaling via PI3Kinase/ MAPKinase etc

Castration Resistant Prostate Cancer - New Clinical Insights

• Most men with CRPC do not yet have radiographic metastases

• Median time to metastasis is 2-3 years

• Determinants of time to onset of metastases are level of PSA and PSADT
Randomized Phase 3 IMPACT Trial

Asymptomatic or minimally symptomatic metastatic CRPC

N=512

2:1

Sipuleucel-T q 2 weeks x 3

Placebo q 2 weeks x 3

Primary endpoint: Overall survival
Secondary endpoint: Objective disease progression

IMPACT Study

- PROVENGEx improved median survival by 4.1 months compared to the control group (25.8 months versus 21.7 months). Overall, PROVENGEx reduced the risk of death by 22.5%

- No effect on the time to disease progression was observed

- No evidence of a favorable effect on PSA, tumor regression, or stabilization of soft tissue or bony disease radiographically, or health-related quality of life

Kantoff PW, et al, NEJM July, 2010
Novel Hormonal Agents

- Abiraterone - CYP 17 inhibitors
- Enzalutamide - Antiandrogen
Abiraterone Acetate
17α hydroxylase, c17-20 lyase inhibitor

Enzalutamide (MDV3100)

- Oral investigational drug rationally designed to target AR signaling, impacting multiple steps in AR signaling pathway.

- No demonstrated agonist effects in pre-clinical models.

CRPC therapies that offer a survival benefit

<table>
<thead>
<tr>
<th>Year approved</th>
<th>Agent</th>
<th>Indication</th>
<th>PFS benefit</th>
<th>OS benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Docetaxel</td>
<td>mCRCP</td>
<td>?</td>
<td>√</td>
</tr>
<tr>
<td>2010</td>
<td>Sipuleucel-T</td>
<td>a-or minimally symptomatic mCRPC</td>
<td>No</td>
<td>√</td>
</tr>
<tr>
<td>2010</td>
<td>Cabazitaxel</td>
<td>Post-docetaxel mCRPC</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>2011 and 2012</td>
<td>Abiraterone</td>
<td>mCRPC</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>2012 and 2014</td>
<td>Enzalutamide</td>
<td>mCRPC</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>2013</td>
<td>Radium-223</td>
<td>Symptomatic bone predominant mCRCP</td>
<td>SSRE</td>
<td>√</td>
</tr>
</tbody>
</table>
## OS Benefit in Recent CRPC Trials

<table>
<thead>
<tr>
<th>Trial/Agent</th>
<th>Mechanism</th>
<th>Comparator</th>
<th>Survival (months)</th>
<th>Hazard Ratio</th>
<th>P-value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFFIRM Enzalutamide</td>
<td>Androgen Receptor Signaling Inhibitor</td>
<td>Placebo</td>
<td>18.4 vs. 13.6</td>
<td>0.631</td>
<td>&lt;0.0001</td>
<td>de Bono et al, ASCO 2012</td>
</tr>
<tr>
<td>COU-AA-301 Abiraterone + prednisone</td>
<td>CYP17 Inhibitor</td>
<td>Placebo + prednisone</td>
<td>14.8 vs. 10.9</td>
<td>0.646</td>
<td>&lt;0.0001</td>
<td>de Bono et al, NEJM 2011</td>
</tr>
<tr>
<td>TROPIC Cabazitaxel + prednisone</td>
<td>Cytotoxic</td>
<td>Mitoxantrone + prednisone</td>
<td>15.1 vs. 12.7</td>
<td>0.70</td>
<td>&lt;0.0001</td>
<td>de Bono et al, Lancet 2010</td>
</tr>
<tr>
<td>Radium 223*</td>
<td>Alpha-particle emitting radionuclide</td>
<td>Placebo</td>
<td>14.9 vs 11.3</td>
<td>0.69</td>
<td>0.0018</td>
<td>Parker et al, ESMO 2011</td>
</tr>
</tbody>
</table>

* Only 60% of these patients were post-docetaxel patients
Prostate Cancer Landscape: 2017

**Hormone Sensitive**

**Newly diagnosed, Localized disease**
- Surgery
- Radiation
- Active surveillance

**Rising PSA, No mets**
- ADT or observation

**Metastatic, Hormone-naïve**
- ADT +/- Chemotherapy

**Castration Resistant**

**Non-metastatic**
- No standard Second-line hormones

**Metastatic, Chemotherapy-naïve Asymptomatic**
- Sipuleucel-T
- Enzalutamide
- Abiraterone
- Docetaxel
- Zoledronic acid
- Denosumab

**Metastatic, Chemotherapy-naïve Symptomatic**
- Docetaxel
- Abiraterone
- Enzalutamide
- RAD 223

**Metastatic, Post-docetaxel**
- Cabazitaxel
- RAD 223

mCRPC = metastatic castration-resistant prostate cancer
2 Major Milestones in 2015

Genetic Blueprint of Prostate Cancer

SU2C

TCGA

A clearer view of targets for therapy
333 primary prostate carcinomas – 74% associated with a molecular abnormality

Seven subtypes defined by ETS fusions or mutations in SPOP, FOXA1, and IDH1

Substantial epigenetic heterogeneity, including a hypermethylated IDH1 mutant subset

Presumed actionable lesions in the PI3K, MAPK, and DNA repair pathways
Sites of Biopsy Acquisition
(as of 12/1/15; n = 220)

- Bone (N=118)
- Lymph Node (N=60)
- Liver (N=23)
- Lung (N=3)
- Adrenal (N=3)
- Soft Tissue (N=9)
- Brain (N=1)
- Bladder (N=3)
Histology of 124 Evaluable Biopsies

- 13% classic small cell/neuroendocrine cancer (SCNC)
- 26% of biopsies are an Intermediate Atypical Carcinoma (IAC) distinct from AdenoCa and SCNC
- 26% of biopsies had distinct, but mixed populations
Identifying Molecular Alterations in CRPC


Presented By Tomasz Beer at Genitourinary Cancers Symposium 2016
Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

RESULTS

Presented By Peter Nelson at 2016 ASCO Annual Meeting
# RESULTS

<table>
<thead>
<tr>
<th>Case Series</th>
<th>n</th>
<th>Mutated</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SU2C/PCF Discovery</td>
<td>150</td>
<td>15</td>
<td>10.0%</td>
</tr>
<tr>
<td>SU2C/PCF Validation</td>
<td>84</td>
<td>9</td>
<td>10.7%</td>
</tr>
<tr>
<td>MSKCC</td>
<td>124</td>
<td>23</td>
<td>18.5%</td>
</tr>
<tr>
<td>Royal Marsden</td>
<td>131</td>
<td>16</td>
<td>12.2%</td>
</tr>
<tr>
<td>University of Washington</td>
<td>91</td>
<td>8</td>
<td>8.8%</td>
</tr>
<tr>
<td>Weill Cornell</td>
<td>69</td>
<td>7</td>
<td>10.1%</td>
</tr>
<tr>
<td>University of Michigan</td>
<td>43</td>
<td>4</td>
<td>9.3%</td>
</tr>
<tr>
<td><strong>Combined</strong></td>
<td>692</td>
<td>82</td>
<td><strong>11.8%</strong></td>
</tr>
</tbody>
</table>
Biomarker based treatment

**DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer**


**A** Radiologic Progression–free Survival

- Biomarker-positive, median: 9.8 mo
- Biomarker-negative, median: 2.7 mo

P<0.001 by log-rank test

**B** Overall Survival

- Biomarker-positive, median: 13.8 mo
- Biomarker-negative, median: 7.5 mo

P=0.05 by log-rank test