Updates in the Treatment of Metastatic Prostate Cancer

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Clinical Specialist Pharmacist – Oncology
May 1, 2018
Objectives

- **Pharmacist**
  - Review background, pathophysiology, and treatment of metastatic prostate cancer
  - Evaluate recent literature for treatment of hormone sensitive prostate cancer
  - Discuss future treatment considerations
  - Apply new literature to patient cases

- **Technician**
  - Understand the similarities and differences between treatments for metastatic prostate cancer
  - Identify the generic and brand names for treatments for metastatic prostate cancer
Patient Case

- JD is a 64 year old male with newly diagnosed prostate cancer. He was diagnosed after presenting with difficulty urinating, intermittent stream, and frequent nocturia. His provider completed a digital rectal exam, which was concerning for prostate cancer. He underwent appropriate staging and work-up, with results below:

- Prostate biopsy + for prostate adenocarcinoma
- Gleason score 4+4
- PSA 42 ng/dL
- SCr and Liver Function Tests within normal limits
- Bone scan: 4 bone lesions, including 1 lesion in the pelvis.

What treatment should JD receive?
Prostate Cancer

- Most frequently diagnosed cancer in men
  - 1 in 9 will be diagnosed in lifetime
- Second leading cause of cancer-related death in men
- 2018 statistics
  - ~164,690 new cases
  - ~29,430 deaths
- Trends
  - New diagnoses: ↓ 5.8% each year last 10 years
  - Death rates: ↓ 3.4% each year from 2005-2014

Prostate Cancer

- Most frequently diagnosed cancer in men
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- Second leading cause of cancer-related death in men
- 2018 statistics
  - ~164,690 new cases
  - ~29,430 deaths
- Trends
  - New diagnoses: ↓ 5.8% each year last 10 years
  - Death rates: ↓ 3.4% each year from 2005-2014

Median age at diagnosis = 66
Median age at death = 80

Pathophysiology

- Majority are adenocarcinomas
- Androgen interaction with androgen receptor
  - Necessary for prostate function and development
  - ~80-90% of prostate cancers depend on androgen

*Endocrine Reviews* 2004; 25:276-308.
Image: American Cancer Society.
Risk Factors

- **Age**
  - Median age at diagnosis: 66 years

- **Race**
  - African American men: higher risk
  - Asian men: less common

- **Family History**
  - First degree relative – doubles lifetime risk

Diagnosis and Work-Up

- **Prostate Specific Antigen (PSA):** glycoprotein secreted by prostate cells
  - Specific to the prostate - **NOT** prostate cancer
  - Provides prognostic information
  - Used to monitor treatment response and disease recurrence

- **Prostate biopsy**
  - Transrectal approach
  - Numerous punch biopsies taken
  - Determine Gleason score

- **Radiographic imaging**
  - X-rays, CT scans, Bone scans
  - Determine extent of disease involvement
Gleason Score

- Tumors can exhibit more than one pattern of cell growth
- Two most prevalent growth patterns added together to determine Gleason score (range 2-10)
- Predicts likelihood of the cancer spreading
Treatment: Hormone Therapy

- **Gold Standard** = Androgen Deprivation Therapy
- Goal: castration
  - Testosterone < 50 ng/dL
- Initial treatment for metastatic disease
  - Castrate-sensitive (also referred to as hormone-sensitive)

### Treatment: Hormone Therapy

<table>
<thead>
<tr>
<th>Antiandrogens</th>
<th>LHRH Agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicalutamide (Casodex®)</td>
<td>Leuprolide (Lupron®, Eligard®)</td>
</tr>
<tr>
<td>Nilutamide (Nilandron®)</td>
<td>Goserelin (Zoladex®)</td>
</tr>
<tr>
<td>Flutamide (Eulexin®)</td>
<td></td>
</tr>
</tbody>
</table>

**LHRH Antagonist**

- Degarelix (Firmagon®)

*References*

*The James*

Castrate-Resistant Prostate Cancer (CRPC)

- Progression to castrate-resistance is inevitable
- **Definition**: rising PSA despite castrate testosterone levels

**Treatment Options:**

- Secondary hormone manipulation
  - Switch antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole/hydrocortisone
- Palliative benefits only until 2004
Treatment Timeline: Castrate-Resistant Studies

- **Docetaxel** 2004
- **Cabazitaxel** 2010
- **Sipuleucel-T** 2010
- **Abiraterone** before Chemo 2011
- **Enzalutamide** before Chemo 2012
- **Abiraterone** after Chemo 2011
- **Enzalutamide** after Chemo 2012
- **Radium-223** 2013
- **Enzalutamide** after Chemo 2014
# CRPC Treatment: Therapeutic Classes

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Treatment</th>
<th>Dose/Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy</strong></td>
<td>Docetaxel (Taxotere®)</td>
<td>75 mg/m² IV every 3 weeks</td>
</tr>
<tr>
<td></td>
<td>Cabazitaxel (Jevtana®)</td>
<td>25 mg/m² IV every 3 weeks</td>
</tr>
<tr>
<td><strong>Immunotherapy</strong></td>
<td>Sipuleucel-T (Provenge®)</td>
<td>IV infusion every 2 weeks x 3 doses</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td>Radium-223 (Xofigo®)</td>
<td>50 kBq/kg IV every 4 weeks x 6 doses</td>
</tr>
<tr>
<td><strong>Hormonal Therapy</strong></td>
<td>Abiraterone (Zytiga®)</td>
<td>1000 mg PO daily + prednisone 5 mg PO BID</td>
</tr>
<tr>
<td></td>
<td>Enzalutamide (Xtandi®)</td>
<td>160 mg PO daily</td>
</tr>
</tbody>
</table>

The James
## CRPC Treatment: Survival Benefit

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Study</th>
<th>Comparator</th>
<th>Survival Benefit (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
<td>TAX 327</td>
<td>Mitoxantrone</td>
<td>18.9 vs 16.5</td>
</tr>
<tr>
<td>Cabazitaxel</td>
<td>TROPIC</td>
<td>Mitoxantrone</td>
<td>15.1 vs 12.7</td>
</tr>
<tr>
<td>Sipuleucel-T</td>
<td>IMPACT</td>
<td>Placebo</td>
<td>25.8 vs 21.7</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>COU-AA-301</td>
<td>Placebo</td>
<td>14.8 vs 10.9</td>
</tr>
<tr>
<td></td>
<td>COU-AA-302</td>
<td>Placebo</td>
<td>NR* vs 27.2</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>AFFIRM</td>
<td>Placebo</td>
<td>18.4 vs 13.6</td>
</tr>
<tr>
<td></td>
<td>PREVAIL</td>
<td>Placebo</td>
<td>32.4 vs 30.2</td>
</tr>
<tr>
<td>Radium-223</td>
<td>ALSYMPCA</td>
<td>Placebo</td>
<td>14.9 vs 11.3</td>
</tr>
</tbody>
</table>

*NR: not reached

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**References**

Recent Literature

- Early Docetaxel
  - GETUG-AFU 15
  - CHAARTED (ECOG 3805)
  - STAMPEDE

- Early Abiraterone
  - LATITUDE
  - STAMPEDE
Recent Literature

- Early Docetaxel
  - GETUG-AFU 15
  - CHAARTED (ECOG 3805)
  - STAMPEDE

- Early Abiraterone
  - LATITUDE
  - STAMPEDE
Metastatic Prostate Cancer

*ADT allowed if started no more than 2 months prior to enrollment

ADT + Docetaxel
N = 192
*Docetaxel 75 mg/m2 x 9 cycles

ADT Alone
N = 193

GETUG-AFU 15: Design

Metastatic Prostate Cancer

*ADT allowed if started no more than 2 months prior to enrollment

ADT + Docetaxel
N = 192
*Docetaxel 75 mg/m2 x 9 cycles

ADT Alone
N = 193

Primary Endpoint: Overall Survival
Secondary Endpoints:
- Time to clinical progression (cPFS)
- Time to PSA progression (bPFS)

# GETUG-AFU 15: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ADT + Docetaxel</th>
<th>ADT Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63</td>
<td>64</td>
</tr>
<tr>
<td>Initial Gleason Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-6</td>
<td>18 (10%)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>7</td>
<td>66 (35%)</td>
<td>64 (34%)</td>
</tr>
<tr>
<td>8-10</td>
<td>103 (55%)</td>
<td>113 (59%)</td>
</tr>
<tr>
<td>Metastatic at diagnosis</td>
<td>128 (67%)</td>
<td>144 (75%)</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>26.7</td>
<td>25.8</td>
</tr>
</tbody>
</table>

GETUG-AFU 15: Results

- **Median Overall Survival**
  - ADT + Docetaxel = 58.9 months
  - ADT Alone = 54.2 months

- **3-year Overall Survival**
  - ADT + Docetaxel = 64.2%
  - ADT Alone = 62.9%

- **Secondary Endpoints**

<table>
<thead>
<tr>
<th></th>
<th>ADT + Docetaxel</th>
<th>ADT Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>bPFS</td>
<td>22.9 mos</td>
<td>12.9 mos</td>
</tr>
<tr>
<td>cPFS</td>
<td>23.5 mos</td>
<td>15.4 mos</td>
</tr>
</tbody>
</table>

GETUG-AFU 15: Safety

- **ADT + Docetaxel**
  - Grade 3-4 Toxicities
    - Neutropenia – 32%
    - Febrile neutropenia – 7%
    - Fatigue – 7%

- **ADT Alone**
  - Few Grade 3-5 toxicities
  - Erectile dysfunction most common = 8%
    - Similar incidence in ADT + Docetaxel arm

GETUG-AFU 15: Conclusions

- Addition of docetaxel did not show survival benefit
  - bPFS, cPFS, and PSA response improved

- Limitations
  - Insufficient power
  - Smaller sample size
Primary Objective

Docetaxel therapy at beginning of ADT for metastatic hormone-sensitive prostate cancer result in longer overall survival than ADT alone

Inclusion Criteria

- Radiologic evidence of metastatic disease
- ECOG 0, 1, 2
- Prior adjuvant ADT
  - If duration < 24 months AND
  - Progression occurred after 12 months
- Treatment with ADT for metastatic disease allowed within 120 days

CHAARTED

CHAARTED: Design

Castrate-Sensitive Metastatic Prostate Cancer

Docetaxel + ADT
N = 397

ADT Alone
N = 393

Docetaxel Arm:
- Docetaxel 75 mg/m² IV every 3 weeks x 6 cycles
- Dexamethasone pre-medication 8 mg PO 12, 3, and 1 hour before infusion
- Prednisone not required
- Growth factor use per investigator

### CHAARTED: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ADT + Docetaxel</th>
<th>ADT Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (year)</strong></td>
<td>64</td>
<td>63</td>
</tr>
<tr>
<td><strong>Volume of metastases – no (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>134 (33.8)</td>
<td>143 (36.4)</td>
</tr>
<tr>
<td>High</td>
<td>263 (66.2)</td>
<td>250 (63.6)</td>
</tr>
<tr>
<td><strong>Visceral metastases – no (%)</strong></td>
<td>57 (14.4)</td>
<td>66 (16.8)</td>
</tr>
<tr>
<td><strong>Gleason score – no (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-6</td>
<td>21 (5.3)</td>
<td>21 (5.3)</td>
</tr>
<tr>
<td>7</td>
<td>96 (24.2)</td>
<td>83 (21.1)</td>
</tr>
<tr>
<td>8-10</td>
<td>241 (60.7)</td>
<td>243 (61.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>39 (9.8)</td>
<td>46 (11.7)</td>
</tr>
<tr>
<td><strong>Median PSA level at start of ADT – ng/ml</strong></td>
<td>50.9</td>
<td>52.1</td>
</tr>
</tbody>
</table>
Primary Endpoint

- **Median overall survival**
  - ADT + Docetaxel = 57.6 months
  - ADT Alone = 44.0 months

13.6 Month Difference
CHAARTED: Results

Primary Endpoint

- Median overall survival
  - ADT + Docetaxel = 57.6 months
  - ADT Alone = 44.0 months
  - 13.6 Month Difference

- Significant benefit in high-volume disease
  - ADT + Docetaxel = 49.2 months
  - ADT Alone = 32.2 months
  - 17 Month Difference

\[ N\text{ Engl J Med 2015; 373:737-46.} \]
CHAARTED: Results

Primary Endpoint

- **Median overall survival**
  - ADT + Docetaxel = 57.6 months
  - ADT Alone = 44.0 months
  - 13.6 Month Difference

- **Significant benefit in high-volume disease**
  - ADT + Docetaxel = 49.2 months
  - ADT Alone = 32.2 months
  - 17 Month Difference

**High-Volume Disease:**
- Visceral metastases
- ≥ 4 bone lesions with ≥ 1 beyond the vertebral bodies and pelvis

Secondary Endpoints

- **PSA decrease < 0.2 ng/mL at 12 months**
  - ADT + Docetaxel = 27.7%
  - ADT Alone = 16.8%

- **Median time to CRPC**
  - ADT + Docetaxel = 20.2 months
  - ADT Alone = 11.7 months

- **Median time to clinical progression**
  - ADT + Docetaxel = 33.0 months
  - ADT Alone = 19.8 months
Secondary Endpoints

- **PSA decrease < 0.2 ng/mL at 12 months**
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- **Median time to CRPC**
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- **Median time to clinical progression**
  - ADT + Docetaxel = 33.0 months
  - ADT Alone = 19.8 months

*All statistically significant*
CHAARTED: Safety

- **ADT + Docetaxel**
  - Grade 3 or 4 allergic reaction = ~2%
  - Grade 3 fatigue = 4%
  - Grade 3 diarrhea, stomatitis, motor neuropathy, sensory neuropathy = < 1% each

- **Neutropenia and Infection:**
  - Neutropenia = ~12.%
  - Neutropenic fever = ~6%
  - Grade 3 or 4 infection with neutropenia = ~2%
CHAARTED: Conclusions

- ADT + Docetaxel x 6 cycles
  - Significantly improved overall survival
  - Benefit noted in men with high volume disease
- Addition of Docetaxel improved secondary endpoints
  - PSA level decrease at 12 months
  - Time to CRPC
  - Time to clinical progression
Newly Diagnosed Prostate Cancer

SOC* + Zoledronic Acid
N = 593

SOC* + Docetaxel
N = 592

SOC* + Zoledronic Acid + Docetaxel
N = 593

Metastatic Node positive
High-risk locally advanced

SOC*: standard of care; hormone therapy for at least 2 years

Multiarm, multistage platform design
Endpoints:
- overall survival, failure-free survival

STAMPEDE: Design

Multiarm, multistage platform design
Endpoints:
- overall survival, failure-free survival

*SOC: standard of care; hormone therapy for at least 2 years

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SOC</th>
<th>SOC + Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age – years</strong></td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td><strong>Median PSA – ng/mL</strong></td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td><strong>Metastases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>460 (39%)</td>
<td>230 (39%)</td>
</tr>
<tr>
<td><strong>Any metastases</strong></td>
<td>724 (61%)</td>
<td>362 (61%)</td>
</tr>
<tr>
<td><strong>Gleason score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 7</td>
<td>282 (24%)</td>
<td>110 (19%)</td>
</tr>
<tr>
<td>8-10</td>
<td>810 (68%)</td>
<td>436 (74%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>92 (8%)</td>
<td>46 (8%)</td>
</tr>
</tbody>
</table>

*STAMPEDE: Patient Characteristics*

STAMPEDE: Results

<table>
<thead>
<tr>
<th></th>
<th>SOC + Docetaxel</th>
<th>SOC Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>81 months</td>
<td>71 months</td>
</tr>
<tr>
<td>Failure-Free Survival</td>
<td>37 months</td>
<td>20 months</td>
</tr>
<tr>
<td>5-year Failure-Free Survival</td>
<td>38%</td>
<td>28%</td>
</tr>
</tbody>
</table>

# STAMPEDE: Safety

<table>
<thead>
<tr>
<th>Adverse Event (grade 3-5)</th>
<th>SOC + Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile neutropenia</td>
<td>84 (15%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>66 (12%)</td>
</tr>
<tr>
<td>General disorder</td>
<td>34 (7%)</td>
</tr>
<tr>
<td>- lethargy, fever, asthenia</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>32 (6%)</td>
</tr>
<tr>
<td>- bone pain, generalized pain</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>45 (8%)</td>
</tr>
<tr>
<td>- diarrhea, abdominal pain, constipation, vomiting</td>
<td></td>
</tr>
<tr>
<td><strong>Most common adverse event in SOC arm:</strong></td>
<td></td>
</tr>
<tr>
<td>Endocrine disorder (impotence, hot flushes) = 145 (12%)</td>
<td></td>
</tr>
</tbody>
</table>

STAMPEDE: Conclusions

- SOC + Docetaxel
  - Improved overall survival
  - Increased adverse events
- Zoledronic acid showed no improvement

Early Docetaxel - Summary

- **CHAARTED and STAMPEDE**
  - Improved overall survival with addition of docetaxel to ADT
- **GETUG-AFU 15**
  - No survival benefit with addition of docetaxel
- **Safety**
  - Similar adverse events noted

**NCCN Category 1 Recommendation**
Recent Literature

- Early Docetaxel
  - GETUG-AFU 15
  - CHAARTED (ECOG 3805)
  - STAMPEDE

- Early Abiraterone
  - LATITUDE
  - STAMPEDE
Newly Diagnosed Metastatic Prostate Cancer

At least two:
1. Gleason > 8
2. At least 3 bone lesions
3. Measurable visceral metastasis

ADT + Abiraterone/Prednisone
N = 597

ADT + Placebo
N = 602

## LATITUDE: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Abiraterone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>68</td>
<td>67</td>
</tr>
<tr>
<td><strong>Gleason score at diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>4 (0.7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>7</td>
<td>9 (2%)</td>
<td>15 (2%)</td>
</tr>
<tr>
<td>≥ 8</td>
<td>584 (98%)</td>
<td>586 (97%)</td>
</tr>
<tr>
<td><strong>High risk at screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gleason ≥ 8 and ≥ 3 bone lesions</td>
<td>573 (96%)</td>
<td>569 (95%)</td>
</tr>
<tr>
<td>Gleason ≥ 8 and measurable visceral disease</td>
<td>82 (14%)</td>
<td>87 (14%)</td>
</tr>
<tr>
<td>≥ 3 bone lesions and measurable visceral disease</td>
<td>84 (14%)</td>
<td>85 (14%)</td>
</tr>
<tr>
<td>Gleason ≥ 8 and ≥ 3 bone lesions and measurable visceral disease</td>
<td>71 (12%)</td>
<td>70 (12%)</td>
</tr>
</tbody>
</table>
# LATITUDE: Results

<table>
<thead>
<tr>
<th>Primary Endpoints</th>
<th>Abiraterone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>Not reached</td>
<td>34.7 mos</td>
</tr>
<tr>
<td>3 year survival rate</td>
<td>66%</td>
<td>49%</td>
</tr>
<tr>
<td>Radiographic Progression-Free Survival</td>
<td>33.0 mos</td>
<td>14.8 mos</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Endpoints* (months)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to pain progression</td>
<td>NR</td>
<td>16.6</td>
</tr>
<tr>
<td>Time to PSA progression</td>
<td>33.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Time to next symptomatic skeletal event</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Time to chemotherapy</td>
<td>NR</td>
<td>38.9</td>
</tr>
<tr>
<td>Time to subsequent prostate cancer therapy</td>
<td>NR</td>
<td>21.6</td>
</tr>
</tbody>
</table>

*All secondary endpoints are median times

LATITUDE: Safety

- **Abiraterone Group**
  - Most common Grade 3 or 4 toxicities
    - Hypertension = 20%
    - Hypokalemia = 11%
    - ALT increased = ~6%
    - Hyperglycemia and AST increased = ~5%

- **Placebo Group**
  - Most common Grade 3 or 4 toxicity
    - Hypertension = ~11%
LATITUDE: Conclusions

- Addition of abiraterone and prednisone
  - Overall survival benefit
  - Radiographic progression free survival benefit
- Safety profile similar to CRPC studies

STAMPEDE: Design

Multiarm, multistage platform design
Endpoints:
- overall survival, failure-free survival

Newly Diagnosed Prostate Cancer

ADT Alone
N = 957

ADT + Abiraterone
N = 960

Metastatic
Node positive
High-risk locally advanced

## STAMPEDE: Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ADT Alone</th>
<th>ADT + Abiraterone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age – years</strong></td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td><strong>PSA level before ADT – ng/mL</strong></td>
<td>56</td>
<td>51</td>
</tr>
<tr>
<td><strong>Disease group – no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Node-negative, nonmetastatic disease</td>
<td>256 (27)</td>
<td>253 (26)</td>
</tr>
<tr>
<td>Node-positive, nonmetastatic disease</td>
<td>187 (20)</td>
<td>182 (19)</td>
</tr>
<tr>
<td>Metastatic disease</td>
<td>476 (50)</td>
<td>465 (48)</td>
</tr>
<tr>
<td><strong>Gleason score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 7</td>
<td>223 (23)</td>
<td>221 (23)</td>
</tr>
<tr>
<td>8-10</td>
<td>721 (75)</td>
<td>715 (74)</td>
</tr>
<tr>
<td>Unknown</td>
<td>13 (1)</td>
<td>24 (2)</td>
</tr>
</tbody>
</table>
STAMPEDE: Results and Safety

- **Overall Survival**
  - 3 year survival: 83% abiraterone vs 76% ADT alone

- **Failure-Free Survival**
  - 3 year rate: 75% abiraterone vs 45% ADT alone

**Safety**

<table>
<thead>
<tr>
<th>Grade 3-5 Adverse Events</th>
<th>ADT Alone</th>
<th>ADT + Abiraterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine disorders</td>
<td>133 (14%)</td>
<td>129 (14%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13 (1%)</td>
<td>44 (5%)</td>
</tr>
<tr>
<td>Hepatic disorders</td>
<td>12 (1%)</td>
<td>70 (7%)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>3 (&lt; 1%)</td>
<td>12 (1%)</td>
</tr>
</tbody>
</table>

STAMPEDE: Conclusions

- Abiraterone + ADT
  - 71% relative improvement in time to treatment failure
  - 37% difference in overall survival
- Consistent for metastatic and nonmetastatic disease

Early Abiraterone - Summary

- **LATITUDE and STAMPEDE**
  - Survival benefit of abiraterone addition to ADT
- Similar side effects reported in CRPC studies
Docetaxel or Abiraterone?

**Docetaxel**
- Significant survival benefit
- Short duration of therapy
- Side effect profile

**Abiraterone**
- Significant survival benefit
- Extended duration of therapy
- Manageable safety profile
- Long-term prednisone
## Early Docetaxel and Abiraterone Summary

<table>
<thead>
<tr>
<th></th>
<th>Overall Survival</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Docetaxel + ADT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GETUG-AFU 15</td>
<td>58.9 mos vs 54.2 mos</td>
<td>Not statistically significant</td>
</tr>
<tr>
<td>CHAARTED</td>
<td>57.6 mos vs 44.0 mos</td>
<td>High-volume disease</td>
</tr>
<tr>
<td>STAMPEDE</td>
<td>81 mos vs 71 mos</td>
<td>No benefit with zoledronic acid</td>
</tr>
<tr>
<td><strong>Abiraterone + ADT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LATITUDE</td>
<td>NR vs 34.7 mos</td>
<td>High-risk population</td>
</tr>
<tr>
<td>STAMPEDE</td>
<td>83% vs 76% 3-year survival</td>
<td></td>
</tr>
</tbody>
</table>
## CRPC Treatment: Survival Benefit

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Study</th>
<th>Comparator</th>
<th>Survival Benefit (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
<td>TAX 327</td>
<td>Mitoxantrone</td>
<td>18.9 vs 16.5</td>
</tr>
<tr>
<td>Cabazitaxel</td>
<td>TROPIC</td>
<td>Mitoxantrone</td>
<td>15.1 vs 12.7</td>
</tr>
<tr>
<td>Sipuleucel-T</td>
<td>IMPACT</td>
<td>Placebo</td>
<td>25.8 vs 21.7</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>COU-AA-301</td>
<td>Placebo</td>
<td>14.8 vs 10.9</td>
</tr>
<tr>
<td></td>
<td>COU-AA-302</td>
<td>Placebo</td>
<td>NR* vs 27.2</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>AFFIRM</td>
<td>Placebo</td>
<td>18.4 vs 13.6</td>
</tr>
<tr>
<td></td>
<td>PREVAIL</td>
<td>Placebo</td>
<td>32.4 vs 30.2</td>
</tr>
<tr>
<td>Radium-223</td>
<td>ALSYMPCA</td>
<td>Placebo</td>
<td>14.9 vs 11.3</td>
</tr>
</tbody>
</table>


*NR: not reached
# Clinical Trials in Progress

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metastatic disease, no previous ADT</strong></td>
<td>STAMPEDE, Group J &lt;br&gt;SOC with or without enzalutamide, abiraterone, and prednisolone</td>
</tr>
<tr>
<td>ENZAMET</td>
<td>ADT + Antiandrogen vs ADT + Enzonlumamide</td>
</tr>
<tr>
<td>PEACE-1</td>
<td>ADT with or without docetaxel, with or without prostate irradiation, with or without abiraterone and prednisolone</td>
</tr>
<tr>
<td>ARASENS</td>
<td>ADT + docetaxel with or without darolutamide</td>
</tr>
<tr>
<td>SWOG 1216</td>
<td>ADT + bicalutamide vs ADT + orteronel</td>
</tr>
<tr>
<td><strong>Metastatic CRPC</strong></td>
<td></td>
</tr>
<tr>
<td>Alliance A031201</td>
<td>Enzalutamide with or without abiraterone and prednisone</td>
</tr>
<tr>
<td>IMbassador250</td>
<td>Enzalutamide with or without atezolizumab</td>
</tr>
<tr>
<td><strong>CRPC with bone metastasis</strong></td>
<td></td>
</tr>
<tr>
<td>PEACE-3</td>
<td>Enzalutamide with or without radium-223</td>
</tr>
<tr>
<td>ERA 223</td>
<td>Abiraterone with or without radium-223</td>
</tr>
</tbody>
</table>

JD is a 64 year old male with newly diagnosed prostate cancer. He was diagnosed after presenting with difficulty urinating, intermittent stream, and frequent nocturia. His provider completed a digital rectal exam, which was concerning for prostate cancer. He underwent appropriate staging and work-up, with results below:

- Prostate biopsy + for prostate adenocarcinoma
- Gleason score 4+4
- PSA 42 ng/dL
- SCr and Liver Function Tests within normal limits
- Bone scan: 4 bone lesions, including 1 lesion in the pelvis.

What treatment should JD receive?
Patient Case

What treatment should JD receive?
- A. Abiraterone + Prednisone x 6 months + ADT
- B. Docetaxel x 6 cycles + ADT
- C. Abiraterone + Prednisone + Docetaxel
- D. Abiraterone + Prednisone + ADT
AB is an 74 year old male with newly diagnosed metastatic prostate cancer. During initial work-up for metastatic disease, the following information was found:

- Gleason 4+5
- PSA 25 ng/dL
- Bone scan: 4 lesions, 1 of which on spine, near T4
- CT scans: liver metastases
- ECOG performance status 2
- SCr and Liver Function Tests within normal limits

During his visit, he states that he does not want chemotherapy.
Patient Case

- What treatment option(s) is(are) appropriate for AB?
  - A. Abiraterone + prednisone + ADT
  - B. ADT Alone
  - C. Docetaxel x 6 cycles + ADT
  - D. Cabazitaxel + ADT
Conclusions

- Prostate cancer is the most common cancer in men.
- Treatment advances have led to regimens that provide overall survival benefit for men with castrate-resistant prostate cancer.
- New literature supports the use of docetaxel and abiraterone in newly diagnosed metastatic prostate cancer, demonstrating overall survival benefit.
- Further research is being done to evaluate new therapies in different stages of disease, as well as combination of existing therapies.
Updates in the Treatment of Metastatic Prostate Cancer

Megan Hinkley, PharmD, BCOP
Clinical Specialist Pharmacist – Oncology
May 1, 2018