Treatment of Advanced Disease and Hereditary Genetics

Chethan Ramamurthy, M.D.
Assistant Professor, Dept Hematology-Oncology
UT Health San Antonio
Prostate Cancer Disease States

Initial Prostate Evaluation:
- No Cancer Diagnosis
- Clinically Localized Disease
- Rising PSA
- Clinical Metastases
  - Non-Castrate
  - Castrate

Death from other causes

Death from Prostate Cancer

Scher, H. Urology, March 2000, Pages 323-327
The Nobel Prize...in 1966

Studies on Prostatic Cancer: I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate by Huggins and Hodges, April 1941

Androgen deprivation remains the backbone of treatment for advanced prostate cancer.
What do you expect from Androgen Deprivation Therapy (Hormone Therapy)?

- Hot Flashes/Sweats
- Fatigue
- Depression
- Irritability
- Decreased mental acuity
- Loss of muscle mass
- Gain of fat and weight
- Weakness
- Loss of libido
- Erectile dysfunction
- Loss of bone density
- Low red blood cell counts
- Increased chance of cardiovascular disease
New Prostate-Specific FDA Approvals

- Abiraterone (Zytiga) – 2011, 2012, 2018
- Enzalutamide (Xtandi) – 2012, 2018
- Radium-223 (Xofigo) – 2013
- Apalutamide (Erleada) – 2018
- Sipuleucel-T (Provenge) – 2010
Advanced Androgen Targeting

Enzalutamide

Abiraterone
## Therapy Options for Advanced Prostate Cancer

### Pre-2010 Era

- ADT

### Castration-Sensitive

<table>
<thead>
<tr>
<th>Nonmetastatic</th>
<th>Metastatic, asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADT</td>
<td>Clinical Trials</td>
</tr>
<tr>
<td>ADT +/- Docetaxel or Abiraterone</td>
<td>2º hormonal therapy</td>
</tr>
<tr>
<td>Radiation for oligometastatic disease</td>
<td>Sipuleucel-T</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>Abiraterone</td>
</tr>
</tbody>
</table>

### Castration-Resistant

<table>
<thead>
<tr>
<th>Metastatic, asymptomatic</th>
<th>Metastatic, symptomatic</th>
<th>Metastatic, advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Trials</td>
<td>Clinical Trials</td>
<td>Clinical Trials</td>
</tr>
<tr>
<td>Radium-223</td>
<td>Enzalutamide</td>
<td></td>
</tr>
<tr>
<td>Abiraterone</td>
<td>Docetaxel</td>
<td>Abiraterone</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Cabazitaxel</td>
<td>Carboplatin</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>PARP inhibitors</td>
<td>Checkpoint blockade</td>
</tr>
</tbody>
</table>

### Modern Era

- Clinical Trials
- Radium-223
- Docetaxel
- Cabazitaxel
- Carboplatin
- PARP inhibitors
- Checkpoint blockade

---

*Mays Cancer Center*

UT Health San Antonio  
MD Anderson Cancer Center
Hereditary Genetics in Prostate Cancer

Representative Pedigree of Pca Patient

unknown, 50

Prostate, 53
Breast, 60
BRIP1 mutation