

# OK Doc. Now What?

John P. Delisio, MD

Virginia Urology

# Prostate Cancer

- Most prevalent male cancer in the US
- Approximately 1 in 7 men diagnosed each year
- 2017: 161,360 men were diagnosed with Prostate Cancer
- 2017: 3,306,760 men were prostate cancer survivors
- Prostate Cancer is now a chronic illness

# PSA

- 1979: First purified from the prostate by Wang, et al
- 1980: Measured in the blood by Papsidero, et al
- 1987: Usefulness as a tumor marker shown by Stamey, et al
- 4.0
- Age Specific Ranges

# PSA

- NOT CANCER SPECIFIC
- Elevated in BPH, infection, inflammation
- PSA increases as men get older

# D'Amico Classification

- Developed in 1998
- Very Low Risk
- Low Risk
- Favorable Intermediate Risk
- Unfavorable Intermediate Risk
- High Risk
- Very High Risk

# Treatment

- Surgery
- Radiation
- Follow PSA post treatment

# Biochemical Failure

- Surgery: PSA > 0.2
- Radiation: Nadir PSA + 2
- PSA doubling time

# Biochemical Failure

- Median survival 13 years
- Dependent upon multiple clinical factors



# Metastatic Evaluation

- CT Scan
- Bone Scan
- PET CT Scan
- MRI

# Treatment

- 1941: Charles Huggins and Clarence V. Hodges
- Androgen Deprivation Therapy
- Prostatic Acid Phosphatase (PAP)
- ANDROGEN DEPRIVATION THERAPY REMAINS THE MAINSTAY FOR TREATING BIOCHEMICAL RECURRENT PROSTATE CANCER
- ALL TREATMENTS FOR RECURRENT/ADVANCED PROSTATE CANCER ARE BASED UPON KEEPING TESTOSTERONE AT CASTRATE LEVELS

# Treatment

- Androgen ablation
- Castration
- Injection therapy

# Castrate Resistance

- Castrate testosterone levels
- Rising PSA
- M0
- M1

# Castrate Resistance

- Upregulation of the Androgen receptor
- 'Promiscuity' of the Androgen receptor
- Auto stimulation of the Androgen receptor
- Other mechanisms

# Castrate Resistance

- Median survival 11 months
- Disease Management
- Quality of life

# Treatment Options

- M0
- Rising PSA
- No evidence of metastatic disease on imaging
- Androgen receptor blockers
  - Enzalutamide
  - Apalutamide
  - Darolutamide

# Androgen Receptor Blockers

- Prevent testosterone binding to the androgen receptor
- Prevent androgen receptor from binding to DNA
- Prevent androgen receptor from entering the nucleus and binding to DNA



# Androgen Receptor Blockers

- Improvement in overall survival as compared to standard therapy:
  - Androgen ablation only
  - 10%
- Improvement in progression free survival at 3 years:
  - 27%

# Androgen Receptor Blockers

- Asthenia (Tiredness)
- Seizures
- Decreased appetite
- Facial flushing
- Hypertension

# Treatment Options

- M1
- Androgen Receptor Blockers
- Immunotherapy
- Abiraterone Acetate
- Radium 223

# Immunotherapy

- Immune Surveillance
- Self vs. Nonself
- Abnormal cells
  - Cancer cells

# Immunotherapy

- Plasmapheresis
- White blood cells separated from red cells
- White blood cells sent to a lab
- 'Train' the White blood cells to attack prostate cancer cells

# Immunotherapy

- Autologous immunotherapy
- Sipuleucel-T
  - Provenge
- Induces both a cellular and humoral immune response
- Antigen found on Prostate cancer cells
- Prostate Antigen Phosphatase (PAP)
- THE EXACT MECHANISM OF ACTION IS UNKNOWN

# Sipuleucel-T

- First treatment approved for metastatic castrate resistant prostate cancer
- 2010
- Minimally symptomatic
- 4 month survival benefit
- Patient's with lower PSA do better
- Better response in the African American population

# Sipuleucel-T

- Acute infusion reactions
  - Fever
  - Nausea
  - Rigors/Chills
- Premedicate
  - Antipyretic
  - Antihistamines



# Sipuleucel-T

- 1 hour infusion in the office
- Series of 3 plasmapheresis/infusion
- No boosters

# Abiraterone Acetate

- Zytiga
- Androgen biosynthesis inhibitor
- Blocks androgen synthesis at a very early step
- Need to take prednisone 5mg twice a day

# Abiraterone Acetate

- 3 year survival standard therapy:
  - 76%
- 3 year survival Zytiga:
  - 83%
- Lowered the risk of death by 37%

# Abiraterone Acetate

- 4 tablets once a day
  - Dosing adjustments
- Hypertension
- Hypokalemia
- Fluid retention
- Cardiac issues

# Radium 223

- Patients with metastases to the bone
- Symptomatic
- No other metastatic sites

# Radium 223

- Xofigo
- Alpha emitting particle
- 6 injections
- 4 week intervals

# Radium 223

- Nausea
- Vomiting
- Diarrhea
- Edema
- Anemia
- Thrombocytopenia
- DO NOT USE IN COMBINATION WITH ZYTIGA

# Radium 223

- Improvement in pain
  - Quality of life
- 3 month overall improvement in survival as compared to placebo
- Helps prevent future skeletal related events



# Chemotherapy

- Docetaxel
- Given in combination with prednisone
- IV administration
- Oncologist

# Chemotherapy

- Fever
- Neutropenia
- Fatigue
- Neuropathy
- Cardiac toxicity