Grand Rounds in Prostate Cancer

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Disclosure

- Dr. Dreicer has acted as a consultant for Millennium, Janssen, Astellas, Roche, Merck, Dendreon, and Medivation.
- Dr. Narus has nothing to disclose.

Learning Objectives

- Define current therapies for castration-resistant prostate cancer (CRPC), particularly the roles of active prostate cancer surveillance vs. definitive therapy
- Summarize the potential benefits of chemotherapy in patients with locally advanced CRPC
- Discuss the sexual side effects from prostate cancer interventions
- List three strategies for the treatment of erectile dysfunction
Management of Castration-Resistant Prostate Cancer: Envisioning a Chronic Disease Paradigm

Robert Dreicer, MD, MS, FACP, FASCO

A. Abiraterone should be considered in all men with CRPC if asymptomatic or minimally symptomatic
B. One should wait 6–8 wk post stopping steroids before considering sipuleucel-T after finishing chemotherapy
C. Cabazitaxel is a good option for all men with symptomatic mCRPC
D. Radium 223 is of potential utility in all men with mCRPC post-doxetaxel
E. Abiraterone is a potent CYP17 lyase inhibitor

Which of the following statements about new agents in the management of prostate cancer is true?

A. Radium-223
B. Docetaxel
C. Cabazitaxel
D. Abiraterone/prednisone
E. Enzalutamide

Your patient has castrate metastatic prostate cancer with a rising PSA and new and progressive bone pain and moderate fatigue. He has both extensive bone and nodal metastases.

Which of the following is the most appropriate next therapeutic intervention?

A. Radium-223
B. Docetaxel
C. Cabazitaxel
D. Abiraterone/prednisone
E. Enzalutamide
Interdisciplinary GU Medical Oncology Care at the Cleveland Clinic

- 5 academic GU medical oncologists
- 2 advanced practitioners (1 PA, 1 NP)
- 1 GU oncology clinical RN
- Multiple GU oncology clinical research RNs

A Brief History of the Management of Advanced Prostate Cancer

- Pre-PSA era (Pre-1989)
  - Patient presents with de novo metastatic disease
  - ADT → response → symptomatic progression
- PSA-directed therapy era (1989-)
  - Rare de novo presentation metastatic disease
  - ADT → response assessed by PSA
  → biochemical progression
  → secondary hormonal maneuvers
  → chemotherapy

Death from other causes

Initial Prostate Evaluation: No Cancer Diagnosis
Clinically Localized Disease
Rising PSA Salvage Rx
Clinical Metastases Noncastrate
Clinical Metastases Castrate

Death from disease

Clinical States in Prostate Cancer

- Locally Advanced Disease
- Rising PSA: Hormonal Failure
- Locally Advanced Disease (De novo)
- Castrate Metastases
- Castrate Resistant Asymptomatic Metastases
- Castrate Resistant Symptomatic Metastases
- Organ Confined

Why Terminology Matters: Hormone Refractory/Androgen Independent: NOT

- Limits in molecular level understanding, available therapeutics influence view of CRPC
- Mixed retrospective clinical data
  - SWOG/ECOG
- French-American rule
- Clinical utility of “second-line" hormonal therapy
  - "Bicalutamide (Casodex) shuffle"

Lymph node metastases

(i) H & E
(ii) Nuclear AR expression
(iii) PSA stain with cytoplasmic PSA expression

PSA and FKBP5 are androgen regulated genes

SWOG = Southwest Oncology Group; ECOG = Eastern Cooperative Oncology Group.
**Testosterone Suppression With Current Therapies**

- Bilateral orchiectomy: Testosterone falls, on average, to 15 ng/dL (0.5 nmol/L).
- LHRH agonists range of suppression averages 30–40 ng/dL.
- Escape occurs in subset of patients.

**Steroid Synthesis**

Low-dose steroid replacement decreases ACTH and minimizes mineralocorticoid-related toxicity.
Progressive chemo-naive mCRPC patients (planned N = 1,088)
Asymptomatic or mildly symptomatic

1:1
AA 1,000 mg daily Prednisone 5 mg bid (Actual n = 546)
Placebo daily Prednisone 5 mg bid (Actual n = 542)

- Co-Primary
  - rPFS by central review
- OS
- Secondary
  - Time to opiate use (cancer-related pain)
  - Time to initiation of chemotherapy
  - Time to ECOG-PS deterioration
  - TTPP

Patients
Efficacy endpoints

Overall Study Design of COU-AA-302

- Phase III multicenter, randomized, double-blind, placebo-controlled study conducted at 151 sites in 12 countries; USA, Europe, Australia, Canada
- Stratification by ECOG performance status: 0 vs. 1

AA = abiraterone acetate; rPFS = radiographic progression-free survival; OS = overall survival; TTPP = time to PSA progression.

COU-AA-301: Abiraterone Acetate Improves Overall Survival in mCRPC

Placebo
10.9 mo (95% CI: 10.2–12.0 mo)
0
Survival (%)
Days from Randomization
Abiraterone acetate
14.8 mo (95% CI: 14.1–15.4 mo)
14.0 mo AA vs. 10.3 mo placebo
15.4 mo AA vs. 11.5 mo placebo

80
60
40
20
0

HR = 0.646 (0.54–0.77), p < .0001

Placebo
10.9 mo (95% CI: 10.2–12.0 mo)

2 prior chemos OS
1 prior chemos OS

Overall Study Design of COU-AA-302

- Phase III multicenter, randomized, double-blind, placebo-controlled study conducted at 151 sites in 12 countries; USA, Europe, Australia, Canada
- Stratification by ECOG performance status: 0 vs. 1
Radiographic PFS

OS

Enzalutamide (MDV3100)

- First-in-class androgen receptor signaling (ARS) inhibitor
- Affects multiple steps in ARS pathway
- Reduces efficiency of nuclear translocation
- Impairs DNA binding, recruitment of coactivators

AFFIRM: A Phase III Trial of Enzalutamide vs. Placebo in Post-Chemotherapy Treated Castration-Resistant Prostate Cancer (CRPC)

- Patient Population: 1,199 patients with progressive CRPC
- * Failed docetaxel chemotherapy

* Glucocorticoids were not required but allowed
AFFIRM: Enzalutamide Alters the Natural History of mCRPC After Chemotherapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td>0.63</td>
</tr>
<tr>
<td>PSA-PFS</td>
<td>0.25</td>
</tr>
<tr>
<td>R-PFS</td>
<td>0.40</td>
</tr>
</tbody>
</table>

PREVAIL: Study Design

Phase III Trial of MDV3100 (Enzalutamide) vs. Placebo in Chemonaive CRPC

Patients:
- 1,717 men with progressive mCRPC
- Asymptomatic/mildly symptomatic
- Chemotherapy naive
- Steroids allowed, but not required

Randomization:
- MDV3100 160 mg daily (capsules) n = 872
- Placebo n = 845

Primary Endpoints:
- Overall survival
- Radiographic progression-free survival
- PSA progression-free survival
Next-Generation AR-Targeting Agents: Lessons Learned

- Optimal timing to initiate therapy undefined
- Clinical judgment
  - Disease biology
  - Patient comfort
  - Pharmacoeconomics
- 1/3 response rule

Next-Generation AR-Targeting Agents: Lessons Learned: Evidence of Cross Resistance

- Retrospective studies
  - Lower response rates
  - Patients who progress on abiraterone; shorter response with enzalutamide, vice versa
- Impact on docetaxel response rates?
- Potential mechanisms of cross resistance
  - Glucocorticoid activation of AR1
  - Gain of function mutation in DHT2

Second-Line Hormonal Therapy: This Time With Drugs That Actually Work

Many issues remain
- Optimal timing
- Role of combination therapy
- When to stop androgen biosynthesis inhibitors
  - Major issue in the prechemotherapy setting
- Optimal dose of steroids for ABIs
- Issues of divergent practice urology vs. oncology
Second-Line Hormonal Therapy: This Time With Drugs That Actually Work

- Pharmacoeconomics
  - Bone-targeted agent with drugs that already impact skeletal-related events (SREs)?
- AR-directed therapy: Biochemical, earlier disease
  - Cure possible?
- Sorting out “personalized medicine,” i.e., identifying responders pretherapy

ALLIANCE (A031201): Enzalutamide vs. Enzalutamide/Abiraterone, Chemonaive mCRPC

Randomized

Patient Population
1,224 patients with progressive CRPC
- ECOG PS 0-1
- No prior treatment with taxane-based chemotherapy or mets
- No prior abiraterone, enzalutamide or other novel antiandrogen or androgen synthesis inhibitor

Primary Endpoint
Overall Survival
Tx continues until progression or toxicity

Active Cellular Immunotherapy (Sipuleucel-T)

Patient’s white blood cells harvested
- Short-term culture with protein “cassette”
- Prostatic acid phosphatase
- Cells infused back into patient (IV)
Randomized Phase III IMPACT Trial (IMmunotherapy Prostate AdenoCarcinoma Treatment)

- Primary endpoint: overall survival
- Secondary endpoint: time to objective disease progression

Asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer (N = 512)

- Sipuleucel-T q2wk x 3
- Placebo q2wk x 3

Treated at physician discretion

- Placebo q2wk x 3
- Treated at physician discretion and/or salvage protocol

The Sipuleucel-T Conundrum

- Sipuleucel-T appears to provide: Improved patient survival
- What sipuleucel-T DOES NOT DO: Not a therapy replacement for patients who need objective antitumor response

- Unprecedented development, integration of a novel therapy
  - No improvement in OR/PFS
  - Limited access dampens learning curve
  - Cost

TROPIC: Phase III Registration Study

- mCRPC patients who progressed during and after treatment with a docetaxel-based regimen (N = 755)

Stratification factors:
- ECOG PS (0, 1 vs. 2)
- Measurable vs. nonmeasurable disease

Primary endpoint: Overall survival

Secondary endpoints: Progression-free survival (PFS), response rate, and safety

Inclusion: Patients with measurable disease must have progressed by RECIST; otherwise must have had new lesions or PSA progression

- Cabazitaxel 25 mg/m² q 3 wk + prednisone* for 10 cycles (n = 378)
- Mitoxantrone 12 mg/m² q 3 wk + prednisone* for 10 cycles (n = 377)

*Oral prednisone/prednisolone: 10 mg daily

TROPIC: Overall Survival

![Graph showing overall survival rates for Cabazitaxel (CBZP) and Mitoxantrone (MP)]

- Median OS, mo
  - MP: 12.7
  - CBZP: 15.1
- HR: 0.72
- 95% CI: 0.61–0.84
- p value: < .0001

Patients at Risk, n

<table>
<thead>
<tr>
<th>Months</th>
<th>MP</th>
<th>CBZP</th>
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<tbody>
<tr>
<td>2</td>
<td>277</td>
<td>378</td>
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<tr>
<td>4</td>
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<tr>
<td>58</td>
<td>1</td>
<td>1</td>
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</tbody>
</table>

HR: Hazard Ratio, CI: Confidence Interval, p: p-value

Radium-223 Targets Bone Metastases

- Acts as a calcium mimic
- Targets new bone growth in, around bone metastases
- Excreted by gut

![Image of the Periodic Table highlighting Radium-223]

Critical Differences in Alpha and Beta Particles

<table>
<thead>
<tr>
<th></th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative particle mass</td>
<td>7300</td>
<td>1</td>
</tr>
<tr>
<td>Initial energy (MeV) per particle</td>
<td>3–8</td>
<td>0.01–2.5</td>
</tr>
<tr>
<td>Range in tissue (µm)</td>
<td>40–100</td>
<td>50–5,000</td>
</tr>
<tr>
<td>LET (KeV/µm)</td>
<td>60–230</td>
<td>0.015–0.4</td>
</tr>
<tr>
<td>DNA hits to kill cells</td>
<td>1–10</td>
<td>100–1,000</td>
</tr>
</tbody>
</table>

LET = linear energy transfer

Radium-223 Targets Bone Metastases

- α-particles cause double-strand DNA breaks in nearby tumor cells
  - Limited penetration of α-emitters (~2–10 cell diameters) results in highly localized killing of tumor cells with minimal collateral damage to normal tissue in surrounding area

**TREATMENT**

6 injections at 4-wk intervals
- Radium-223 (50 kBq/kg) + Best standard of care
- Placebo (saline) + Best standard of care

**PLACEBO VS. RADON**

N = 922

**STRATIFICATION**

- Confirmed symptomatic CRPC
- ≥ 2 bone metastases
- No known visceral metastases
- Post-docetaxel or unfit for docetaxel


**Overall Survival Benefit**

**mCRPC Studies: 2010–2014**

<table>
<thead>
<tr>
<th>Agents</th>
<th>Disease State</th>
<th>Median OS</th>
<th>HR (p value)</th>
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</thead>
<tbody>
<tr>
<td>Sipuleucel-T vs. placebo</td>
<td>Chemonaive</td>
<td>25.8 mo</td>
<td>0.789 (.017)</td>
</tr>
<tr>
<td>Docetaxel vs. mitoxantrone/prednisone</td>
<td>Chemonaive</td>
<td>18.9 mo</td>
<td>0.76 (.009)</td>
</tr>
<tr>
<td>Cabazitaxel vs. mitoxantrone/prednisone</td>
<td>Post-docetaxel</td>
<td>15.1 mo</td>
<td>0.70 (&lt; .0001)</td>
</tr>
<tr>
<td>Abiraterone/prednisone vs. placebo/prednisone</td>
<td>Post-docetaxel</td>
<td>14.8 mo</td>
<td>0.646 (&lt; .0001)</td>
</tr>
<tr>
<td>Abiraterone/prednisone vs.placebo/prednisone</td>
<td>Progressive chemotherapy</td>
<td>Not reached</td>
<td>0.75 (.01)</td>
</tr>
<tr>
<td>Enzalutamide vs. placebo</td>
<td>Post-docetaxel</td>
<td>18.4 mo</td>
<td>0.631 (&lt; .0001)</td>
</tr>
<tr>
<td>Enzalutamide vs. placebo</td>
<td>Progressive chemotherapy</td>
<td>32.4 mo</td>
<td>0.70 (&lt; .0001)</td>
</tr>
<tr>
<td>Radium-223 vs. placebo</td>
<td>Post-docetaxel</td>
<td>14.9 mo</td>
<td>0.695 (.003)</td>
</tr>
</tbody>
</table>
“Everyone has a photographic memory. Some just don’t have film.”  
–Steven Wright

Men’s Sexual and Reproductive Health  
Joseph B. Narus, DNP, GNP-BC, ANP

I am confident about addressing the sexual and reproductive health issues of male patients.  
A. Yes  
B. No
I routinely take a sexual history for male patients.

A. Yes
B. No

Sexual Discussion Barriers

- Clinician barriers
  - Embarrassment to raise subject
  - Focused on other health issues
  - Lack of training on sexual medicine issues
  - Discomfort using psychosocial counseling interventions
  - Lacks awareness of association with other conditions

- Patient barriers
  - Emotional factors (anxiety, embarrassment)
  - Age
  - Perception not a medical problem
  - Lack of knowledge of treatment options
  - Insurance coverage

Taking a Sexual History

- Explore your cultural, religious, gender-based concepts of sexuality
- Respect patient’s cultural, religious, gender-based concepts of sexuality
- Appropriate setting
- Your attitude, ability to communicate provide reassurance
- Eye-to-eye contact, pauses, avoid writing or typing as patient discloses personal information (if possible)
- Explain why you are taking a history: Potential sexual sequelae from treatment
- Note that you realize information is highly personal, and encourage the patient to be open and direct
Sexual History

- Sexual response
  - “How is your sexual function?”
  - Reality vs. internet (appearance and endurance)
  - “Are you satisfied with your relationship and sexual function?”
  - “Have you maintained interest in sex?”
  - Are you able to achieve and maintain an erection?
  - Partner vs. masturbation
  - Spouse/partner’s interest, health

- Neutral questions: Sexual orientation, gender, sexual identity
  - “Do you identify/describe yourself as heterosexual, gay, bisexual, or undefined?”
  - “Are you currently in a relationship?”
  - Appropriate pronouns
  - Appropriate terms: Penetrating/receptive (“top/bottom”)

Assessment of Sexual Dysfunction

- Medical history
- Surgical history
- Social history
  - Relationship status
  - Alcohol, recreational drugs, tobacco use
- Physical examination
  - Vital signs, waist circumference, gynecomastia, hair distribution
  - Genital exam (suprapubic fat, penis & scrotum)
  - Prostate
- Tests
  - Laboratory (blood, urine)
  - Biothesiometry
  - Duplex Doppler ultrasound
  - Penile nocturnal tumescence test (Rigi-Scan)

Case Study

- Mr. Smith: Married 58-year-old with prostate cancer
- 18 mo post robotic-assisted laparoscopic prostatectomy (RALP); 12 mo post external-beam radiotherapy (EBRT) with androgen deprivation therapy (ADT) for biochemical recurrence. PSA = < 0.05
- Presents with spouse; reports worsening erectile dysfunction (ED) since EBRT and inconsistent ability to achieve an orgasm. Denies ED prior to RALP; was responding to sildenafil 100 mg post-op. Reports sexual intercourse with spouse 2 times a week prior to prostatectomy.
- Recently attempted intercourse with sildenafil 100 mg; achieved 40% rigid erection. Also distressed about ejaculating urine with delayed orgasm.

How would you manage Mr. Smith?
Male Sexual Dysfunction

- Erectile dysfunction
  - Organic
  - Psychogenic
  - Mixed
- Ejaculation/Orgasm disorders
  - Anejaculation
  - Dysorgasmia (painful orgasm)
  - Anorgasmia/Retarded orgasm
  - Premature
- Sexual incontinence
  - Arousal Incontinence
  - Climacturia
- Penile morphologic changes
  - Curvature (Peyronie’s disease)

Physiology of Sexual Function

- Complex cascade of events
  - Neurologic
  - Vascular
  - Hormonal
  - Psychological
- Any disruption affects erectile function

Penile Anatomy: Serial Section

- Dorsal penile artery
- Sinusoidal spaces
- Cavernosal artery
- Corpus cavernosum
- Urethral artery
- Corpus spongiosum
- Deep dorsal vein
- Superficial dorsal vein
- Dorsal penile nerve
- Buck’s fascia
- Circumflex veins
- Tunica albuginea
- Urethra
Erectile Dysfunction

- ... is the consistent inability to achieve or maintain a penile erection sufficient for "adequate" sexual relations.
- The effects of ED interfere with:
  - Man's self-esteem
  - Interpersonal relationships
  - Sense of well-being
- Post-prostatectomy ED rates range from 12%–96%² with a meta-analysis reporting an overall erectile function recovery rate of 58%³.
- Incidence of radiation-associated ED post-external beam or brachytherapy for prostate cancer is 15%–60%⁴.

Instruments to Evaluate Erectile Dysfunction

Sexual Health Inventory for Men (SHIM)
- Questionnaire-based, reliable self-administered symptom scales
- Maximum score = 25
- Abridged version of the International Index of Erectile Function
- 2 domains (5 questions, rating 1–5):
  - Erectile function (4 questions)
  - Satisfaction (1 question)
- Results:
  - 5–7 = severe
  - 8–11 = moderate
  - 12–16 = mild to moderate
  - 17–21 = mild
  - 22–25 = normal

Instruments to Measure Erectile Dysfunction

International Index of Erectile Function
- Questionnaire-based, reliable self-administered symptom scales
- Maximum score = 75
- 5 domains (15 questions, rating 0 or 1–5):
  - Erectile function (6 questions)
  - Orgasmic function (2 questions)
  - Sexual desire (2 questions)
  - Intercourse satisfaction (3 questions)
  - Overall satisfaction (2 questions)
- Results:
  - ≤ 10 = severe
  - 11–17 = moderate
  - 18–25 = mild
  - 26 = normal
**Etiology of Erectile Dysfunction**

- Arteriogenic (accessory pudendal artery injury)
- Venogenic (erectile tissue damage)
- Neurogenic (cavernosal nerve injury)
- Psychogenic (confidence erosion)

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**Flaccid**
- $P_0 = 35-40$ mm Hg
- Increased TGF-$\beta_1$ Secretion
- Collagen Production
- Fibrosis and venous leak

**Erect**
- $P_0 = 70-100$ mm Hg
- Increased cGMP Secretion
- Decreased Collagen Production
- Preserved erectile tissue integrity

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**Venous Leak**

- Tunica albuginea
- Subtunical venule
- Smooth muscle
Management of Erectile Dysfunction

- Treatment options generally motivated by clinician, patient, and/or patient’s spouse/partner
- Risks and benefits for each
- Advantage/disadvantage (including costs)

First-line therapy
- Lifestyle modification, reversible causes
- Oral agents

Second-line therapy
- Vacuum erection device
- Intracavernosal injection
- Intracorporeal suppository

Third-line therapy
- Implantable penile prosthesis

Oral Agents: PDE5 Inhibitors

- Nitric oxide dependent mechanism
- Success depends on
  - Time of trial
  - Degree of nerve-sparing
  - Responsiveness of corporal cavernosal smooth muscle
- Post-pelvic surgery response
  - 20% at 3 mo
  - 50% at 12 mo
  - Slightly higher at 18 mo
- Penile rehabilitation
  - Low-dose PDE5 inhibitors for endothelial protection
**Oral Agents**

**Advantages**
- Quick and easy to administer
- Discreet
- Suitable for travel

**Disadvantages**
- Poor efficacy post-prostatectomy (early post-op)
- Insurance coverage
- Side effects
  - Headache
  - Back/muscle pain (tadalafil)
  - Nasal congestion
  - GI upset
  - Facial flushing
  - Tinnitus (<1%)
  - Visual changes

**Correct PDE5 Inhibitor Use**
- Timing
  - Sildenafil and vardenafl (1 hr prior to activity)
  - Tadalafil (2–4 hr pre-activity)
  - Avanafil (30 min)
- Take on empty stomach
- Tadalafil and avanafil no food effect
- Avoid taking when tired or under stress
- Must be engaged in sexual activity (partner or masturbatory)
- Contraindicated
  - Unstable angina requiring nitroglycerine use
  - History of hypotension (SBP < 90 or DBP < 60)
  - History of retinitis pigmentosa
  - Macular degeneration
  - Inability to walk up 2 flights of stairs
  - Caution with retroviral drugs

**PDE5 Inhibitor Cost**
- **Sildenafil**
  - 25 mg, 50 mg, 100 mg
- **Vardenafil**
  - 2.5 mg, 5 mg, 10 mg, 20 mg
- **Tadalafil**
  - 5 mg, 10 mg, 20 mg
- **Avanafil**
  - 50 mg, 100 mg, 200 mg

Not covered by Medicare or Medicaid

Insurance plans cover between 4–10 tabs  
425–30 days (copayments vary)
Intracavernosal Injection (ICI) Therapy

- Involves direct injection of papaverine, phentolamine, and alprostadil separately or in combination into the corpus cavernosum
- Utilized when oral agents not effective or side effects not tolerated
- Results in inhibition of PDE5, leading to increased cAMP and cGMP in penile erectile tissue

ICI Therapy

**Advantages**
- High efficacy rate
- Reliable
- Suitable for travel but agents with PGE1 require refrigeration

**Disadvantages**
- Invasiveness and anxiety of injecting needle into penis
- Cost/insurance coverage
- Side effects:
  - Priapism
  - Bruising/bleeding/hematoma
  - PGE1 pain

**Precautions**
- Obese abdomen
- History vasovagal response
- Dexterity problems
- Uncontrolled hypertension
- Predisposition to priapism due to hematologic disorders (e.g., sickle cell anemia, multiple myeloma, leukemia)

**Contraindications**
- Concurrent use of MAO inhibitors
- Penile prosthesis
- Sexual activity is inadvisable or contraindicated

ICI Training

Instructed to angle needle at 10 o’clock or 2 o’clock position on shaft directly behind midline

ICI Agent Costs

- Alprostadil
  - Kit
    - 10 µg (1) = $108
    - 20 µg (1) = $140
    - 40 µg (1) = $191
  - Solution (reconstituted)
    - 20 µg (1) = $10
    - 40 µg (1) = $79
- Compounded agents
  - 500 units (5 mL vial) = $50–$70
  - 29-gauge syringe
    - (30) = $20–$25

- Not covered by Medicare or Medicaid
- Some insurance plans provide coverage with limited quantity in 25–30 day period (co-payments vary)
- Some insurance plans have started providing limited coverage for compounded agents with restrictions

Implantable Penile Prosthesis

- Utilized in patients who have failed drug therapy, cannot tolerate, or patient burnout with therapies
- Implant types
  - Mechanical
    - Malleable
  - Inflatable
    - Two piece
    - Three piece (reservoir placed in abdomen)
- Does increase girth, but not length
### Penile Prosthesis: 2 Piece

- **Advantages**
  - High efficacy
  - Generates a 100% rigid erection in 15–30 sec
  - High satisfaction rate
  - Simple to use
  - Can use multiple times in 24 hr
  - Limited travel issues (may show up on TSA scan)

- **Disadvantages**
  - Invasive permanent/irreversible surgical procedure
  - Risk of infection (approx. 2%)
  - Mechanical breakdown (15% within 10 yr)
  - Autoinflation
  - Surgical side effects
    - Pain/edema/bruising
    - Scrotal hematoma

### Penile Prosthesis: 3 Piece

**Advantages**

**Disadvantages**

### Implantable Penile Prosthesis

**Advantages**

**Disadvantages**

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References:

Penile Prosthesis Cost

- Surgery: $8,000 to $12,000
- Time associated with absence from work
- Covered by Medicare and Medicaid
- Covered by most insurance plans

Ejaculation Disorders

- Anejaculation
- Dyseorgasmia (painful orgasm)
  - Tamsulosin HCL (0.4 mg)
  - Alfuzosin (10 mg)
  - Patient education regarding side effects of α-blockers
- Anorgasmia (no orgasm)/Retarded orgasm (delayed)
  - Neuropathy (chemotherapy/radiation)
  - Psychogenic
  - SSRI
  - Low testosterone (ADT)
- Premature
  - SSRI and sprays

Sexual Incontinence

- Common after radical pelvic cancer surgeries
- Two types
  - Arousal
  - Climacturia (orgasm leakage)
- Patient and partner distress
- Interventions
  - Kegel exercise
  - Condom
  - Penile constriction loop
  - Artificial urinary sphincter

Penile Changes

Curvature (Peyronie’s Disease)

- Localized connective tissue disorder affecting tunica albuginea of penis where fibrous scar tissue replaces normal elastic fibers
- Manifests as curvature, indentation, shortening, hourglass deformity
- Precise process of plaque formation uncertain but may be related to post-prostatectomy fibrotic changes, secondary to denervation and/or local ischemia
- Early assessment and intervention upon discovery by patient or clinician recommended to stabilize and prevent progression
- Study of 1,100 men incidence was 15.9% post-prostatectomy

Penile Changes

- Peyronie’s assessment
  - Duplex Doppler ultrasound
  - Dynamic infusion cavernosometry
- Peyronie’s treatment
  - Intraligamental verapamil
  - Collagenase clostridium histolyticum
  - Penile traction device
  - Colchicine/pentoxifylline

Case Study Revisited

- Mr. Smith: Married, 58-yr-old with prostate cancer.
- 18 mo post robotic assisted laparoscopic prostatectomy (RALP); 12 mo post external-beam radiotherapy (EBRT) with androgen deprivation therapy (ADT) for biochemical recurrence. PSA = <0.05
- Presents with spouse; reports worsening erectile dysfunction (ED) since EBRT and inconsistent ability to achieve an orgasm. Denies ED prior to RALP; was responding to sildenafil 100 mg post-op. Reports sexual intercourse with spouse 2 times a week prior to prostatectomy.
- History of elevated cholesterol, HTN. Denies tobacco, recreational drug use.
- Current medications: sildenafil 25 mg qhs, HCTZ 25 mg daily, simvastatin 10 mg daily.
- Recently attempted intercourse with sildenafil 100 mg; achieved 40% rigid erection. Also distressed about ejaculating urine with delayed orgasm.

How would you manage Mr. Smith?

- Discontinue PDE5 inhibitors
- Intracavernosal injection therapy
- Penile constriction loop/lifestyle modification
- Lifestyle/sexual counseling
Summary

- Important to counsel patients pre and post prostate cancer treatment
- Set realistic expectations
- Early intervention and initiative to assess and manage patient can be key to post treatment satisfaction
- Refer to a sexual and reproductive medicine program/clinician when applicable and available
- narusj@mskcc.org

Questions?

- Rajeev’s Institute for Erectile Dysfunction