Introduction: Prostate Cancer

- Most commonly diagnosed cancer in men in the United States
  - Approximately 164,690 new cases were diagnosed in 2018
- Second leading cause of cancer-related death in men in the United States
  - Approximately 29,430 deaths in 2018
  - Approximately 50% of patients who die from prostate cancer have metastases at diagnosis
- 5-year survival for distant stage prostate cancer is <30%, compared to nearly 100% for local- and regional disease

Introduction, cont’d.

- Gains in survival over the last decade have been modest, but recent years have seen an acceleration in life-extending drug development
- The role of oncology nursing in mPRCA management is primarily focused on providing information and support to patients and families
  - AEs related to treatment can impact adherence and outcomes
  - Sexual and urinary function, perceptions of self, and quality of life can be major stressors for patients
  - Nurses can provide patient education on identifying, reporting, and mitigating AEs and other stressors
Role of Androgens in Prostate Cancer

• Prostate cancer cells usually require androgen hormones, such as testosterone, to grow
• Androgen deprivation therapy (ADT) is the gold standard of therapy for advanced disease
  - ADT reduces the levels of androgen hormones with surgery or drugs to prevent prostate cancer cells from growing
• Newer and emerging agents act at different steps along the androgen-AR signaling pathway to further block androgen activity and inhibit the cancer’s growth

Therapy for mPRCA

Past:
- Standard hormonal therapy for all (ADT)

Present:
- Intensified medical therapy for many
  - Docetaxel for high-volume disease
  - Abiraterone for high and low-volume disease

Future:
- More and more individualized approaches
- Molecularly selected agents in addition to hormonal therapy
- Perhaps metastases-directed therapy and/or local therapy

Metastatic Hormone-Sensitive Prostate Cancer
Case 1: Mr. Reynolds

Initial Management of Patients with mPRCA

- ADT (medical or surgical) has been first-line standard of care for mPRCA for nearly 80 years
  - Medical castration with luteinizing hormone-releasing hormone (LHRH) agonist/antagonist treatment
  - Surgical castration (bilateral orchiectomy)
- ADT is moderately effective but associated with side effects and resistance

Options for Medical Castration

<table>
<thead>
<tr>
<th>Agent</th>
<th>Administration/Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide</td>
<td>Subcutaneous injection; 1, 3, 4, or 6-month administration (7.5 mg for 1-month, 22.5 mg for 3-month, 30 mg for 4-month, and 45 mg for 6-month)</td>
</tr>
<tr>
<td>Degarelix</td>
<td>Subcutaneous injection; treatment is started with a dose of 240 mg given as two injections of 120 mg each, followed by maintenance doses of 80 mg administered as a single injection every 28 days</td>
</tr>
<tr>
<td>Triptorelin</td>
<td>Intramuscular injection; recommended dosage is 3.75 mg once every 4 weeks, 11.25 mg once every 12 weeks, or 22.5 mg once every 24 weeks</td>
</tr>
<tr>
<td>Goserelin</td>
<td>Subcutaneous implant; recommended dosage is 3.6 mg every 4 weeks or 10.8 mg every 12 weeks</td>
</tr>
<tr>
<td>Histrelin</td>
<td>Annual subcutaneous implant; 50 mg</td>
</tr>
</tbody>
</table>
Potential Side Effects of ADT

- Side effects impair quality of life and treatment adherence
- Side effects of ADT, whether medical or surgical, can include:
  - Hot flashes
  - Erectile dysfunction
  - Loss of libido
  - Bone loss (which can lead to spine and hip fractures)
  - Decreased muscle mass
  - Weight gain
  - Fatigue
  - Gynecomastia
  - Impaired glucose tolerance
  - Metabolic syndrome
  - Increased risk of CVD
  - Psychological effects
  - and/or mood changes
  - Others…

Considerations for Addressing Side Effects Associated with ADT

- Inquire about patient concerns at every visit
- Discuss short and long-term side effects with patients and families, including
  - Strategies for prevention
  - Recognition/reporting
  - Strategies for mitigation
- Discuss importance of continued adherence/compliance

Multi Modality Treatment for mPRCA

- Radiation therapy can be used in combination with ADT and consists of external irradiation or brachytherapy
  - External radiotherapy AEs include diarrhea, fatigue, cystitis, erectile dysfunction
  - Brachytherapy can cause pain, hematuria, infection, cystitis, fatigue
- Docetaxel is a cytotoxic chemotherapy agent that may be used with ADT
  - Associated with increased risk of myelosuppression, peripheral neuropathy, hypersensitivity reaction, and gastrointestinal AEs
Multi Modality Treatment for mPRCA

- Patients are likely to be on different treatment modalities concurrently; side effects may potentiate each other
- Recognizing which modality is causing which side effect can be difficult
- Consistently discuss side effects of concern with patients

Metastatic Castration-Resistant Prostate Cancer

Case 2: Mr. Smith
Metastatic Castration-Resistant Prostate Cancer

Most patients with mPRCA treated with ADT experience disease progression within 2 to 3 years, to a disease state known as metastatic castration-resistant prostate cancer (mCRPC).

Until recently, docetaxel was the primary treatment for mCRPC.

Since 2010, 5 new agents have been approved for mCRPC: abiraterone, cabazitaxel, enzalutamide, radium-223, sipuleucel-T.

Optimal use, sequence, timing of these agents not yet established.

All have different indications and toxicity profiles.

Systemic Treatments Approved Since 2010 for mCRPC

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Key Trial</th>
<th>Year of FDA Approval</th>
<th>Sequencing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabazitaxel</td>
<td>TROPIC</td>
<td>2010</td>
<td>Post-docetaxel</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>AFFIRM, PREVAIL</td>
<td>2012, 2014</td>
<td>Post-docetaxel, First-line</td>
</tr>
<tr>
<td>Radium-223</td>
<td>ALSYMPCA</td>
<td>2013</td>
<td>Bone-metastatic disease only</td>
</tr>
<tr>
<td>Sipuleucel-T</td>
<td>IMPACT</td>
<td>2010</td>
<td>First-line</td>
</tr>
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</table>

Abiraterone:
- Inhibits CYP17
- Approved for mCRPC in combination with low-dose prednisone
- Fatigue, edema, arthralgia, constipation
- Liver toxicity may also be seen and liver function should be measured at baseline and throughout treatment; dose reductions may be necessary depending on transaminase levels

Cabazitaxel:
- Novel taxane
- Approved for mCRPC previously treated with docetaxel
- Increased risk of abnormal blood counts (e.g., anemia, neutropenia), diarrhoea, fatigue, and nausea or vomiting
- Patients receiving cabazitaxel should be educated on infection monitoring and prevention measures and undergo regular blood monitoring

Systemic Treatments Approved Since 2010 for mCRPC

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<th>MOA and Indications</th>
<th>Possible Side Effects</th>
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| Abiraterone | Inhibits CYP17
- Approved for mCRPC in combination with low-dose prednisone | Fatigue, edema, arthralgia, constipation
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| Cabazitaxel | Novel taxane
- Approved for mCRPC previously treated with docetaxel | Increased risk of abnormal blood counts (e.g., anemia, neutropenia), diarrhoea, fatigue, and nausea or vomiting
- Patients receiving cabazitaxel should be educated on infection monitoring and prevention measures and undergo regular blood monitoring |
Systemic Treatments Approved Since 2010 for mCRPC

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<tr>
<td>Enzalutamide</td>
<td>• Androgen receptor inhibitor</td>
<td>• Fatigue, back pain, arthralgia, gastrointestinal side effects, hypertension, and anorexia</td>
</tr>
<tr>
<td></td>
<td>• Radioisotopic that selectively targets bone metastases</td>
<td>• Anemia, gastrointestinal effects, fatigue, bone pain, fatigue, myelosuppression, and peripheral edema</td>
</tr>
<tr>
<td></td>
<td>• Approved for mCRPC with symptomatic bone metastases without visceral metastases</td>
<td></td>
</tr>
<tr>
<td>Radium-223</td>
<td>• Radiopharmaceutical that selectively targets bone metastases</td>
<td>• Chills, fever, headache, influenza-like illness, hematuria, somnolence, and events</td>
</tr>
<tr>
<td>Sipuleucel-T</td>
<td>• Therapeutic cancer vaccine</td>
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Managing Side Effects

### Toxicity (Drug)

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<tr>
<th>Toxicity (Drug)</th>
<th>Key Considerations</th>
<th>Management Recommendations</th>
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</thead>
<tbody>
<tr>
<td>Administration</td>
<td>Adverse effects (sipuleucel-T)</td>
<td>• Personal and digital triaging, shift, triage, and framing</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>• Perioral and digital tingling, chills, nausea, and fainting</td>
<td>• Discuss the procedure in advance, including the long duration and resulting need to be well hydrated, to avoid caffeine, and to consume a calcium-rich meal on the day of the procedure</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Abnormalities (abiraterone)</td>
<td>• Grade 3 or greater diarrhea can lead to dose delay or reduction</td>
</tr>
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<td>Abnormalities</td>
<td>• Grade 3 or greater diarrhea can lead to dose delay or reduction</td>
<td>• Educate patients about hydration or antidiarrheal medication, and administer when required</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Abnormalities (abiraterone)</td>
<td>• Causes of fatigue are multifactorial, and dose modification may reduce the impact on patient functioning</td>
</tr>
<tr>
<td>Hematologic AEs</td>
<td>Abnormalities (cabazitaxel)</td>
<td>• Causes of fatigue are multifactorial, and dose modification may reduce the impact on patient functioning</td>
</tr>
<tr>
<td>Infection</td>
<td>Abnormalities (cabazitaxel)</td>
<td>• Causes of fatigue are multifactorial, and dose modification may reduce the impact on patient functioning</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Abnormalities (cabazitaxel)</td>
<td>• Causes of fatigue are multifactorial, and dose modification may reduce the impact on patient functioning</td>
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<td>Administration</td>
<td>Food effect (abiraterone)</td>
<td>• Abnormalities may increase by as much as 10-fold when taken with meals, increasing the likelihood of toxicity</td>
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</tr>
<tr>
<td>Hematologic AEs</td>
<td>Abnormalities (abiraterone)</td>
<td>• Colorectal malignancies have been reported with cabozantinib, so frequent blood monitoring is recommended to determine if growth factor support and/or dose modification is needed</td>
</tr>
<tr>
<td>AEs or infection</td>
<td>Abnormalities (abiraterone)</td>
<td>• Consider primary prophylaxis in high-risk patients (aged older than 65 years, poor performance status, previous medical history, extensive radiation ports, prior radiotherapy, or other serious comorbidities)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Abnormalities (abiraterone)</td>
<td>• All patients should receive premedication with IV antihistamine, corticosteroids, and an H2 antagonist</td>
</tr>
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<td>Food effect (abiraterone)</td>
<td>• Educate patients about the risks of taking abiraterone with food</td>
</tr>
<tr>
<td>Food effect</td>
<td>• Abnormalities may increase by as much as 10-fold when taken with meals, increasing the likelihood of toxicity</td>
<td></td>
</tr>
<tr>
<td>Hematologic AEs</td>
<td>Abnormalities (abiraterone)</td>
<td>• Educate patients about the high risk of infection at neoplastic/radiation and how to recognize the signs of hematologic toxicity (eg, headache, cough, dyspnea, diarrhea, fever, chills)</td>
</tr>
<tr>
<td>AEs or infection</td>
<td>Abnormalities (abiraterone)</td>
<td>• Advise patients to monitor their temperature and seek immediate advice if it exceeds 100.4°F for any duration or 99.5°F for more than one hour</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Abnormalities (abiraterone)</td>
<td>• Advise patients that antihistamines and NSAIDs can mask symptoms like fever</td>
</tr>
</tbody>
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Managing Side Effects

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</tr>
</thead>
<tbody>
<tr>
<td>Liver function abnormalities (abiraterone)</td>
<td>Patients with moderate hepatic impairment should receive a reduced abiraterone dose (250 mg) and more frequent monitoring. Liver function tests should be performed before treatment.</td>
<td>Patients with normal transaminase levels at baseline should be monitored every two weeks for the first three months, and then monthly thereafter. Marked increases in liver enzymes may require treatment discontinuation or a dose reduction.</td>
</tr>
<tr>
<td>Nausea and vomiting (cabazitaxel)</td>
<td>Prolonged periods of uncontrolled vomiting may require hospital admission to correct fluid and electrolyte deficits. Patients should be monitored for the development of constipation and peroperative antibiotics. Inform patients that antiemetics will be included in their medications for cabazitaxel. Instruct patients to maintain adequate fluid intake.</td>
<td>Inform patients that antiemetics will be included in their medications for cabazitaxel. Discuss the incidence of nausea and vomiting at each visit, potentially assisted by a patient diary. Instruct patients to maintain adequate fluid intake.</td>
</tr>
<tr>
<td>Peripheral neuropathy (cabazitaxel)</td>
<td>Chemotherapy-induced peripheral neuropathy can be extremely painful and lead to significant loss of functional abilities and decreased quality of life. The clinical course commonly begins with paresthesia (tingling) and dysesthesia (e.g., pain, itching, “pins and needles”) in fingers and toes and spreads to arms and legs. No treatments are known: Provide educational support and monitor symptoms over time. Interruption of chemotherapy can alleviate symptoms, but recovery tends to be slow.</td>
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</tr>
<tr>
<td>Renal failure (cabazitaxel)</td>
<td>Most cases occurred in association with sepsis, dehydration, or obstruction urinary tract. Identify causes of renal failure and treat aggressively.</td>
<td>Refer patients to specialist management as needed. Refer patients for specialist management as needed.</td>
</tr>
<tr>
<td>Seizures (enzalutamide)</td>
<td>Patients with predisposing factors for seizure were excluded from phase III trials of enzalutamide.</td>
<td>Inform patients receiving enzalutamide about the risk of seizures and sudden loss of consciousness. Advise patients not to participate in activities that could lead to serious harm should a seizure occur.</td>
</tr>
<tr>
<td>Toxicity associated w/elevated steroid synthesis (abiraterone)</td>
<td>Monitor for fluid retention, hypertension, and hypokalemia at least once per month. Abiraterone should be used with caution in patients with a history of CVD, particularly when underlying medical conditions may be complicated by fluid retention, hypertension, and hypokalemia. Consider concurrent administration of abiraterone with low-dose glucocorticoids.</td>
<td>Obtain an accurate patient history related to cardiovascular conditions. Hypertension and hypokalemia should be controlled before and during therapy with abiraterone. Hypertension-related side effects can be treated using the mineralocorticoid receptor antagonist spironolactone in combination with a salt-restricted diet.</td>
</tr>
</tbody>
</table>

Bone Health in mPRCA
Bone Health in mPRCA

- Bone loss related to ADT and prostate cancer metastatic to bone can lead to fragility fractures in the wrist, spine, and hip
- The risk of bone loss is particularly high among older men treated with ADT, with a 50% rate of osteoporosis at 4 years and 80% at 10 years
- 80-90% of men with mCRPC have radiologically detectable bone metastases

Bone Health in mPRCA, cont’d.

- Use of a bone-protective therapy is an important aspect of PRCA management
- Bone protective therapy can decrease the risk of skeletal related events (SREs) by
  - Relieving bone pain
  - Preventing fractures
  - Decreasing the need for surgery and radiation to the bones
  - Lowering the risk of spinal cord compression

Management Recommendations

- Provide patient education on bone health and fracture risk
- Screen for and identify patients at increased risk of treatment-related osteoporosis or bone fragility due to bone metastases
  - Baseline bone mineral density scan (dual-energy x-ray absorptiometry, or DEXA, scan) prior to beginning ADT
  - Regular follow-up DEXA scans to monitor for bone loss
- Recommended lifestyle changes, including weight-bearing and strengthening exercises and avoiding smoking and excessive alcohol use
Supplemental Calcium and Vitamin D

- Consider supplemental calcium and vitamin D3 based on age and fracture risk
  - Calcium (1000-1200 mg daily from food and supplements)
  - Vitamin D3 (400-1000 IU daily)
- Calcium supplements are available as calcium carbonate or calcium citrate
  - Calcium carbonate requires gastric acid for optimal absorption and should be taken with food
  - Calcium citrate does not require gastric acid for absorption and can be taken in between meals
  - Calcium supplements should be taken in divided doses of no more than 600 mg at one time
  - Whether calcium supplements raise the risk of CVD is currently debated
  - Increasing dietary calcium in food is associated with a lower risk for nephrolithiasis compared with calcium supplements
- Vitamin D plays a role in gastrointestinal calcium absorption and is essential for maintaining normal bone mineralization

Bone Protective Therapy

- Zoledronic Acid
  - Highly potent bisphosphonate
  - Intravenous administration
  - Patients must be adequately hydrated and a serum creatinine level should be assessed prior to administration
- Denosumab
  - RANKL inhibitor
  - Subcutaneous administration
- Hypocalcemia is a common side effect of both agents
  - Recommend starting vitamin D before the initiation of therapy and monitor calcium levels during therapy

Osteonecrosis of the Jaw

- Both zoledronic acid and denosumab are associated with an increased risk of osteonecrosis of the jaw (ONJ)
  - Severe and painful condition characterized by exposure of mandibular or maxillary bone through lesions in the gingiva that do not heal
- Preventive measures can minimize the risk of ONJ
- Refer for a dental evaluation before starting either agent
Additional Supportive Care Needs for Patients with mPRCA

Supportive Nursing Care

- Supportive nursing care is associated with the following
  - Improved symptoms from treatment-related complications and the disease itself
  - Decreased psychological and emotional distress
  - Increased patient knowledge and self-management
  - Decreased use of acute services
- Features of supportive nursing care include
  - Education and support at diagnosis
  - Guidance with decision-making regarding treatment
  - Management of side effects during and immediately after treatment
  - Continued support for long-term sequelae of the disease or treatment

Additional Supportive Care Measures in mPRCA

- Address psychosocial issues
- Provide information on disease and health systems (eg, disease education, home care, reducing risk of comorbidities)
- Address concerns related to bladder, bowel, and sexual dysfunction
- Address patient concerns about imaging modalities used to monitor for disease progression (eg, risk vs benefit)
- Monitor for and address pain
- Monitor for and address complications (eg, spinal cord compression, urinary obstruction)

Conclusions and Key Summary Points

• Nurses can help in the management of patients with prostate cancer in numerous ways, including
  - Identifying patients with existing comorbidities that overlap with toxicity profiles of therapies
  - Monitoring for disease progression
  - Providing support as part of the treatment team

• Treatment decisions are likely to be influenced by side-effect manageability, past experiences, and patient perspectives

Conclusions and Key Summary Points, cont’d.

• Optimize the treatment decision-making process by identifying patient needs and enabling patients to have an informed and involved role
• Optimize the management of both ADT- and metastasis-related bone health in patients with mPRCA
• It’s important to have an understanding of the treatment journey, be familiar with treatment options, and coordinate patient care to improve patient management, quality of experience, and outcomes
Nursing Management of Treatment-Related Side Effects in Metastatic Prostate Cancer

References


LUPRON DEPOT (leuprolide) [package insert]. North Chicago, IL: AbbVie Inc.


ZOLADEX (goserelin) [package insert]. Lake Forest, IL: AstraZeneca.