Establishing an Advanced Prostate Cancer Clinic: Nursing Focus

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How to Start the Clinic

- Collaborate with one primary urologist
- Have support from all urology partners
- Set up protocols
- Consider starting with ADT clinic
- Decide how to schedule, morning or afternoon clinic
- RN or Advanced Practice Provider
- Use of EMR, what functionality do you have

Suggested Protocols

- ADT therapy
- Imaging Guidelines
- Abiraterone (Zytiga)
- Enzalutamide (Xtandi)
- Radium 223 (Xofigo)
- Sipuleucel T (Provenge)
- Denosumab (Prolia, Xgeva)
- Docetaxel (Taxotere, Docefrez)
- Cabazitaxel (Jevtana)

Assemble Patient Education

- Decide on written patient education information for the therapies.
- Load education information into EMR
- Can obtain from pharmaceutical reps, company drug websites, create your own.

Androgen Deprivation

- **ADT is the Gold Standard for men with metastatic disease**
  - Treatment with ADT is not curative and we know that most men will become resistant
- LHRH agonist or antagonist (Medical Castration)
  - **Leuprolide acetate (agonist)**
  - **Goserelin acetate (agonist)**
  - **Degarelix (antagonist)**
- Combined androgen blockade
- Anti-androgen treatment
  - **Bicalutamide**

ADT Adverse Effects

- Hot flashes (a sudden wave of mild or intense body heat), sweating, or clamminess
- Fatigue
- Decrease in bone density
- Decrease in size of testicles
- Decrease in sexual ability or desire
- Possible weight gain of 10-15 pounds
- Depression
- Loss of muscle mass, weakness

Identification of Metastatic Disease

- Presence of metastases is an important determinant in treatment selection
- Frequent post-treatment PSA surveillance has resulted in earlier detection of progression and metastases
- Factors related to time to onset of metastases includes baseline **PSA** , **PSADT**, and **PSA velocity**.
  - Associated with time to first bone metastasis, bone metastasis-free survival, and overall survival[1,2]
- The RADAR Group considers **PSADT** to be the best and the most consistent predictor of metastases[3]

[1]. Smith et al. *J Clin Oncol*. 2005;23:2918–2925. [2] Smith et al. *Cancer*. 2011;117:2077–2085. [3] Crawford et al. Urology. 2014;83(3):664-669

Recommendations for Early Identification of Metastatic Disease: RADAR Group

Newly Diagnosed Patients

- Scan high-risk patient and intermediate-risk patient with at least 2 of the following criteria:
  - **PSA level > 10 ng/mL**
  - Gleason score = 7
  - Palpable disease (≥T2b)

Biochemical Recurrent Patients

- 1st scan when **PSA level 5 ≥ 10 ng/mL**
- If negative on previous scan:
  - 2nd scanning when **PSA = 20 ng/mL** and every doubling of PSA level thereafter (based on PSA testing every 3 months)

M0 Castrate-Resistant Patients

- 1st scan when **PSA level ≥2 ng/mL**
- If negative on previous scan:
  - 2nd scanning when **PSA = 5 ng/mL** and every doubling of PSA level thereafter (based on PSA testing every 3 months)

Crawford et al. Urology. 2014;83(3):664-669

mCRPC: Clinical Perspective

- Most men with newly diagnosed CRPC do not have radiographic metastases
  - **Median time to metastasis is 2-3 years**
  - **>80% of men with CRPC will develop metastases**
- Metastatic CRPC (mCRPC)
  - 90% of men have rising PSA
  - >80% have bone metastases
  - >20% have soft tissue metastases, primarily in lymph nodes
- mCRPC is the indication for newest recently approved therapies
- Multidisciplinary care evolving as options increase

Scher HI et al. *J Clin Oncol*. 2008;26:1148–1159. Smith MR et al. *Cancer.* 2011;117:2077-2085. Kirby M et al. *Int J Clin Pract*. 2011;65:1180-1192.

Sipuleucil T

- Indicated for the treatment of **asymptomatic or minimally symptomatic metastatic CRPC**
  - Sipuleucel-T activates patients' immune cells
- Assess patients veins, if unable to place 18 g IV, may need vascular access device inserted for therapy.
- Process
  - Undergo leukopheresis at American Red Cross Sites
  - Recombinant prostatic acid phosphatase and GM-CSF combine with patient's antigen presenting cells
  - Infused 3 days later

Kantoff P et al. *N Engl J Med*. 2010;363:411-422. Gomella LG, Oliver Sartor A. Urol Oncol. Feb 20 2013. N.D. Shore, et al. *Cancer Control*. 2013: 20(1).

Sipuleucil T Patient Teaching

- No markers at this time to measure effectiveness
- **Does not lower PSA**, so is not a marker for response
- Need to follow infusion schedule, if misses infusion will need additional leukapheresis
- Possible side effects that may occur and are normal, when to call office.

Kanoff PW et al .*N Eng J Med* 2010, 363:411-422

Sipuleucil T Nursing Considerations

- Acute transfusion reaction within 24 hours
- Most common adverse reactions
  - Chills, fever, fatigue
  - Back pain, headache
  - Nausea, vomiting
  - Hypertension, tachycardia
  - Dyspnea, hypoxia and bronchospasm
- Usually resolve within 48 hours
- Most are mild to moderate symptoms

Kanoff PW et al. *N Eng J Med* 2010, 363:411-422. PROVENGE[package insert]. Dendreon Corporation; June 2011. http://www.provenge.com/pdf/prescribing-information.pdf.

Sipuleucil T Infusion

- Administer 3 doses at approximately 2 week intervals
  - Each dose is at least 50 million autologous activated CD54 cells in 250 mL Lactated Ringer's
- **Premedicate** 30 minutes before infusion with acetaminophen 650 mg PO and an antihistamine (eg, diphenhydramine 50 mg PO)
- Have someone drive patient to and from infusion site.
- Patient observation for 30 minutes after infusion

Kantoff P et al. *N Engl J Med*. 2010;363:411-422. Gomella LG, Oliver Sartor A. Urol Oncol. Feb 20 2013. N.D. Shore, et al. *Cancer Control*. 2013: 20(1).

Sipuleucil T Infusion

- Contents of bag will be slightly cloudy, with a cream to pinkish color
- Gently mix and resuspend the contents, small clumps of material should disperse with mixing
- Infuse intravenously over a period of 60 minutes
  - Do **NOT** use a cell filter
- Monitor patient during infusion and for 30 minutes once completed

Sipuleucil T Infusion Reactions

- If infusion reaction occurs:
  - Slow or stop infusion based on severity of reaction until symptoms improve
- When symptoms improve:
  - Restart infusion as long as it has not been 3 hours since start of infusion

Treatment Infusion Reactions

- For **severe rigors or pain** use intravenous **meperidine**
  - Start with 10 mg dosage
  - Dilute meperidine with LR (10mg to 1 mL) and administer **slowly** IV push
  - May repeat dosage after 5 minutes if needed
- For **nausea/vomiting**
  - H1 or H2 blockers such as hydroxyzine, promethazine or famotidine, ranitidine IVP

Sipuleucil T Resources

- http://www.provengehcp.com
- Provides in formation for patients and healthcare providers
- Has a video on how to administer Sipuleucil T

Radium 223 Administration

- Indicated for the treatment of patients with **CRPC, symptomatic bone metastases, and no known visceral metastatic disease**
- HGB > 10 at baseline
- Administer every 4 weeks IV push x 6 injections
  - Dosed by weight: 50 kBq (1.35 microcurie) per kg body weight
  - IV infused over 1 minute in urology clinic or outpatient nuclear medicine setting.
- **Bone marrow suppression may occur**

Den, RB et al. *The Canadian Journal of Urology.* 2014;21:70 – 76.

Radium 223 Adverse Effects

- Most common side effects:
  - Diarrhea
  - Peripheral edema
  - Nausea

- Bone marrow suppression (myelosuppression)
  - thrombocytopenia
  - neutropenia
  - pancytopenia and leukopenia.

Radium 223 Nursing Considerations

- Obtain CBC with differential before each treatment with radium-223. Monitor Alkaline phosphatase levels.
- Discontinue radium-223 if hematologic values do not recover within 6-8 weeks after that last administration despite receiving supportive care

Before first administration of Radium 223 confirm:

- Absolute neutrophil count ≥1.5 x 10^9/L
- Platelet count ≥100 x 10^9/L
- Hemoglobin ≥10 g/dL

Before subsequent administration of Radium 223 confirm:

- Absolute neutrophil count ≥1 x 10^9/L
- Platelet count ≥50 x 10^9/L

Xofigo® (radium Ra 223 dichloride) injection [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc.; May 2013.

Radium 223 Nursing Considerations

- Radiation protection precautions must be taken in accordance with national and local regulations
- Therapeutic benefits
  - Patients reported a meaningful improvement in quality of life
  - Prolonged overall survival by 3.6 months
  - Prolonged time to symptomatic skeletal related events
  - Decline in alkaline phosphatase
- Management of Side Effects
- Education and Emotional Support
- Reimbursement issues

Radium 223 Patient Teaching

- Stay well hydrated and report any signs of dehydration, urinary, or kidney problems.
- No restrictions regarding contact with other people after receiving injection.
- Wear condoms for intercourse during treatment and for 6 months after completed.
- Bathroom hygiene is important for 1 week after treatment, as radioactivity is present primarily in feces, but 5% in urine.
  - After going to the bathroom, wash hands and flush the toilet several times
  - Promptly clean up spilled body waste, wearing gloves.

Radium 223 Resources

- www.**xofigo**-us.com
- Provides information for patients and healthcare providers.

Abiraterone Acetate

- An androgen biosynthesis inhibitor
- Indicated for the **treatment of mCRPC**
  - Used in combination with prednisone
- More selective and specific than ketoconazole
- Due to its action on the adrenal glands, can lead to increased mineralocorticoid production
  - This excess can cause fluid retention, hypokalemia and hypertension

Attard G, et al. *J Clin Oncol*. 2008;26:4563-4571. ZYTIGA® (abiraterone acetate) [package insert]. Horsham, PA: Centocor Ortho Biotech Inc.; 2011. Ang JE, et al. *Br J Cancer*. 2009;100:671-675.

Abiraterone Acetate Administration

- Administration
  - 1,000 mg (4 , 250mg tablets) once daily on an empty stomach
  - Given with prednisone 5mg BID (minimize hypokalemia and hypertension)
- Dose Modifications
  - Dosage adjustment necessary if hepatotoxicity occurs
    - ALT/AST 5x NL or bilirubin 3x NL stop medication
    - Resume at 750mg daily once ALT/AST 2.5x NL or bilirubin 1.5x NL

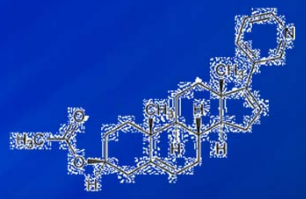
J.M. Gaya, et al. *Expert Review Anticancer Therapy*. 2013:13: 819-827. ZYTIGA® (abiraterone acetate) [package insert]. Horsham, PA: Centocor Ortho Biotech Inc.; 2011.

Abiraterone Acetate Adverse Effects

- Most AEs occurred during the first 3 months of treatment
- Most common AEs
  - Fatigue
  - Arthralgia
  - Fluid retention-peripheral edema
  - Hypokalemia
  - Hypertension
  - Cardiac Disorders
  - Atrial fibrillation
  - ALT and AST increased
  - Increased hot flashes

De Bono J et al. *N Engl J Med*. 2011;364:1995-2005.

Abiraterone Acetate Nursing Considerations



- Monitor patients for blood pressure, edema, and hypokalemia
  - Control hypertension and correct hypokalemia before treatment
  - Monitor blood pressure, serum potassium, and symptoms of fluid retention monthly
- Measure serum AST, ALT, and bilirubin
  - Prior to the start of treatment
  - Every 2 weeks for the first 3 months of treatment
  - Monthly thereafter

Attard G, et al. *J Clin Oncol*. 2008;26:4563-4571. ZYTIGA® (abiraterone acetate) [package insert]. Horsham, PA: Centocor Ortho Biotech Inc.; 2011. Ang JE, et al. *Br J Cancer*. 2009;100:671-675.

Abiraterone Acetate Nursing Considerations

- If AST, ALT rise above 5x the upper limit of normal (ULN) or bilirubin rises above 3x ULN $\rightarrow$ hold abiraterone until return to baseline then restart abiraterone at a reduced dosage

Abiraterone Acetate Patient Teaching

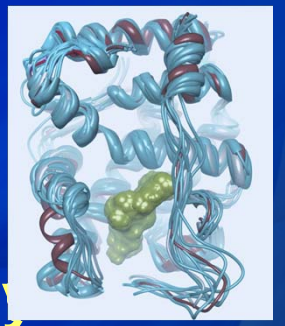
- Abiraterone must be taken on an empty stomach.
  - No food for at least 2 hours before and 1 hour after taking
  - Food increases absorption by 10-17 times
- Do not crush or chew pills.
- Need blood work and blood pressure monitored closely.

ZYTIGA® (abiraterone acetate) [package insert]. Horsham, PA: Centocor Ortho Biotech Inc.; 2011.

Abiraterone Acetate Patient Teaching

- Avoid co-administration with:
  - Dextromethorphan
  - Ketoconazole
  - Itraconazole
  - Clarithromycin
  - Phenytoin
  - Carbamazepine
  - Phenobarbital

Enzalutamide

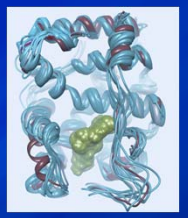


Approved both pre- and post- chemotherapy

- Post chemotherapy OS of 4.8 months (18.4 vs 13.6)
- Pre-Chemotherapy: September 2014
  - PREVAIL phase III trial of enzalutamide in asymptomatic or mildly symptomatic mCRPC
    - Significant improvement in OS
    - Delayed time to radiographic progression or death
    - Delayed time to initiation of chemotherapy (17 months)
    - Delayed time to a skeletal related event

FDA Grants Expanded Indication for Enzalutamide (*Xtandi*). September 11, 2014. Available at http://www.medscape.com/viewarticle/831548

Enzalutamide Administration

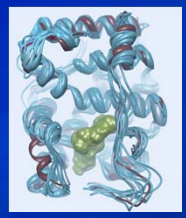


- Administration
  - 160mg (4, 40mg capsules) once daily
  - May be taken with or without food
  - Do not chew, crush, dissolve or open the capsule.

- Dose Modifications
  - If ≥ grade 3 toxicity, delay for 1 week or until symptoms improve to ≤ grade 2, then continue at same or reduced dose

J.M. Gaya, et al. *Expert Review Anticancer Therapy*. 2013:13: 819-827. XTANDI® (enzalutamide) [package insert]. Northbrook, IL:Astellas Pharma US, Inc.; 2013.

Enzalutamide Adverse Events

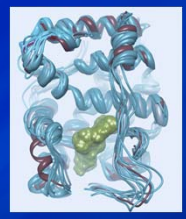


- Fatigue
- Dizziness
- Hot flash
- Musculoskeletal Pain
- Headache
- Hypertension
- Peripheral edema
- Infections
- Falls and related injuries
- LFT abnormalities
- Lowers seizure threshold
- Diarrhea

Hallucinations

Escher H et al. *N Engl J Med*. 2012;367:1187-1197.
. XTANDI® (enzalutamide) [package insert]. Northbrook, IL:Astellas Pharma US, Inc.; 2013.

Enzalutamide Nursing Considerations



- Prior to starting, evaluate for potential drug interactions and history of seizures.
- No required monitoring.
- Monitor routinely
  - CBC
  - CMP
  - Additional INR monitoring may be needed if patient if on warfarin therapy

J.M. Gaya, et al. *Expert Review Anticancer Therapy*. 2013:13: 819-827. Enzalutamide [prescribing information]. 2013.

Docetaxel

- **Indication: FDA-approved standard of care 1st line chemotherapy for men with CRPC**

Patient survival with docetaxel-based therapy is improved by 20% to 24% when compared with survival with mitoxantrone and prednisone therapy.

Docetaxel

- Docetaxel is a type of chemotherapy drug known as a *taxane*.
  - Docetaxel interferes with microtubules, which are part of the internal structure cells need when they are dividing: This leads to cell death.
- **Indication: FDA-approved standard of care 1st-line chemotherapy for men with CRPC**
- **Transforming care: Men with newly diagnosed metastatic prostate cancer—New Standard of Care**

Docetaxel Adverse Effects

- Adverse effects (most common)
  - Low white blood cell count with increased risk of serious infection
  - Fever
  - Retaining fluid (may include swelling in hands or feet, shortness of breath)
  - Nausea
  - Diarrhea
  - Hair loss, including face and body hair
  - Feeling very tired or weak
  - Anemia
  - Skin rash

Docetaxel. American Cancer Society. Available at: http://www.cancer.org/treatment/treatmentsandsideeffects/guidetocancerdrugs/docetaxel.

Docetaxel Nursing Considerations

Assessment & Drug Effects

- Lab tests:
  - Monitor bilirubin, AST or ALT, and alkaline phosphatase prior to each drug cycle.
  - Generally, do not give to patients with elevations of bilirubin or with significant elevations of transaminases concurrent with elevations of alkaline phosphatase.
- Frequently monitor CBCs with differential
  - Withhold drug if platelets <100,000 or neutrophils <1500 cells/mm^3

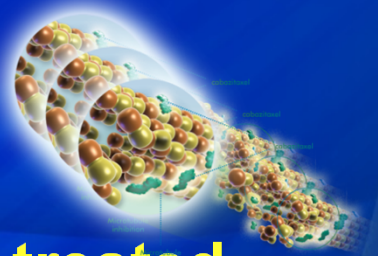
Docetaxel
Nursing Considerations

- Monitor for S&S of hypersensitivity which may develop within a few minutes of initiation of infusion.
  - It is usually not necessary to discontinue infusion for minor reactions (i.e., flushing or local skin reaction).
- Assess throughout therapy and report:
  - Cardiovascular dysfunction, respiratory distress; fluid retention
  - Development of neurosensory symptoms, neuropathy
  - S&S of infection.

Docetaxel
Nursing Considerations

- **Nadir (**low point): The nadir is the point in time between chemotherapy cycles in which you experience low blood counts.
  - **Onset:** 4-7 days
  - **Nadir:** 5-9 days
  - **Recovery:** 21 days
- Low white blood cell count
  - Increases risk for infection
  - Prevent with use of pegfilgrastim
    - helps prevent febrile neutropenia on day 2
- Low red blood cell count
  - Anemia

Cabazitaxel Administration

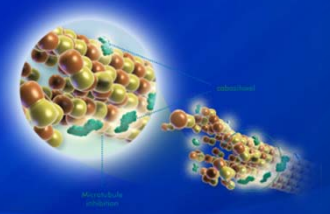


- Indicated for **men with mCRPC previously treated with docetaxel**
- **Black box warning**: risk of severe hypersensitivity and neutropenia related deaths.

- Administration
  - 25mg/m^2 IV as 1 hour infusion every 3 weeks
  - Prednisone 10mg QD
- Premedicate with antihistamine, corticosteroid and H2 antagonist 30 minutes prior to each dose

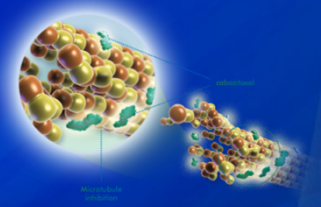
Lheureux S, Joly F. *Bull Cancer*. 2012;99:875-80. Cabazitaxel [prescribing information]. 2013

Cabazitaxel Administration



- Use Granulocyte Colony Stimulating Factors (G-CSF) to prevent the severe neutropenia
- Dose modifications
  - Delay and reduce dose to 20 mg/m^2:
    - Febrile neutropenia
    - Prolonged neutropenia ≥ grade 3 (> than 1 week)
    - ≥ grade 3 diarrhea or persisting diarrhea

Cabazitaxel Nursing Considerations



- Neutropenia, febrile neutropenia, anemia, thrombocytopenia
  - Use of pegfilgrastim to help prevent febrile neutropenia on day 2
  - Evaluate CBC weekly during 1st cycle and prior to each treatment thereafter
- Diarrhea, taste changes, nausea, vomiting, anorexia, constipation, abdominal pain
  - Prepare patient for diarrhea: dietary changes, use of loperamide, diphenoxylate/atropine
  - Dietary changes for taste changes