PROSTATE CANCER TREATMENT REGIMENS (Part 1 of 2)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Castration-Resistant Prostate Cancer[1]

First-Line Therapy[1]

Note: All recommendations are Category 2A unless otherwise indicated.

No Visceral Metastases

REGIMEN	DOSING
Enzalutaminde (Category 1)[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.
Abiraterone acetate + prednisone (Category 1)[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Docetaxel + prednisone (Category 1)[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Radium-223 (for symptomatic bone metastases) (Category 1)[9]	Radium-223 50kBq/kg every 4 weeks for 6 injections.

Visceral Metastases

Docetaxel + prednisone (Category 1)[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Enzalutaminde (Category 1)[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.
Abiraterone acetate + prednisone[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Mitoxantrone[7]	**Day 1:** Mitoxantrone 12mg/m^2 IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily. Repeat for up to 10 cycles if tolerated.

Subsequent Therapy[1]

No Visceral Metastases

Prior Therapy Enzalutamide/Abiraterone

Docetaxel + prednisone (Category 1)[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Abiraterone acetate + prednisone[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Enzalutaminde[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.
Radium-223 (if bone predominant disease) (Category 1)[9]	Radium-223 50kBq/kg every 4 weeks for 6 injections.
Sipuleucel-T[10*]	Sipuleucel-T three complete doses (50 million autologous CD54+ cells), given at 2-week intervals (range 1–15 weeks).

Prior Therapy Docetaxel

Enzalutaminde (Category 1)[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.
Abiraterone acetate + prednisone (Category 1)[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Radium-223 (if bone predominant disease) (Category 1)[9]	Radium-223 50kBq/kg every 4 weeks for 6 injections.
Cabazitaxel + prednisone (Category 1)[11-13]	**Day 1:** Cabazitaxel 25mg/m^2 IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily throughout cabazitaxel treatment. Repeat for up to 10 cycles if tolerated.
Sipuleucel-T[10*]	Sipuleucel-T three complete doses (50 million autologous CD54+ cells), given at 2-week intervals (range 1–15 weeks).

continued

PROSTATE CANCER TREATMENT REGIMENS (Part 2 of 2)

Castration-Resistant Prostate Cancer[1] (continued)

Subsequent Therapy[1] (continued)

No Visceral Metastases (continued)

Prior Therapy Docetaxel (continued)

REGIMEN	DOSING
Docetaxel rechallenge[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Mitoxantrone[7,12]	**Day 1:** Mitoxantrone 12mg/m^2 IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily. Repeat for up to 10 cycles if tolerated.

Visceral Metastases

Prior Therapy Enzalutamide/Abiraterone

Docetaxel + prednisone (Category 1)[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Abiraterone acetate + prednisone[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Enzalutaminde[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.

Prior Therapy Docetaxel

Enzalutaminde (Category 1)[2,3]	Enzalutamide 160mg/day orally without regard to food intake; with or without prednisone.
Abiraterone acetate + prednisone (Category 1)[4-6]	Abiraterone 1,000mg orally once daily, plus prednisone 5mg orally twice daily on an empty stomach.
Cabazitaxel + prednisone (Category 1)[11-13]	**Day 1:** Cabazitaxel 25mg/m^2 IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily throughout cabazitaxel treatment. Repeat for up to 10 cycles if tolerated.
Docetaxel rechallenge[7,8]	**Day 1:** Docetaxel 75mg/m^2 IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated.
Mitoxantrone[7,12]	**Day 1:** Mitoxantrone 12mg/m^2 IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily. Repeat for up to 10 cycles if tolerated.

General treatment notes:

- Encourage men with advanced prostate cancer to participate in clinical trials and refer early to a medical oncologist.
- Reserve systemic chemotherapy for men with castration-resistant metastatic prostate cancer except when enrolled in a clinical trial.
- Secondary hormone therapy (eg, antiandrogens, antiandrogen withdrawal, ketoconazole, corticosteroids) is also an option for patients with castration-resistant prostate cancer.

* The maximum dosing interval has not been established.[4]

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology™. Prostate Cancer. v 1.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed January 30, 2015.
2. Xtandi [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc.; 2013.
3. Scher HI, Fizazi K, Saad F, et al; AFFIRM Investigators. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med.* 2012;367:1187–1197.
4. Zytiga [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2013.
5. de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med.* 2011;364:1995–2005.
6. Fizazi K, Scher HI, Molina A, et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. *Lancet Oncol.* 2012;13:983–992.
7. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med.* 2004;351:1502–1512.
8. Tannock IF, Fizazi K, Ivanov S, et al; VENICE investigators. Aflibercept versus placebo in combination with docetaxel and prednisonefor treatment of men with metastatic castration-resistant prostate cancer (VENICE): a phase 3, double-blind randomised trial. *Lancet Oncol.* 2013;14:760–768.
9. Xofigo [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2013.
10. Provenge [prescribing information]. Seattle, WA: Dandreon Corp.; 2011.
11. Jevtana [prescribing information] Bridgewater, NJ: sanofi-aventis US LLC; 2014.
12. de Bono JS, Oudard S, Ozguroglu M, et al; TROPIC Investigators. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet.* 2010;376:1147–1154.
13. Heidenreich A, Scholz HJ, Rogenhofer S, et al. Cabazitaxel plus prednisone for metastatic castration-resistant prostate cancer progressing after docetaxel: results from the German compassionate-use programme. *Eur Urol.* 2013;63:977–982.

(Revised 2/2015)