

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-Recurrent Prostate Cancer¹

First-Line Therapy¹

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

No Visceral Metastases

REGIMEN	DOSING
Enzalutamide (Category 1) ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.
Abiraterone acetate + prednisone (Category 1) ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Docetaxel + prednisone (Category 1) ^{9,10}	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) ^{11,12}	Radium-223 50kBq/kg every 4 weeks for 6 injections.

Visceral Metastases

Docetaxel + prednisone (Category 1) ^{9,10}	Day 1: Docetaxel 75mg/m ² IV once every 3 weeks + prednisone 5mg orally twice daily. Repeat for up to 10 cycles if tolerated. Addition of estramustine to this regimen is not recommended.
Enzalutamide (Category 1) ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.
Abiraterone acetate + prednisone ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Mitoxantrone + prednisone ^{9,10}	Day 1: Mitoxantrone 12–14mg/m ² IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily. Repeat for up to 10 cycles if tolerated.

Subsequent Therapy¹

No Visceral Metastases

Prior Therapy Enzalutamide/Abiraterone

Docetaxel + prednisone (Category 1) ^{9,10}	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 ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Enzalutamide ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.
Radium-223 (for symptomatic bone metastases) (Category 1) ^{11,12}	Radium-223 50kBq/kg every 4 weeks for 6 injections.
Sipuleucel-T (if no or minimal symptoms, no liver metastases, life expectancy >6 months, and an ECOG score of 0 or 1) ^{13,14*}	Sipuleucel-T three complete doses (50 million autologous CD54+ cells), given at 2-week intervals (range 1–15 weeks).

Prior Therapy Docetaxel

Enzalutamide (Category 1) ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.
Abiraterone acetate + prednisone (Category 1) ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Radium-223 (for symptomatic bone metastases) (Category 1) ^{11,12}	Radium-223 50kBq/kg every 4 weeks for 6 injections.
Cabazitaxel + prednisone (Category 1) ¹⁵⁻¹⁷	Day 1: Cabazitaxel 25mg/m ² IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily throughout cabazitaxel treatment (starting doses are reduced by 5 mg/m ² and 10 mg/m ² for mild and moderate hepatic impairment, respectively). Repeat for up to 10 cycles if tolerated.
Sipuleucel-T (if no or minimal symptoms, no liver metastases, life expectancy >6 months, and an ECOG score of 0 or 1) ^{13,14*}	Sipuleucel-T three complete doses (50 million autologous CD54+ cells), given at 2-week intervals (range 1–15 weeks).
Docetaxel rechallenge ^{9,10}	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 + prednisone ^{9,10}	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.

continued

PROSTATE CANCER TREATMENT REGIMENS (Part 2 of 2)

Castration-Recurrent Prostate Cancer¹ (continued)

Visceral Metastases

Prior Therapy Enzalutamide/Abiraterone

REGIMEN	DOSING
Docetaxel + prednisone (Category 1) ^{9,10}	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 ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Enzalutamide ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.

Prior Therapy Docetaxel

Enzalutamide (Category 1) ²⁻⁴	Enzalutamide 160mg (four 40mg capsules) orally daily with or without food; prednisone can be given concurrently but is not required.
Abiraterone acetate + prednisone (Category 1) ⁵⁻⁸	Abiraterone 1,000mg orally once daily on an empty stomach, plus prednisone 5mg orally twice daily.
Cabazitaxel + prednisone (Category 1) ¹⁵⁻¹⁷	Day 1: Cabazitaxel 25mg/m ² IV every 3 weeks + prednisone 10mg orally daily or 5mg twice daily throughout cabazitaxel treatment (starting doses are reduced by 5 mg/m ² and 10 mg/m ² for mild and moderate hepatic impairment, respectively). Repeat for up to 10 cycles if tolerated.
Docetaxel rechallenge ^{9,10}	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 + prednisone ^{9,10}	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.
- All prostate cancer patients should receive best supportive care throughout treatment.

* The maximum dosing interval has not been established.¹³

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology™. Prostate Cancer. v 2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 15, 2016.
2. Xtandi [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc.; 2015.
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. Beer TM, Armstrong AJ, Rathkopf DE, et al; PREVAIL Investigators. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med*. 2014;371:424-433.
5. Zytiga [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2015.
6. 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.
7. 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.
8. Logothetis CJ, Basch E, Molina A, et al. Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: exploratory analysis of data from the COU-AA-301 randomised trial. *Lancet Oncol*. 2012;13:1210-1217.
9. 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.
10. Berthold DR, Pond GR, Soban F, de Wit R, Eisenberger M, Tannock IF. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. *J Clin Oncol*. 2008;26:242-245.
11. Xofigo [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2013.
12. Parker C, Nilsson S, Heinrich D, et al; ALSYMPCA Investigators. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med*. 2013;369:213-223.
13. Provenge [prescribing information]. Seattle, WA: Dandreon Corp.; 2011.
14. Kantoff PW, Higano CS, Shore ND, et al; IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med*. 2010;363:411-422.
15. Jevtana [prescribing information] Bridgewater, NJ: sanofi-aventis US LLC; 2014.
16. 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.
17. Bahl A, Oudard S, Tombal B, et al; TROPIC Investigators. Impact of cabazitaxel on 2-year survival and palliation of tumour-related pain in men with metastatic castration-resistant prostate cancer treated in the TROPIC trial. *Ann Oncol*. 2013;24:2402-2408.

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