

Established efficacy from PREVAIL and new data from TERRAIN



PREVAIL
(N = 1717)

PREVAIL was a multinational, double-blind, randomized, placebo-controlled phase 3 trial of XTANDI + GnRH therapy* in patients with metastatic castration-resistant prostate cancer who were asymptomatic or mildly symptomatic.^{1,2}

EXTENDED SURVIVAL

23% reduction in risk of death with XTANDI + GnRH therapy* vs placebo + GnRH therapy* (HR = 0.77 [95% CI, 0.67-0.88])¹

Median overall survival was **35.3 months** (95% CI, 32.2-not reached) for patients receiving XTANDI + GnRH therapy* vs **31.3 months** (95% CI, 28.8-34.2) for those receiving placebo + GnRH therapy*¹

IMPROVED RADIOGRAPHIC PROGRESSION-FREE SURVIVAL

83% reduction in risk of radiographic progression or death with XTANDI + GnRH therapy* vs placebo + GnRH therapy* (HR = 0.17 [95% CI, 0.14-0.21]; $P < 0.0001$)¹

Median radiographic progression-free survival was **not reached** (95% CI, 13.8-not reached) for patients receiving XTANDI + GnRH therapy* vs **3.7 months** (95% CI, 3.6-4.6) for those receiving placebo + GnRH therapy*¹

TERRAIN
(N = 375)

TERRAIN was a multinational, double-blind, randomized trial comparing XTANDI + GnRH therapy* with bicalutamide + GnRH therapy* in patients who were asymptomatic or mildly symptomatic.^{1,3}

IMPROVED RADIOGRAPHIC PROGRESSION-FREE SURVIVAL VS BICALUTAMIDE

40% reduction in risk of radiographic progression or death with XTANDI + GnRH therapy* vs bicalutamide + GnRH therapy* (HR = 0.60 [95% CI, 0.43-0.83])¹

Median radiographic progression-free survival was **19.5 months** (95% CI, 11.8-not reached) for patients receiving XTANDI + GnRH therapy* vs **13.4 months** (95% CI, 8.2-16.4) for patients receiving bicalutamide + GnRH therapy*¹

➤ **Please contact your local Astellas Account Manager for more information.**

GnRH, gonadotropin-releasing hormone; HR, hazard ratio; CI, confidence interval.

*Or after bilateral orchiectomy.¹

Indication

XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

Important Safety Information

Contraindications

XTANDI is not indicated for women. XTANDI can cause fetal harm and potential loss of pregnancy.

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In placebo-controlled studies, 8 of 1671 (0.5%) patients treated with XTANDI and 1 of 1243 (0.1%) patients treated with placebo experienced a seizure. In patients who previously received docetaxel, 7 of 800 (0.9%) patients treated with XTANDI experienced a seizure and no patients treated with placebo experienced a seizure. In a placebo-controlled study in chemotherapy-naïve patients, 1 of 871 (0.1%) patients treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo experienced a seizure. In bicalutamide-controlled studies conducted in chemotherapy-naïve patients, 3 of 380 (0.8%) patients treated with XTANDI and 1 of 387 (0.3%) patients treated with bicalutamide experienced a seizure. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Please see additional Important Safety Information on back and [click here](#) for Full Prescribing Information.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Posterior Reversible Encephalopathy Syndrome (PRES) In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

Adverse Reactions

The most common adverse reactions ($\geq 10\%$) that occurred more commonly ($\geq 2\%$ over placebo) in the XTANDI patients from the two placebo-controlled clinical trials were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo. In the bicalutamide-controlled study of chemotherapy-naïve patients, the most common adverse reactions ($\geq 10\%$) reported in XTANDI patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, upper respiratory tract infection, diarrhea, and weight loss.

In the study of patients taking XTANDI who previously received docetaxel, Grade 3 and higher adverse reactions were reported among 47% of XTANDI patients and 53% of placebo patients. Discontinuations due to adverse events were reported for 16% of XTANDI patients and 18% of placebo patients. In the placebo-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to adverse events were reported for 6% of both study groups. In the bicalutamide-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 38.8% of XTANDI patients and 37.6% of bicalutamide patients. Discontinuations due to adverse events were reported for 7.6% of XTANDI patients and 6.3% of bicalutamide patients.

Lab Abnormalities: In the two placebo-controlled trials, Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and 6% of placebo patients (0.5% Grade 3-4). Grade 1-4 thrombocytopenia occurred in 6% of XTANDI patients (0.3% Grade 3-4) and 5% of placebo patients (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of XTANDI patients (0.2% Grade 3-4) and 16% of placebo patients (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients (0.1% Grade 3-4) and 2% of placebo patients (no Grade 3-4).

Infections: In a study of patients taking XTANDI who previously received docetaxel, 1% of XTANDI patients compared to 0.3% of placebo patients died from infections or sepsis. In the placebo-controlled study of chemotherapy-naïve patients, 1 patient in each treatment group (0.1%) had an infection resulting in death.

Falls (including fall-related injuries) occurred in 9% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients, and included non-pathologic fractures, joint injuries, and hematomas.

Hypertension occurred in 11% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in $< 1\%$ of patients in each arm.

Drug Interactions

Effect of Other Drugs on XTANDI Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

Effect of XTANDI on Other Drugs Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please [click here](#) for Full Prescribing Information.

Sincerely,



Kenton Stewart
Vice President, Health Systems
Astellas Pharma US, Inc.

References: **1.** XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med* 2014;371(5):424-33. **3.** Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. *Lancet Oncol* 2016;17(2):153-63.

