

Name: Hong Tang, MD, FACP
Title: Executive Medical Director Oncology
Company: Astellas Pharma, Medical Affairs, Americas
Address: 1 Astellas Way
Northbrook, IL 60062
Phone: 224-205-8839
Email: hong.tang@astellas.com

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NCCN Guidelines Panel: Prostate Cancer

On behalf of Astellas and Medivation, we are submitting this request to the NCCN Prostate Cancer Guideline Panel on Xtandi® (enzalutamide), for review of data from two multicenter, randomized, double blind clinical trials (TERRAIN and STRIVE), which compared enzalutamide to bicalutamide in men with castration-resistant prostate cancer (CRPC).^{1,2} The TERRAIN trial enrolled 375 men with metastatic CRPC and the STRIVE trial enrolled 396 men with either metastatic or non-metastatic CRPC.

Specific Changes: We are providing data from the TERRAIN and STRIVE trials, which evaluated the use of enzalutamide compared to bicalutamide in men with CRPC as described above; data from these trials have been published in Lancet Oncology (TERRAIN) and in the Journal of Clinical Oncology (STRIVE).^{1,2}

FDA Clearance: Enzalutamide is currently approved for the treatment of patients with metastatic CRPC.³

Rationale: Two multicenter, randomized, double-blind clinical trials, TERRAIN and STRIVE, demonstrated significant increases in progression-free survival (PFS) for enzalutamide 160 mg/day compared to bicalutamide 50 mg/day in men with CRPC.^{1,2} In TERRAIN, enzalutamide treated patients had a median PFS (time from randomization to centrally confirmed radiographic progression, skeletal related event, initiation of new anti-neoplastic therapy or death, whichever occurs first) of 15.7 months (95% confidence interval [CI] 11.5–19.4) compared to 5.8 months (95% CI 4.8–8.1) for bicalutamide treated patients (hazard ratio 0.44 [95% CI 0.34–0.57; p<0.0001]).¹ In STRIVE, the median PFS (time from randomization to radiographic progression, prostate-specific antigen progression, or death due to any cause, whichever occurs first) was 19.4 months (95% CI 16.5 to NR) with enzalutamide versus 5.7 months (95% CI 5.6 to 8.1) with bicalutamide (HR 0.24 [95% CI 0.18–0.32; p<0.001]).² The most common adverse events in patients treated with enzalutamide (> 10% incidence in either trial) were: fatigue, back pain, hot flush, fall, hypertension, dizziness, decreased appetite, nausea, constipation, diarrhea, weight decrease, pain in extremity, and arthralgia.^{1,2}

Additional details of the trial can be accessed here:

TERRAIN: [http://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045\(15\)00518-5.pdf](http://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045(15)00518-5.pdf)

STRIVE: <http://ico.ascopubs.org/content/early/2016/01/21/JCO.2015.64.9285.full.pdf+html>

Respectfully submitted,



Hong Tang, MD, FACP
Executive Medical Director Oncology
Oncology Medical Affairs, Americas



Elaine K. Wong, MSc, MD
Vice President, Medical Affairs
Medivation, Inc.

Encl: Xtandi prescribing information

Cited References

1. Shore N, 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* (Epub) 01-13-2016. Accessible online at: [http://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045\(15\)00518-5.pdf](http://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045(15)00518-5.pdf).
2. Penson D, Armstrong A, Concepcion R, et al. Enzalutamide Versus Bicalutamide in Castration-Resistant Prostate Cancer: The STRIVE Trial. *J Clin Oncol* (Epub) 01-25-2016. Accessible online at: <http://jco.ascopubs.org/content/early/2016/01/21/JCO.2015.64.9285.full.pdf+html>.
3. XTANDI [package insert]. Northbrook, IL: Astellas, Inc. and San Francisco, CA: Medivation, Inc.