P080 Testosterone recovery for relugolix vs. leuprolide in men with advanced prostate cancer: Results from the phase 3 HERO study

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Tombal B.[1], Tutrone R.F.[2], Saad F.[3], George D.J.[4], Bailen J.L.[5], Cookson M.S.[6], Saltzstein D.R. [7], Brown B.[8], Lu S.[8], Shore N.D.[9]

[1]Cliniques Universitaires Saint Luc, Dept. of Urology, Brussels, Belgium, [2]Chesapeake Urology, Dept. of Urology, Towson, United States of America, [3]University of Montreal Hospital Centre, Dept. of Surgery, Montreal, Canada, [4]Duke Cancer Institute Center for Prostate and Urologic Cancers, Duke University, Durham, United States of America, [5]First Urology, Dept of Urology, Jeffersonville, United States of America, [6]The University of Oklahoma Health Sciences Center, Dept. of Urology, Oklahoma City, United States of America, [7]Urology San Antonio, Dept. of Urology, San Antonio, United States of America, [8]Myovant Sciences, Inc., Brisbane, United States of America, [9]Carolina Urologic Research Center, Dept. of Surgery and Oncology, Myrtle Beach, United States of America

Introduction & Objectives: In the phase 3 HERO study, the oral GnRH receptor antagonist, relugolix, showed sustained testosterone (T) suppression superior to that of leuprolide (96.7% vs 88.8%; difference: 7.9% [95% CI, 4.1 to 11.8; P<0.001]). Herein, we provide an analysis of the testosterone recovery data in a subgroup of 184 men from the HERO study who were not indicated to continue androgen deprivation therapy.

Materials & Methods: The phase 3 HERO study was designed to evaluate relugolix in men with advanced prostate cancer. Overall, 934 men were randomized 2:1 to receive relugolix 120 mg orally once daily after a single oral loading dose of relugolix 360 mg on Day 1 or leuprolide injections every 12 weeks for 48 weeks. T recovery was assessed in 184 patients who completed 48 weeks of treatment and who did not plan to start alternative androgen deprivation therapy within the following 12 weeks (or within 24 weeks following the last injection of leuprolide 3-month depot). During the 90-day recovery period, assessments included time to T recovery (≥ 280 ng/dL, the lower limit of the normal range) using the Kaplan-Meier method, PSA concentrations in T recovery phase, and adverse events during the recovery phase. All analyses were conducted in a modified intent to treat population.

Results: Overall, 137 men in the relugolix group and 47 men in the leuprolide group were included in these analyses. Mean (standard deviation) T levels for men entering the recovery assessment were 427±142 ng/dL and 404±127 ng/dL in the relugolix and leuprolide groups, respectively. The cumulative incidence rate of T recovery to ≥ 280 ng/dL at 90 days after drug discontinuation was 53.9% in the relugolix group compared with 3.2% in the leuprolide group (nominal p = 0.0017). Overall, 74 of the 137 men in relugolix group recovered T with a median time to recovery of 86.0 days (95% CI: 65.0, 92.0), versus 2 of the 47 men in leuprolide group with a median time to recovery of 112.0 days (95% CI: 112.0, not estimable). At the 90-day follow-up visit, the median PSA values were 0.39 ng/mL (range: 0 to 233.1) and 0.06 ng/mL (0 to 14.0) in the relugolix and leuprolide groups, respectively. Incidence of adverse events were generally similar in the treatment groups during the recovery phase, with 96% of men experiencing at least one adverse event and 15% of men experiencing a grade ≥3 adverse event in both treatment groups during the recovery phase.

Conclusions: Relugolix, an oral nonpeptide GnRH receptor antagonist, had a faster and more complete recovery of T to normal levels after treatment discontinuation versus leuprolide in a subgroup of men from the phase 3 HERO study.

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