Phase 3 HERO Study Design: Evaluation of the Safety and Efficacy of Relugolix, a Novel Oral GnRH Receptor Antagonist, in Men with Advanced Prostate Cancer

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HERO: INTRODUCTION

RELUGOLIX, AN ORAL GnRH RECEPTOR ANTAGONIST

- Androgen deprivation therapy (ADT) is the mainstay of treatment for unresectable, locally advanced or metastatic prostate cancer.[1]
- Relugolix is an oral, once daily, potent and selective non-peptide gonadotropin-releasing hormone (GnRH) receptor antagonist in development for the treatment of men with advanced prostate cancer (Figure 1).
- Unlike injectable GnRH agonists, oral relugolix lowers testosterone within 2 days by inhibiting pituitary release of both follicle-stimulating hormone (FSH) and luteinizing hormone (LH). [2, 3]

PHASE 2 CLINICAL TRIALS

- Demonstrated sustained testosterone suppression to below castration levels in > 90% of men over 24 weeks in two Phase 2 studies:
  - Men with androgen-sensitive prostate cancer (n = 95) randomized to relugolix, 80 or 120 mg orally once daily or leuprolide acetate injections, q 3 months.[2]
  - Men with localized prostate cancer and neo/adjuvant ADT with external beam radiation therapy randomized to relugolix 120 mg orally once daily or degarelix injection, monthly. [3]
    - Higher median levels of testosterone were demonstrated 12 weeks after treatment discontinuation with 120 mg once daily relugolix vs degarelix 4-week depot (257 vs 30 ng/dL).[3]

FIGURE 1 : Relugolix Mechanism of Action

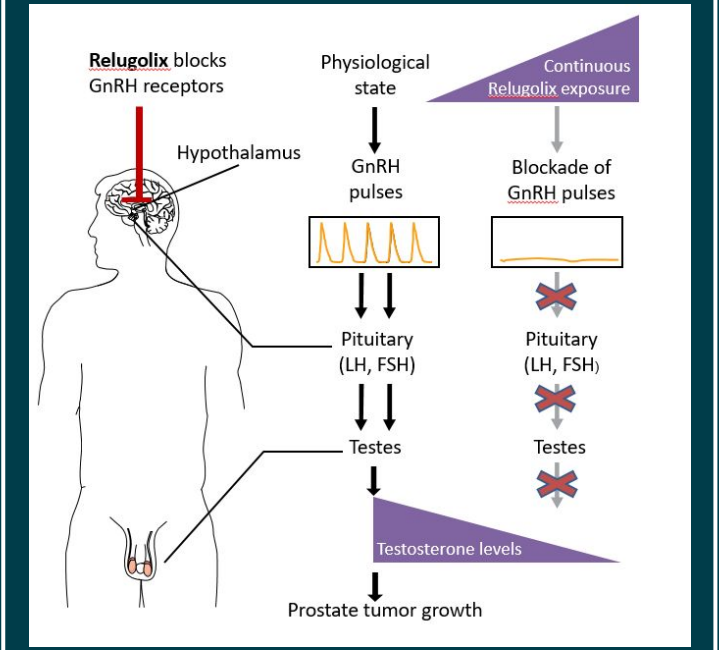


Figure adapted from MacLean D., et al. J Clin Endocrinol. Metab. 2014;99:E1455-53.

1. Shroder F, et al. BJU Int 2012; 109(Suppl 6):1-12. 100: 2. Saad, et al. Presented at ASCO GU, 2016; . 3. Dearnaley, et al. Presented at ESMO, 2016.

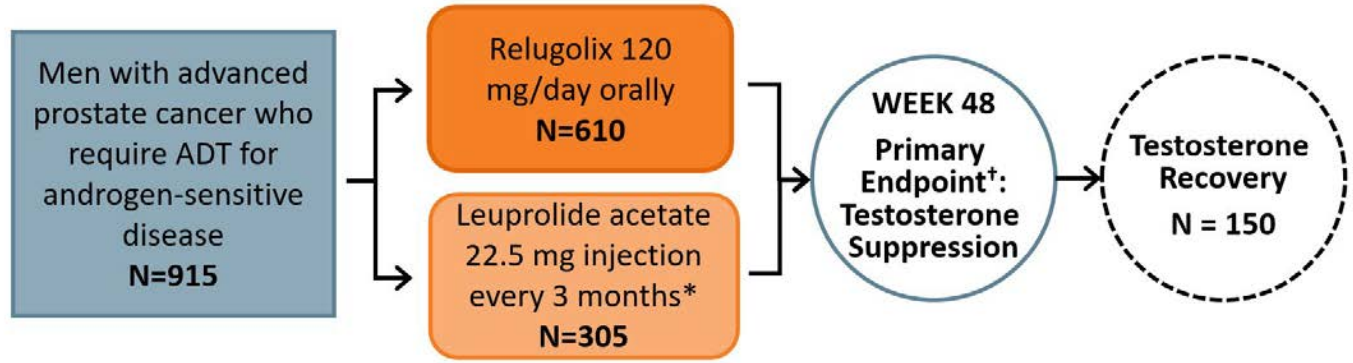
HERO STUDY DESIGN / SUMMARY

STUDY DESIGN

- The Phase 3 HERO study was designed to gain regulatory approval, if successful, in the US, Canada, EU, Japan and China.
- Approximately 1100 men with advanced prostate cancer will be enrolled from ~200 sites globally.
  - 915 were targeted for the primary endpoint analyses (Figure 2).
  - A further 120 men with metastatic disease are targeted for a key secondary endpoint: risk of progression to castration resistance during the 48 week treatment period.

Figure 2. HERO Study Design

DURATION	48-week treatment period
KEY ENDPOINTS	Primary endpoint: maintaining sustained testosterone suppression (≤ 50 ng / dL)
	Key secondary endpoint: risk of progression to castration resistance during the 48 week treatment period



*In some Asian countries, men may receive the approved dose of 11.25 mg leuprolide acetate every 3 months.
†The primary analysis of efficacy and safety will be conducted after the first 915 patients (non-metastatic and metastatic) have completed study treatment.

CURRENT STATUS

- The Phase 3 HERO study in men with advanced prostate cancer has completed enrollment of 934 men for the primary endpoint analysis.
- Top-line results from the HERO study are expected to be announced in 2019.
- The HERO study continues to enroll men with metastatic disease to evaluate a key secondary endpoint designed to demonstrate superiority of relugolix over leuprolide acetate to decrease the risk of progression to castration-resistant disease, and patients in China.