DOI: *10.4081/aiua.2025.14277*

REVIEW

Relugolix as a novel androgen deprivation treatment of prostate cancer: A review

Ioannis Kyriazis [1], Themistoklis Bellos [2], Stamatios Katsimperis [1], Panagiotis Angelopoulos [1], Panagiotis Neofytoy [1], Ioannis Varkarakis [1], Andreas Skolarikos [1], Athanasios Papatsoris [1]

[1] 2nd Department of Urology, University of Athens, Sismanoglio General Hospital, Athens, Greece;
[2] Urology Department, Korgialeneio Benakeio Hospital , Hellenic Red Cross , Athens, Greece.

Summary ***Background: Androgen deprivation therapy (ADT) is a cornerstone treatment for advanced prostate cancer. While effective, traditional injectable luteinizing hormone-releasing hormone (LHRH) agonists are associated with an initial testosterone flare and potential cardiovascular risks. Relugolix is a novel, oral gonadotropin-releasing hormone (GnRH) antagonist developed to provide rapid suppression without a testosterone flare. This review synthesizes the latest evidence on the efficacy, safety, and clinical utility of relugolix.***

Methods: This non-systematic review was conducted via a search of PubMed and MEDLINE databases up to July 2025 using the terms "relugolix" AND "ADT" OR "Androgen Deprivation Therapy" AND "Prostate Cancer." Only original studies in English were included.

Results: The phase III HERO trial established the superiority of relugolix over leuprolide, demonstrating higher rates of sustained castration (96.7% vs. 88.8%) and a significantly faster onset of action. Relugolix also showed a 54% reduction in major cardiovascular adverse events. Furthermore, it exhibited equivalent efficacy to injectable degarelix when combined with radiotherapy, but with more robust testosterone recovery after treatment cessation (52% vs. 16%). Real-world data indicates high patient adherence to the oral regimen, and a cost-effectiveness analysis suggests it is a cost-effective option despite a higher drug cost.

Conclusions: Relugolix represents a significant advancement in ADT, offering a potent, oral alternative with a rapid onset of action, a superior cardiovascular safety profile, and improved testosterone recovery. It provides clinicians with a valuable option for treating advanced prostate cancer, particularly in patients with cardiovascular comorbidities.

KEY WORDS: *Relugolix; Androgen deprivation therapy (ADT); Prostate cancer; Castration.*

Submitted 24 August 2025; Accepted 5 September 2025

INTRODUCTION

More than three decades ago, the first luteinizing hormone-releasing hormone agent was discovered and subsequently utilized in the management of prostate cancer (1). *Androgen deprivation therapy* (ADT) is recognized as the main therapeutic approach for metastatic prostate cancer. Additionally, it is utilized in patients classified as intermediate or high risk who are receiving *external beam radiation* (EBRT) (2). Testosterone levels can be effectively reduced to castration levels through the surgical procedure of bilateral orchiectomy or via the administration of LHRH agonists or GnRH antagonists. Although the initial GnRH antagonists demonstrated notable histamine-related adverse effects that limited their use in clinical settings, later modifications in their structure have led to the development of considerably safer formulations that are now commonly employed in practice (3). In 2008, FDA approved the third-generation GnRH antagonist, degarelix. Subsequently, in 2020, it granted authorization for the first orally administered GnRH antagonist, relugolix, based on the results of the HERO trial (3, 4). This review seeks to emphasize the latest and developing information regarding the therapeutic effectiveness and safety profile of the new oral GnRH antagonist, relugolix.

MATERIALS AND METHODS

This non-systematic review involved a thorough search of the PubMed and MEDLINE databases, conducted up to July 2025. The search utilized the terms: "*relugolix*" AND "*ADT*" OR "*Androgen Deprivation Therapy*" AND "*Prostate Cancer*". The screening process was conducted autonomously by a single author, followed by validation from the remaining authors. Discrepancies were ultimately addressed by the concluding author. Only original studies were considered for inclusion. Exclusion criteria encompassed studies utilizing animal models as well as those published in languages other than English.

RESULTS

Pharmacodynamic data from a phase I trial demonstrated that oral relugolix (360 mg loading dose, followed by 120 mg daily) achieves rapid absorption and reduces testosterone to castrate levels within one week (5). The important phase III HERO trial (n = 930) showed that relugolix worked better than leuprolide. For example, 96.7% of patients stayed castrated for 48 weeks, compared to 88.8% of patients who did not. Also, the drug worked much faster (56% of patients were castrated by day 4, compared to 0% of patients who were not) (4). Also, rel-

ugolix worked well as neoadjuvant/adjuvant therapy with radiotherapy for people with intermediate-risk disease. It had the same castration rates as injectable degarelix, but a much higher rate of testosterone recovery after treatment discontinuation (52% *vs*. 16%) (6).
The safety profile of relugolix reveals a significant occurrence of hot flushes (54.3%), akin to agonists, alongside a higher yet manageable incidence of diarrhoea (4).
Importantly, a meta-analysis and the HERO trial data demonstrate a superior cardiovascular safety profile for GnRH antagonists relative to agonists, with relugolix exhibiting a 54% reduction in major cardiovascular events among at-risk patients (4, 7). Relugolix, like other ADT, makes sexual function worse during treatment, but the stronger testosterone recovery makes life better after treatment (6, 8).
In the clinical trial, 99% of the people who were supposed to take the daily oral regimen did so (4, 9). Initial real-world data confirmed a high adherence rate of 90%. A retrospective analysis reveals that relugolix exhibited a superior 12-month adherence rate of 60.8% and an extended time to discontinuation of 13.5 months, compared to both GnRH agonists and degarelix (10, 11). A US cost-effectiveness analysis determined an incremental cost-effectiveness ratio of $49,571.10 per QALY for relugolix compared to leuprolide, indicating it may be a cost-effective alternative despite a higher monthly drug expenditure (12).

Discussion

Drug development

Miwa et al. achieved the successful synthesis of a potent GnRH antagonist, known as TAK-385, administered orally, building upon previous research aimed at the development of GnRH antagonist compounds (13). This compound shows improved in vivo antagonistic effects on GnRH and presents reduced inhibition of cytochrome P450 compared to other agents such as sufugolix. In preclinical studies, TAK-385 (relugolix) was given orally, resulting in sustained but reversible suppression of the hypothalamic-pituitary-gonadal axis.
This suggests a potential therapeutic way for hormone-dependent disorders, including endometriosis, uterine fibroids, and prostate cancer (14).

Mechanism of action

Since the formulation of the concept by *Huggins and Hodges*, which established the hormonal sensitivity of prostate cancer, *androgen deprivation therapy* (ADT) has emerged as a pivotal treatment approach for metastatic disease. The primary aim of ADT is to lower serum testosterone to levels consistent with castration, which subsequently prevents the activation of the *androgen receptor* (AR). Following the binding of androgens to the AR, the resulting complex undergoes translocation to the nucleus, thereby promoting gene transcription that governs the differentiation and maturation of prostatic cells (15). Although surgical castration represents the most direct approach to suppress testosterone levels, its permanent effects and significant psychological implications for the patient have led to the adoption of medicinal castration as the standard practice.
Medical castration can be achieved through the administration of LHRH agonists or GnRH antagonists. The action of LHRH agonists is characterized by the continuous stimulation of the pituitary gland, which results in the down-regulation and desensitization of LHRH receptors located within the pituitary. This mechanism leads to a reduction in the concentrations of *luteinizing hormone* (LH) and *follicle-stimulating hormone* (FSH), consequently inhibiting testosterone synthesis to levels comparable to those observed in castration. The initial phase of this technique entails the stimulation of LH synthesis, leading to an increase in testosterone levels that may last for 5-12 days, thereby producing a flare phenomenon (16). The clinical implications of this flare phenomenon, which depends on the metastatic burden and the locations of metastasis, may encompass bone pain, bladder outlet obstruction, ureteral obstruction, spinal cord compression, and cardiovascular complications, with a reported incidence varying from 4% to 63% (17). However, nearly 10% of individuals receiving LHRH agonists fail to achieve castration levels (18).
In contrast, GnRH antagonists demonstrate a notably different mechanism of action. The compounds exhibit competitive binding to the LHRH receptors located in the pituitary gland, leading to the inhibition of the rapid and reversible synthesis of LH and FSH. This mechanism results in a reduction of testosterone levels to castration levels while avoiding the occurrence of a flare phenomenon (8). A subtle difference exists between LHRH agonists and GnRH antagonists, with the latter maintaining suppression of FSH (19). Unfortunately, initial GnRH antagonists exhibited considerable adverse effects, particularly histamine-mediated allergic reactions, as well as challenges related to solubility and potency that compromised their clinical utility (20). Despite the initial drawbacks, new GnRH antagonists are characterized by a notably safer profile, demonstrating decreased histamine-release properties, extended biological activity, and enhanced solubility (21). Abarelix represented the inaugural GnRH antagonist; however, its association with severe allergic reactions led to the discontinuation of its research efforts. Degarelix is the most commonly used GnRH antagonist in clinical practice across Europe and the United States, following its initial FDA approval in 2008. Relugolix (TAK-3850) is a recently approved orally administered GnRH antagonist, receiving FDA approval in 2020.

Pharmacodynamics

Relugolix is a nonpeptide GnRH antagonist administered orally, initiating with a loading dose of 320 mg on the first day, succeeded by a daily maintenance dose of 120 mg. The compound demonstrates a significant binding capacity to LHRH receptors located in the pituitary gland, thereby leading to the inhibition of the hypothalamic-pituitary-gonadal axis. Pharmacokinetic data were collected subsequent to the phase I study of TAK-385 in patients with hormone-naive, non-metastatic prostate cancer. TAK-385 demonstrated rapid absorption after a single loading dose. By day 28, during the maintenance

dosing phase, the median steady-state Tmax was observed to be between 1 and 2 hours, while the mean terminal half-life (t1/2z) ranged from 67 to 79 hours. All administered doses rapidly reduced testosterone levels to castration thresholds within a one-week period according to titration by *Suzuki et al.* (5).

Therapeutic outcomes

Relugolix is an orally administered, highly specific non-peptide GnRH antagonist that effectively reduces testosterone levels to castration levels within one week of initiation of treatment. Findings from two completed phase II trials suggest that relugolix, given as a 320 mg loading dose on the first day followed by daily doses of 80 or 120mg, results in a reduction of serum testosterone to castration levels within one week and a decrease in PSA levels of more than 90% by the end of a 24-week treatment period (22, 23).

In 2020, *Shore and colleagues* published the results of a phase III randomized trial that evaluated relugolix against leuprolide in a cohort of 930 patients diagnosed with advanced prostate cancer. Participants were assigned randomly to receive either relugolix 120 mg orally on a daily basis after a single loading dose of 320 mg or leuprolide injections administered every three months, in a 2:1 ratio, for a total duration of 48 weeks (4). The main objective was to achieve and maintain testosterone levels at or below castration thresholds of less than 50 ng/dl. The secondary endpoints encompassed the assessment of non-inferiority concerning the primary objective, specifically targeting castrate testosterone levels on day 4 and testosterone levels falling below 20 ng/dl by day 15. The assessment of testosterone recovery was conducted in a specific group of patients. In a clinical study, relugolix achieved castration levels in 96.7% of patients after 48 weeks, compared to 88.8% of patients treated with leuprolide, indicating its superior efficacy ($p < 0.001$). Furthermore, relugolix exhibited a significant advantage in all primary secondary outcomes ($p < 0.001$). On day 4, 56% of patients receiving relugolix achieved castration, in contrast to 0% of patients in the leuprolide group. A total of 184 participants were evaluated for testosterone recovery 90 days following the discontinuation of treatment. The mean testosterone concentration observed during that period was 288.4 ng/dl among patients administered relugolix, in contrast to 58.6 ng/dl in those treated with leuprolide. Significant adverse events were observed, with notable cardiovascular incidents occurring in 2.9% of the relugolix cohort and 6.2% of the leuprolide cohort (4). As a result of the previously discussed findings, relugolix was granted FDA approval in December 2020 for use in adult patients diagnosed with advanced prostate cancer.

In a phase 2 randomized, open-label, parallel-group study, relugolix was evaluated among 103 patients diagnosed with intermediate-risk prostate cancer. These patients had undergone primary external beam radiation therapy, either in conjunction with adjuvant or neoadjuvant androgen deprivation therapy. Participants in the study were divided into two cohorts, with one group receiving oral relugolix and the other receiving injectable degarelix over a period of 24 weeks. The rates of castration observed during treatment were recorded at 95% and 82% for relugolix, while for degarelix, the rates were 89% and 68%. These figures correspond to thresholds of 1.73 and 0.7 nmol/l, respectively. The median duration until castration in the relugolix cohort was recorded at 4 days. Both cohorts demonstrated a decrease in PSA levels and prostatic dimensions. Three months after the cessation of treatment, testosterone levels were evaluated, indicating that relugolix supported testosterone recovery in 52% of patients, whereas degarelix resulted in recovery for only 16% of patients. The most frequently reported adverse event in both groups was hot flushes (6).

Safety profile

Abufaraj et al. presented the results of a meta-analysis regarding clinical safety and oncological effects of GnRH agonists in comparison to antagonists. The researchers established that GnRH antagonists were significantly associated with a heightened occurrence of injection site reactions. A trend suggests a reduced occurrence of significant adverse events in patients receiving GnRH antagonist treatment (9.8% *versus* 11%). Both groups demonstrated similar dropout rates due to adverse events. Furthermore, GnRH antagonists exhibited an enhanced safety profile concerning musculoskeletal and cardiovascular adverse effects (7).

The HERO trial data indicated that the primary adverse event linked to relugolix was hot flushes, affecting 54.3% of patients; yet, no statistically significant difference was noted when compared to the leuprolide group. No disparity in hepatic function was seen between the two groups. Conversely, diarrhoea was more prevalent in the relugolix group; however, no severe cases were recorded, and no patient was required to terminate treatment due to this adverse event. Concerning severe adverse events, fatal incidents were recorded in 1.1% of patients treated with relugolix, compared to 2.9% of patients treated with leuprolide. Relugolix showed a 54% decrease in the occurrence of significant cardiovascular events, especially notable in patients with a previous history of cardiovascular disease (4). The primary side effects linked to degarelix included skin irritations at the injection sites, which occur infrequently with relugolix due to its composition.

Quality of life

The administration of ADT has been associated with a decline in the quality of life among patients undergoing this treatment. Both agonists and antagonists appear to exert comparable adverse effects on sexual health, with relugolix being no exception to this observation. The neoadjuvant administration of relugolix prior to *external beam radiation* (EBRT) resulted in a notable decrease in various sexual health metrics, encompassing the ability to achieve an erection, the quality and frequency of erections, as well as the capacity to reach orgasm. Relugolix and degarelix have been shown to adversely impact overall health status, sexual function, and symptoms associated with hormonal therapy. The distinction between the two medications lies in the observation that post-treatment recovery of sexual activity is more favourable in patients who received relugolix (6).

Data regarding quality of life are also accessible from the participants of the HERO trial. While no significant differences were observed throughout the treatment duration, relugolix demonstrated a correlation with reduced hormone-related symptoms following testosterone recovery. This effect is likely attributed to the more favorable testosterone recovery observed in the relugolix cohort compared to the leuprolide cohort (4).

Adherence to therapy

The adherence to treatment presents a notable issue when evaluating a daily orally administered GnRH antagonist in comparison to three- or six-month ADT formulations. In the HERO trial, adherence reached 99%, as expected, owing to the rigorous monitoring of patients within the trial setting (9). Real-world statistics indicate that oral adherence is notably high among patients diagnosed with advanced prostate cancer, reaching a rate of 90%. Adherence to injectable or implantable androgen deprivation therapy was observed to range from 71% to 95% (7). Furthermore, a treatment interruption lasting up to 7 days does not have a significant effect on testosterone suppression. In contrast, if the duration exceeds 7 days, it is recommended to consider a re-challenge with a dosage of 360 mg (24). Given that treatment adherence information predominantly comes from clinical trials, the integration of real-world data will be essential for improving our understanding of compliance.

A retrospective analysis of real-world data involving 91 patients revealed that a significant proportion demonstrated remarkable adherence to the prescribed treatment regimen. The primary factor contributing to non-compliance was cost (10). A later retrospective analysis of real-world data indicated that relugolix exhibited a higher adherence rate (≥ 80%) at the 12-month followup, achieving 60.8%. In contrast, adherence rates for degarelix and GnRH agonists were significantly lower, at 13.0% and 46.3%, respectively. The median duration until treatment discontinuation was observed to be greater for relugolix, recorded at 13.5 months, in contrast to degarelix, which was noted at 3.1 months, and GnRH agonists, which had a median of 8.8 months. In cases of metastatic prostate cancer, there was an observed increase in persistence and adherence rates (11).

Cost- effectiveness

The economic viability of relugolix therapy has also faced scrutiny. A cost-effectiveness study published in the United States revealed that the monthly cost associated with relugolix was higher than that of leuprolide. A follow-up investigation demonstrated an incremental effect of 0.46 *quality-adjusted life-years* (QALY) associated with relugolix, alongside an incremental cost-effectiveness ratio of $49,571.10 per QALY (12, 25). The study in question presents a notable limitation due to the lack of reporting on adverse events. This information is essential for accurately assessing the overall cost-effectiveness of the medication when compared to standard GnRH agonist formulations (12). Data derived from everyday clinical practice can yield diverse insights regarding adherence, effectiveness, and safety profiles. The OPTYX observational study seeks to address these enquiries by gathering real-world data from a cohort of 1,000 patients receiving relugolix treatment, obtained from a variety of academic institutions as well as community and government clinics (26).

Future directions

Further information will be provided regarding the application of relugolix, which needs to establish whether the more convenient method of administration will achieve adherence rates similar to those of injectable formulations. Relugolix is set to undergo further evaluation for its efficacy in cases of castrate-resistant prostate cancer. The PRONOUNCE trial is expected to provide critical data and insights concerning the safety profile of GnRH agonists compared to antagonists in the context of cardiovascular disease and related events (27).

Conclusions

Relugolix signifies a transformative advancement in ADT for prostate cancer. As the first oral GnRH antagonist, it offers a highly effective and swift method of castration, surpassing traditional LHRH agonists such as leuprolide, while mitigating the risk of the clinical flare up phenomenon (4, 16).

Its most important clinical benefit is that it is safer, especially because it greatly lowers the risk of major cardiovascular events, which is very important for this group of patients (4, 7). The oral formulation corresponds with patient preference and is linked to elevated treatment adherence (11). Moreover, data shows that testosterone levels recover more quickly after stopping treatment with oral antagonists than with injectable ones. This suggests that patients on time-limited ADT may have a better long-term quality of life (6, 8).

In conclusion, relugolix sets a new standard for medical castration by combining effectiveness, a good safety profile for the heart, and oral administration that is easy for patients to use. Especially for people with heart problems, it is the best choice. Ongoing real-world studies will further solidify its role in the evolving prostate cancer treatment landscape (26).

References

1. Srkalovic G, Bokser L, Radulovic S, et al. Receptors for luteinizing hormone-releasing hormone (LHRH) in Dunning R3327 prostate cancers and rat anterior pituitaries after treatment with a sustained delivery system of LHRH antagonist SB-75. Endocrinology. 1990; 127:3052-60.

Declarations

Ethical approval and consent for participate: *Not appliable.*

Availability of data and material: *Not appliable.*

Competing interests: *Not appliable.*

Funding: *None.*

Acknowledgments: *None.*

2. Bolla M, Van Tienhoven G, Warde P, et al. External irradiation with or without long-term androgen suppression for prostate cancer with high metastatic risk: 10-year results of an EORTC randomised study. Lancet Oncol. 2010; 11:1066-73.

3. Dellis A, Papatsoris A. Therapeutic outcomes of the LHRH antagonists. Expert Rev Pharmacoecon Outcomes Res. 2017; 17:481-488.

4. Shore ND, Saad F, Cookson MS, et al. Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer. N Engl J Med. 2020; 382:2187-2196.

5. Suzuki H, Uemura H, Mizokami A, et al. Phase I trial of TAK-385 in hormone treatment-naïve Japanese patients with nonmetastatic prostate cancer. Cancer Med. 2019; 8:5891-5902.

6. Dearnaley DP, Saltzstein DR, Sylvester JE, et al. The Oral Gonadotropin-releasing Hormone Receptor Antagonist Relugolix as Neoadjuvant/Adjuvant Androgen Deprivation Therapy to External Beam Radiotherapy in Patients with Localised Intermediate-risk Prostate Cancer: A Randomised, Open-label, Parallel-group Phase 2 Trial. Eur Urol. 2020; 78:184-192.

7. Abufaraj M, Iwata T, Kimura S, et al. Differential Impact of Gonadotropin-releasing Hormone Antagonist Versus Agonist on Clinical Safety and Oncologic Outcomes on Patients with Metastatic Prostate Cancer: A Meta-analysis of Randomized Controlled Trials. Eur Urol. 2021; 79:44-53.

8. Hsueh JY, Gallagher L, Koh MJ, et al. Impact of neoadjuvant relugolix on patient-reported sexual function and bother. Front Oncol. 2024; 14:1377103.

9. Limonta P, Montagnani Marelli M, Moretti RM. LHRH analogues as anticancer agents: pituitary and extrapituitary sites of action. Expert Opin Investig Drugs. 2001; 10:709-20.

10. Hafron J, Sangha P, Kung T, Pruett J. Adherence to Hormonal Therapies in Prostate Cancer. Urol Pract. 2023; 10:540-546.

11. Hafron J, Hong A, Ryan MJ, et al. Study of persistence and adherence to ADT in prostate cancer: relugolix, degarelix, and GnRH agonists in the US. Future Oncol. 2025; 21:1219-1230.

12. Kasparian S, Wei O, Tsai NC, et al. A Practical Guide to Relugolix: Early Experience With Oral Androgen Deprivation Therapy. Oncologist. 2023; 28:699-705.

13. Miwa K, Hitaka T, Imada T, et al. Discovery of 1-{4-[1-(2,6-difluorobenzyl)-5-[(dimethylamino)methyl)-3-(6-methoxypyridazin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d)pyrimidin-6-yl)phenyl}-3-methoxyurea (TAK-385) as a potent, orally active, non-peptide antagonist of the human gonadotropin-releasing hormone receptor. J Med Chem. 2011; 54:4998-5012.

14. Nakata D, Masaki T, Tanaka A, et al. Suppression of the hypothalamic-pituitary-gonadal axis by TAK-385 (relugolix), a novel, investigational, orally active, small molecule gonadotropin-releasing hormone (GnRH) antagonist: studies in human GnRH receptor knock-in mice. Eur J Pharmacol. 2014; 723:167-74.

15. Ryan CJ, Tindall DJ. Androgen receptor rediscovered: the new biology and targeting the androgen receptor therapeutically. J Clin Oncol. 2011; 29:3651-8.

16. Frampton JE, Lyseng-Williamson KA. Degarelix. Drugs. 2009; 69:1967-76.

17. van Poppel H, Nilsson S. Testosterone surge: rationale for gonadotropin-releasing hormone blockers? Urology. 2008; 71:1001-6.

18. Crawford ED, Tombal B, Miller K, et al. A phase III extension trial with a 1-arm crossover from leuprolide to degarelix: comparison of gonadotropin-releasing hormone agonist and antagonist effect on prostate cancer. J Urol. 2011; 186:889-97.

19. Garnick MB, Campion M. Abarelix Depot, a GnRH antagonist, v LHRH superagonists in prostate cancer: differential effects on follicle-stimulating hormone. Abarelix Depot study group. Mol Urol. 2000 Fall; 4:275-7.

20. Huirne JA, Lambalk CB. Gonadotropin-releasing-hormone-receptor antagonists. Lancet. 2001; 358:1793-803.

21. Tombal B, Miller K, Boccon-Gibod L, et al. Additional analysis of the secondary end point of biochemical recurrence rate in a phase 3 trial (CS21) comparing degarelix 80 mg versus leuprolide in prostate cancer patients segmented by baseline characteristics. Eur Urol. 2010; 57:836-42.

22. Dearnaley D, Saltzstein DR, Sylvester JE, et al. Neo/adjuvant ADT to EBRT: final results of the randomized phase 2 trial of the oral GnRH antagonist, TAK-385 (relugolix) and degarelix in patients with prostate cancer. Ann Oncol 2016; 27:243-265.

23. Saad F, Bailen JL, Pieczonka CM, et al. Second interim analysis (IA2) results from a phase II trial of TAK-385, an oral GnRH antagonist, in prostate cancer patients (pts). J Clin Oncol. 2016; 34:200.

24. Sari Motlagh R, Abufaraj M, Mori K, et al. The Efficacy and Safety of Relugolix Compared with Degarelix in Advanced Prostate Cancer Patients: A Network Meta-analysis of Randomized Trials. Eur Urol Oncol. 2022; 5:138-145.

25. Adekunle OA, Seoane-Vazquez E, Brown LM. Cost-effectiveness analysis of androgen deprivation therapy with relugolix for the treatment of advanced prostate cancer. J Am Pharm Assoc (2003). 2023; 63:817-824.e3.

26. Spratt DE, Dorff T, McKay RR, et al. Evaluating relugolix for the treatment of prostate cancer in real-world settings of care: the OPTYX study protocol. Future Oncol. 2024; 20:727-738.

27. Melloni C, Slovin SF, Blemings A, et al. Cardiovascular Safety of Degarelix Versus Leuprolide for Advanced Prostate Cancer: The PRONOUNCE Trial Study Design. JACC CardioOncol. 2020; 2:70-81.

Correspondence

Ioannis Kyriazis (Corresponding Author)
ioanniskyriazis93@gmail.com

Stamatios Katsimperis
stamk1992@gmail.com

Panagiotis Angelopoulos
angelopoulospanag@gmail.com

Panagiotis Neofytoy
neo.panagiotis@gmail.com

Ioannis Varkarakis
medvark3@yahoo.com

Andreas Skolarikos
andskol@yahoo.com

Athanasios Papatsoris
agpapatsoris@yahoo.gr

2nd Department of Urology, University of Athens, Sismanoglio General Hospital, Athens, Greece

Themistoklis Bellos
bellos.themistoklis@gmail.com

Urology Department, Korgialeneio Benakeio Hospital , Hellenic Red Cross, Athens, Greece