


Relugolix Plus Enzalutamide For Metastatic Hormone-Sensitive Prostate Cancer: A Case Report

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Background: In the UK, relugolix, an oral gonadotropin-releasing hormone receptor antagonist, is indicated for advanced hormone-sensitive prostate cancer, and as neo-adjuvant and adjuvant treatment in combination with radiotherapy in patients with high-risk localised or locally advanced hormone-dependent prostate cancer. Experience with the combination of oral relugolix plus oral enzalutamide is limited.

Case Presentation: A white British male (66 years old) with a history of myelodysplastic syndrome, chronic neutropenia and indeterminate colitis presented with metastatic adenocarcinoma of the prostate gland. The patient started subcutaneous leuporelin acetate and oral enzalutamide. After 8 weeks, the oral enzalutamide dose was reduced because of fatigue. Following the second leuporelin injection, the patient developed a subcutaneous abscess that required surgical incision and drainage. The patient switched to oral relugolix and continued with oral enzalutamide. Within 3 months of commencing leuporelin and enzalutamide the prostate specific antigen (PSA) concentration fell from a peak of 269.00 ng/mL to 2.55 ng/mL. Following the switch to oral relugolix plus enzalutamide, the PSA remained stable until the most recent assessment 11 months later. Relugolix plus enzalutamide was well tolerated.

Conclusion: Relugolix plus enzalutamide produced a sustained reduction in PSA and the combination was well tolerated. Further research including real world data should assess relugolix in doublet and triplet combinations for prostate cancer.

Plain Language Summary: Oral (by mouth) relugolix can treat certain men with hormone sensitive prostate cancer. Studies are underway looking at relugolix combined with other drugs, such as oral enzalutamide, and at various stages of prostate cancer. Dr Thomson et al report the case of a man with other serious diseases who took oral relugolix and oral enzalutamide after experiencing side effects with injectable drugs. His levels of prostate specific antigen (PSA), which indicates prostate cancer control (the lower the better), fell markedly after starting treatment and, after switching to relugolix, remained stable for 11 months. He tolerated relugolix plus enzalutamide well.

Keywords: relugolix, enzalutamide, prostate cancer, gonadotropin-releasing hormone receptor antagonist, prostate specific antigen

Introduction

In men with prostate cancer, androgen deprivation therapy (ADT) induces cancer cell apoptosis and death.¹ In advanced prostate cancer, regimens combining treatments with distinct modes of action may enhance cell death.¹ For example, combination treatment with ADT plus either androgen receptor pathway inhibitors or chemotherapy shows a consistent survival advantage compared with previous regimens when used early in metastatic prostate cancer.²

In our centre, patients with advanced prostate cancer usually receive long-term ADT using luteinising hormone releasing hormone (LHRH) agonists. The down-regulation of the LHRH hormone-gonadal axis takes several weeks and elicits an initial testosterone surge.³ We, therefore, combine LHRH agonists with a short course of a prophylactic anti-androgen (bicalutamide) starting 1–2 weeks before the first injection of LHRH agonist.

This paper presents the case of a patient with advanced prostate cancer treated with relugolix, an orally active nonpeptide gonadotropin-releasing hormone (GnRH) receptor antagonist that rapidly suppresses testosterone levels.⁴ In the UK, relugolix is indicated for adults with advanced hormone-sensitive prostate cancer, and as neo-adjuvant and adjuvant treatment in combination with radiotherapy in patients with high-risk localised or locally advanced hormone-dependent prostate cancer.⁵

The Phase III HERO study enrolled 930 men with advanced prostate cancer with one of three clinical disease presentations; 50.2% showed evidence of biochemical or clinical relapse after local primary intervention with curative intent; 27.1% had advanced localised disease that was not suitable for primary surgical intervention with curative intent; and 22.7% had newly diagnosed androgen-sensitive metastatic disease.³ The latter group is analogous to our patient. Patients were randomised in a 2:1 ratio to either daily oral relugolix or leuporelin 3-monthly injections.

Relugolix (n=622) produced more rapid and sustained suppression of testosterone levels than leuporelin (n=308). In the relugolix arm, 96.7% (95% confidence interval [CI], 94.9 to 97.9) of men maintained castrate levels of testosterone (the primary endpoint) during 48 weeks treatment compared with 88.8% (95% CI, 84.6 to 91.8) of patients receiving leuporelin. The absolute difference (7.9 percentage points; 95% CI, 4.1 to 11.8) showed noninferiority, with superiority achieved after non-inferiority criteria were met ($P<0.001$ for superiority).³ In the subgroup with newly diagnosed androgen-sensitive metastatic disease treated with relugolix, 97.8% (95% CI, 93.4 to 99.3) of men maintained castrate levels of testosterone during 48 weeks treatment.³

Other secondary end points were also in favour of relugolix compared with leuporelin ($P<0.001$). For instance, 56.0% of the relugolix group versus none of the leuporelin-treated men showed castrate levels of testosterone on day 4. At day 15, 98.7% of the relugolix group versus 12.0% of the leuporelin-treated men showed castrate levels of testosterone. In a subgroup (n=184), mean testosterone levels 90 days after treatment discontinuation were 288.4 ng/dl in the relugolix group and 58.6 ng/dl in the leuporelin group.³ The earlier recovery of testosterone on stopping relugolix compared with leuporelin potentially resolves side effects more rapidly.

Among all patients, the incidence of major adverse cardiovascular events (MACE; nonfatal myocardial infarction, nonfatal stroke, and death from any cause) was 2.9% with relugolix and 6.2% among those receiving leuporelin (hazard ratio, 0.46; 95% CI, 0.24 to 0.88). In patients with a pre-study history of MACE, the incidence of MACE during the study was 3.6% (n=3/84) with relugolix and 17.8% (n=8/45) among those receiving leuporelin.³

Formal prospective combination trials with relugolix are underway (eg NCT06130995).^{6,7} A real-world study from the USA included 47 patients who received relugolix monotherapy and 24 patients who received relugolix combined with one or more of several agents including enzalutamide (n=10), abiraterone (n=8), bicalutamide (n=4), apalutamide (n=3), cabazitaxel (n=2), docetaxel (n=1) and radium 223 (n=1). Enzalutamide was the most commonly co-prescribed agent, used by 43% of those who received combination therapy.⁶

In HERO, participants randomised to receive relugolix or leuporelin could receive combination therapy with either enzalutamide or docetaxel in the event of PSA progression. A total of 57 men (5.3% of the study population) received enzalutamide and/or docetaxel in combination with relugolix (n=37; 5.2% of the study population) or leuporelin (n=20; 5.6%).⁸ Most of the 57 participants (80.3%) who received combination therapy had newly diagnosed androgen-sensitive metastatic disease. The proportion of patients showing castration testosterone levels were similar with and without concomitant enzalutamide or docetaxel. No clinically relevant differences in adverse events emerged with and without concomitant enzalutamide or docetaxel.⁸

To the best of our knowledge, this paper presents the first case in the UK of a patient with advanced prostate cancer treated with a combination of oral relugolix plus oral enzalutamide. The patient provided written informed consent to have the case details, direct quotes and accompanying images published. Ethical approval was not required.

Case Presentation

The patient, a white British male born in 1954, presented in 2020 with an incidental finding of an enlarged prostate gland on pelvic magnetic resonance imaging for inflammatory bowel disease, with a diagnosis of indeterminate colitis. The patient underwent prostate specific antigen (PSA) testing for 34 months. The GP re-referred the patient in October 2022 after the PSA concentration increased to 99 ng/mL (Figure 1).

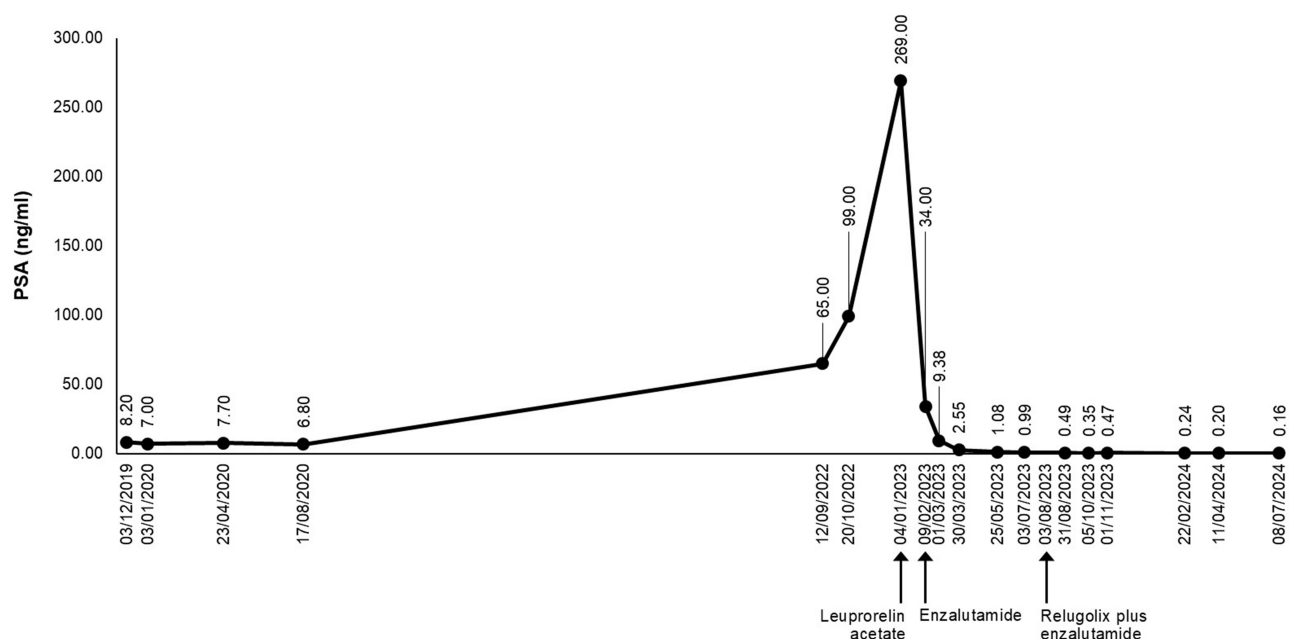


Figure 1 PSA concentrations over time.

The patient had been diagnosed with myelodysplastic syndromes (46, XY) in September 2019, which resulted in chronic neutropenia. As a result the patient received antimicrobial prophylaxis with antibiotics and the anti-fungal posaconazole. The PSA at this stage was 8.2 ng/mL (Figure 1). Due to a risk of infection secondary to the neutropenia, the urology multidisciplinary team (MDT) decided not to proceed with a prostate biopsy and advised a period of PSA surveillance.

At GP re-referral, pelvic MRI and bone scintigraphy showed metastatic prostate cancer (T3a N1 M1b), with low-volume skeletal metastases according to the CHAARTED criteria (<4 bone metastases, no metastases outside the vertebral column or pelvis and no visceral metastases)⁹ as well as left pelvic and para-aortic lymphadenopathy. The patient had an Eastern Cooperative Oncology Group performance status of 0.

Biopsy showed grade group 2 acinar adenocarcinoma of the prostate gland (Gleason score 3+4). The multidisciplinary team (MDT) considered that radiotherapy was not advisable because the patient's history of indeterminate colitis increased the likelihood of radiation colitis.

Pharmacotherapy

The patient started subcutaneous injections with the LHRH agonist leuporelin acetate (3.75 mg once a month) in January 2023. At this time, his PSA concentration was 269 ng/mL (Figure 1). The patient received three-weeks treatment with oral bicalutamide to reduce the risk of tumour flare. Shortly after this he commenced enzalutamide, an androgen receptor blocker, 160 mg daily. After 8 weeks, the dose of oral enzalutamide was reduced to 80 mg daily because of fatigue (grade 2 estimated from clinic letters). The patient's fatigue improved after the enzalutamide dose reduction. The dose of oral enzalutamide was increased to 120 mg daily seven months after the dose reduction. The re-emergence of fatigue prompted a reduction to 80 mg after 8 weeks on the higher dose. The patient remains on 80 mg oral enzalutamide daily.

Following the second leuporelin injection, the patient developed a subcutaneous abscess (5x4 cm) that required surgical incision and drainage (Figure 2). The team considered that oral administration was preferable to injection or bilateral orchidectomy because of the high risk of infection resulting from the chronic neutropenia exemplified by the abscess. Therefore, the patient switched to oral relugolix and continued with oral enzalutamide. The patient received the recommended loading dose of 360 mg relugolix on the first day, followed by 120 mg relugolix taken once daily at approximately the same time each day.⁵



Figure 2 The subcutaneous abscess (5x4 cm) that required surgical incision and drainage following the second leuporelin injection.

The PSA concentration (Figure 1) fell to 0.99 ng/mL on leuporelin and enzalutamide. Following the switch from leuporelin to relugolix, the PSA concentrations declined further, then remained stable until the most recent assessment 11 months after the start of relugolix plus enzalutamide (July 2024; 0.16 ng/mL; Figure 1).

The combination of relugolix plus enzalutamide was well tolerated based on routine assessments and patient self-reports. Routine follow-up continues.

Patient's Experience

The authors asked the patient to describe, in writing, his experiences of treatment. Four themes emerged. Once drafted, the patient reviewed this section to ensure that the edited remarks accurately reflect his experiences.

Theme One

Differentiating the effects of the prostate cancer and treatment from those produced by ongoing health issues, particularly myelodysplastic syndrome, can be difficult. The patient noted, for example, that his anaemia had worsened since starting treatment for prostate cancer. He believes that the anaemia and severe neutropenia probably contributes to his fatigue (vide infra). In addition, he commented that the severe neutropenia:

[L]eaves me more at risk of infections. One consequence of this has been that I have generally avoided situations where there may be a lot of people close together, such as cinemas and theatres, and I have dropped out of a couple of music groups that I used to play in. I have been less confident about committing to things such as holiday trips, as my health can be a bit up and down. So, the prostate cancer and its treatment needs to be seen against that background.

Theme Two

The patient and his partner experienced “a sense of relief” that there was an oral alternative to subcutaneous injections with the LHRH agonist.

I would have been worried about having further [leuporelin acetate] injections, after the effect of the last one [the subcutaneous abscess] ... [I]t has been a relief to me, and my partner, that I have been able to use relugolix as an alternative. I think hot flushes are less common and not so intense [with relugolix compared with leuporelin acetate].

Theme Three

The patient found that fatigue restricted activities of daily living and quality of life. Indeed, up to 90% of patients with advanced prostate cancer experience fatigue, which can arise from the malignancy as well as ADT.^{10,11} The patient reported that disentangling fatigue produced by relugolix plus enzalutamide from that associated with other ongoing health issues, particularly myelodysplastic syndrome, is problematic.

I am fine with the daily routine of cooking, housework, light DIY [do-it-yourself; home repairs and decoration], shopping etc, but I don't feel so confident about, say, a DIY project requiring sustained effort, or a walk longer than say 45–75 minutes. I have been joint editor of a local journal, but I have recently stepped down from this, partly because I wasn't sure I could sustain it. I think I find it harder to get motivated to do things, such as outings beyond the nearest few miles, or something outside the familiar routine, or that adds to stress, though again this has probably been the case since [my] diagnosis with myelodysplastic syndrome.

Theme Four

Deliberate and inadvertent non-adherence is a potential concern with oral chemotherapy taken under a patient's cognisance.^{12–15} The patient did not report any practical, logistical or other difficulties in daily life with the oral medication compared with the injection and devised a method to ensure compliance.

At breakfast, I put the relugolix box on the kitchen worktop. This reminds me to take the relugolix around mid-morning. I then put the box away again. This seems to work. Similarly with the enzalutamide, I put the card container on the kitchen worktop after lunch to remind me to take the tablets mid-afternoon. With the enzalutamide, the tablets are marked with the day of the week so it is easier to keep track. I have quite a few tablets to take during the day, so I follow a routine or schedule to fit these in: breakfast, Adcal D-3 [calcium and vitamin D3] and posaconazole; mid-morning, relugolix; before lunch, ciprofloxacin; after lunch, enzalutamide; and posaconazole about 6 o'clock and about 9 o'clock

Discussion

In our patient, concomitant treatment with relugolix and enzalutamide is well tolerated, which is in line with the finding of the HERO subgroup analysis.⁷ PSA concentrations remained stable until the most recent assessment 11 months after the start of combination treatment (Figure 1). The combination was well tolerated based on routine assessments and patient self-reports. The patient experienced no new side effects of concern when oral relugolix was added to oral enzalutamide. However, more extensive studies with larger samples and a longer follow-up are needed to validate our observations and ascertain long-term efficacy and safety.

The case, which we believe is the first UK patient with advanced prostate cancer treated with a combination of oral relugolix plus oral enzalutamide, also illustrates some points that clinicians could consider when counselling patients and during MDT meetings.

Firstly, clinicians could discuss changing treatments and routes of administration when clinically indicated. Our experience resonates with the results of a small real-world study of 19 patients who filled prescriptions after transitioning from leuporelin or degarelix to relugolix. Fifteen patients felt better and four felt worse after switching.⁶ Moreover, oral treatments are preferable to injectables for patients with needle phobia, which may lead to patients avoiding treatment.¹⁵ Our case also highlights the value of oral options in patients at higher risk of infection, bleeding or both with injections.

Secondly, non-adherence is a potential concern with oral medication taken under the patient's cognisance.^{12–15} Nonadherence rates among prostate cancer patients prescribed oral therapies may reach 25–51%.¹⁵ Real-world evidence from the USA suggests that compliance with relugolix is high: 93% of 101 patients reported never missing a relugolix dose.⁶ Our patient devised a procedure that minimised the likelihood that he would forget to take a medicine despite the

high pill burden. Healthcare professionals could consider whether behavioural, and mixed educational and behavioural interventions may improve adherence to medications for cancer and concomitant disorders.¹⁶

Thirdly, potential drug-drug interactions are common in cancer patients, especially, as with our patient, when receiving multiple medicines to treat conditions unrelated to the malignancy.¹⁷ In addition, drug-drug interactions between cancer treatments are a potential concern with combination therapy. For example, the multidrug transporter P-glycoprotein mediates the absorption of relugolix and limits absolute oral bioavailability to 11.6%.⁸ P-glycoprotein inducers or inhibitors affect relugolix exposure.⁸ This patient received posaconazole, which is a substrate for and inhibits p-glycoprotein.¹⁸ Our patient would have attained steady state posaconazole levels by the time he started relugolix. The effect on relugolix exposure was not assessed, but there seemed to be no safety or efficacy signal suggesting drug-drug interactions in this patient. Nevertheless, relugolix should be prescribed with caution in patients taking strong p-glycoprotein inhibitors.⁵

Enzalutamide strongly induces hepatic CYP3A and both induces and inhibits P-glycoprotein.^{8,19} Posaconazole inhibits CYP3A and inhibits P-glycoprotein.^{18,20} In contrast, relugolix only slightly induces CYP3A. Concomitant use of relugolix plus voriconazole (a strong CYP3A4 inhibitor that does not inhibit P-glycoprotein) did not result in a clinically meaningful increase in relugolix exposure.²¹ Nevertheless, when possible, co-administration of relugolix with combined p-glycoprotein and strong CYP3A inducers should be avoided. If co-administration is unavoidable, the dose of relugolix should be increased.⁵ On-going studies are assessing whether strong CYP3A4 inhibitors (itraconazole or ritonavir) extend relugolix dosing intervals (NCT05679388).

When there are comorbidities and concomitant medications, as in this patient, it is important to consider their possible effect on tolerance of new treatments and the outcomes of that treatment. In this case, regular clinic review and titration of the enzalutamide dose was performed in order to optimise treatment intensity whilst maintaining quality of life. Furthermore, there was a rapid and sustained PSA response to the leuporelin acetate, subsequent relugolix and enzalutamide (Figure 1), indicating good efficacy. Repeat imaging was not performed, with the patient having no symptoms to suggest progressive disease and an ongoing PSA response.

We did not measure testosterone levels or formally assess quality of life, neither of which is part of routine care in our centre. However, the comments from the patient suggest that, while appreciating his limitations, he was able to perform many activities of daily living and maintained his quality of life. The patient also noted that conditions and factors other than the malignancy and the treatment for prostate cancer influenced the quality of life. In any patient, isolating the effect of one disease or factor is difficult. Further studies using validated formal measures would provide more robust quality of life data.

The patient experienced no new side effects of concern with oral relugolix. Initially, oral enzalutamide was associated with grade 2 fatigue. The patient's fatigue improved after the enzalutamide dose reduction. Notably, there was no evidence of cardiac toxicity, an important consideration when evaluating possible combinations. In men with prostate cancer, ADT is associated with prolongation of the QTc interval and, in turn, an increased risk of sudden cardiac death.²² In the HERO study, the incidence of MACE was 2.9% and 6.2% with relugolix and leuporelin respectively, representing a 54% lower risk of MACE with relugolix than with leuporelin.³ A descriptive analysis suggested that relugolix was associated with a reduced risk of MACE compared with leuporelin.⁴ Longer term follow-up studies are, however, needed to fully evaluate cardiac toxicity with relugolix as monotherapy and in combination.

Further research assessing relugolix as the backbone of doublet and triplet combination regimens would be of value, as well as long-term survival data and whether previous and subsequent lines of treatment influence outcomes in people with prostate cancer. Moreover, without a control group, the observed outcomes cannot be attributed definitively to the combination of relugolix and enzalutamide. Studies comparing relugolix and enzalutamide with other standard treatments are underway.

Conclusions

Concomitant relugolix and enzalutamide provided ongoing PSA suppression, which has remained stable until the most recent assessment 11 months after the switch from subcutaneous leuporelin and 18 months since starting treatment overall. The combination was well tolerated based on routine assessments and patient self-reports. The patient

experienced no new side effects of concern with oral relugolix. Further research should assess relugolix as the backbone of doublet and triplet combination regimens.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

Mr Thakrar is an employee of Accord-UK. Dr Thomson reports: speaker fees from Novartis, Roche, Exact Sciences and Gilead; payments for advisory boards from Merck Sharp & Dohme, Exact Sciences, Novartis, Amgen, Seagen and Gilead; support for attending conferences from Bristol Myers Squibb, Merck Sharp & Dohme, Astellas, Ipsen, EUSA, Lilly, Gilead and Novartis; and support for educational meetings from Roche. Ms Victor reports speaker fees from Bayer, Ipsen, Pfizer, Merck and Accord; payments for membership of an educational meeting steering group from Astellas; support for attending conferences from Accord. Dr Gunn reports support for attending conferences from Janssen Pharmaceuticals. Dr Adamson has no affiliations with or involvement in any organisation or entity with any financial or non-financial interests. Relugolix therapy was funded by the NHS through an individual funding request (IFR).

References

1. Etheridge T, Damodaran S, Schultz A, et al. Combination therapy with androgen deprivation for hormone sensitive prostate cancer: a new frontier. *Asian J Urol*. 2019;6(1):57–64. doi:10.1016/j.ajur.2018.09.001
2. Chen K, O'Brien J, McVey A, et al. Combination treatment in metastatic prostate cancer: is the bar too high or have we fallen short? *Nat Rev Urol*. 2023;20(2):116–123. doi:10.1038/s41585-022-00669-z
3. Shore ND, Saad F, Cookson MS, et al. Oral relugolix for androgen-deprivation therapy in advanced prostate cancer. *N Engl J Med*. 2020;382(23):2187–2196. doi:10.1056/NEJMoa2004325
4. Shirley M. Relugolix: a review in advanced prostate cancer. *Target Oncol*. 2023;18(2):295–302. doi:10.1007/s11523-022-00944-4
5. Accord Healthcare. Orgovyx 120 mg film-coated tablets. Summary of Product Characteristics. Available from <https://products.mhra.gov.uk/>. Accessed May 2024.
6. Kasparian S, Wei O, Tsai N-C, et al. A practical guide to relugolix: early experience with oral androgen deprivation therapy. *Oncologist*. 2023;28(8):699–705. doi:10.1093/oncolo/oyad036
7. ClinicalTrials.gov. Relugolix + Enzalutamide Study in High-Risk Prostate Cancer. Available from <https://clinicaltrials.gov/study/NCT06130995>. Accessed June 2024.
8. George DJ, Saad F, Cookson MS, et al. Impact of concomitant prostate cancer medications on efficacy and safety of relugolix versus leuprolide in men with advanced prostate cancer. *Clin Genitourin Cancer*. 2023;21(3):383–392.e2. doi:10.1016/j.clgc.2023.03.009
9. Sweeney CJ, Chen Y-H, Carducci M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. *New Eng J Med*. 2015;373(8):737–746. doi:10.1056/NEJMoa1503747
10. Andersen MF, Midtgaard J, Bjerre ED. Do patients with prostate cancer benefit from exercise interventions? A systematic review and meta-analysis. *Int J Environ Res Public Health*. 2022;19(2). doi:10.3390/ijerph19020972
11. Cornford P, Robijn E, Rogers E, Wassersug R, Fleure L. Fatigue in prostate cancer: a roundtable discussion and thematic literature review. *Eur Urol Open Sci*. 2024;63:119–125. doi:10.1016/j.euros.2024.03.003
12. Verbrugghe M, Verhaeghe S, Lauwaert K, Beeckman D, Van Hecke A. Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: a systematic review. *Cancer Treat Rev*. 2013;39(6):610–621. doi:10.1016/j.ctrv.2012.12.014
13. Huang W-C, Chen C-Y, Lin S-J, Chang C-S. Medication adherence to oral anticancer drugs: systematic review. *Expert Rev Anticancer Ther*. 2016;16(4):423–432. doi:10.1586/14737140.2016.1159515
14. Talens A, Guilbert M, Lumbreras B, Aznar MT, López-Pintor E. Medication experience and adherence to oral chemotherapy: a qualitative study of patients' and health professionals' perspectives. *Int J Environ Res Public Health*. 2021;18(8):4266. doi:10.3390/ijerph18084266
15. Higano C, Hafron J. Adherence with oral anticancer therapies: clinical trial vs real-world experiences with a focus on prostate cancer. *J Urol*. 2023;209(3):485–493. doi:10.1097/JU.0000000000003081
16. Cross AJ, Elliott RA, Petrie K, Kuruvilla L, George J. Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications. *Cochrane Database Syst Rev*. 2020;5(5). doi:10.1002/14651858.CD012419.pub2

17. Chen L, Cheung WY. Potential drug interactions in patients with a history of cancer. *Curr Oncol*. 2014;21(2):e212–20. doi:10.3747/co.21.1657
18. Nagappan V, Deresinski S. Posaconazole: a broad-spectrum triazole antifungal agent. *Clinic Infect Dis*. 2007;45(12):1610–1617. doi:10.1086/523576
19. Otsuka Y, Poondru S, Bonate PL, et al. Physiologically-based pharmacokinetic modeling to predict drug-drug interaction of enzalutamide with combined P-gp and CYP3A substrates. *J Pharmacokinet Pharmacodyn*. 2023;50(5):365–376. doi:10.1007/s10928-023-09867-7
20. Lempers VJ, van den Heuvel JJ, Russel FG, et al. Inhibitory potential of antifungal drugs on atp-binding cassette transporters p-glycoprotein, MRP1 to MRP5, BCRP, and BSEP. *Antimicrob Agents Chemother*. 2016;60(6):3372–3379. doi:10.1128/aac.02931-15
21. De La Cerda J, Dunshee C, Gervasi L, et al. A Phase I clinical trial evaluating the safety and dosing of relugolix with novel hormonal therapy for the treatment of advanced prostate cancer. *Target Oncol*. 2023;18(3):383–390. doi:10.1007/s11523-023-00967-5
22. Gagliano-Jucá T, Travison TG, Kantoff PW, et al. Androgen deprivation therapy is associated with prolongation of QTc interval in men with prostate cancer. *J Endocr Soc*. 2018;2(5):485–496. doi:10.1210/js.2018-00039

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