



Letters to the Editor

Letter: Adherence and Persistence on Relugolix for the Treatment of Prostate Cancer in the United States Medicare Fee-for-Service Population

Urol Pract. 2025;12(6):691-699. doi:10.1097/UPJ.0000000000000886

To the Editor:

In their recent review of over 5000 Medicare claims, McKay et al¹ report a high level of adherence to relugolix when used for androgen deprivation therapy (ADT) by patients with both metastatic and nonmetastatic prostate cancer (PCa). An incentive for their study was a concern that various factors, such as forgetfulness, might lead to poor adherence to this oral medication.

A significant finding in McKay et al was lower adherence to relugolix among nonmetastatic vs metastatic patients, with $P < .0001$ in a log-rank test.¹ The authors proffer the view that this reflects the fact that patients with nonmetastatic PCa are more likely to be prescribed intermittent ADT. This places the onus of poor adherence upon the physicians and ignores the patients' agency in the desire to discontinue treatment. We offer here a different look on prostate cancer patients' adherence and persistence in using relugolix for androgen deprivation therapy.

McKay et al¹ do not ask why patients prescribed relugolix desire drug holidays. The fact is that relugolix shares with other androgen-suppressing medications a vast array of adverse effects (AEs) that reduce patients' quality of life (QoL).² The AEs associated with relugolix are the same as those from standard luteinizing hormone–releasing hormone (LHRH) agonists but are arguably more stressful because they emerge so quickly.^{2,3}

In a recent survey of > 800 PCa patients on their perceived benefits and risks of alternative forms of ADT, relugolix was endorsed over injectable ADT drugs because it could be stopped quickly and testosterone could recover faster.⁴ The PCa patients thus understood that relugolix had the same burdensome AEs as other ADT drugs. They did not view relugolix as more tolerable; it was preferred by some patients simply because they could be on it for a shorter time. This suggests that companies marketing relugolix could both help PCa patients and get better long-term adherence if they

focused on ways to improve the QoL of patients prescribed relugolix.

Take, for example, the concern that forgetfulness may lead patients to not adhere to oral medications. This is a particular concern for patients on LHRH agonists or antagonists since those drugs are associated with increased risk of cognitive impairment. That risk is diminished, however, when estradiol (administered transdermally; currently off-label) is simultaneously prescribed with LHRH drugs. Similarly, patients given some add-back estradiol while on relugolix can expect fewer hot flashes and less risk of osteoporosis.⁵ Their improved QoL could lead to better adherence and persistence in using relugolix for ADT.

The authors conclude their article with suggestions to improve adherence to relugolix. However, to the best of our knowledge, none of these have been tested with this specific medication. They also do not mention the fact that a patient education program about the side effects of ADT has been shown, in a randomized controlled trial, to significantly improve patients' self-efficacy in managing AEs when the patients are informed of the AEs *before* they experience them.⁶ Offering such a program to all patients starting on relugolix might be one of the most cost-effective and beneficial ways for improving both patients' QoL and adherence to treatment.

**Richard Wassersug,¹ Carly Sears,² Paul Schellhammer,³
and Robert Watson⁴**

¹*Department of Cellular and Physiological Sciences
Faculty of Medicine, University of British Columbia
Vancouver, British Columbia, Canada*

²*University of Calgary, Calgary, Alberta, Canada*

³*Urology, Macon and Joan Brock Virginia Health Sciences
Eastern Virginia Medical School, Norfolk, Virginia*

⁴*Sandia National Laboratories (Ret.)
Albuquerque, New Mexico*

Funding/Support: None.

Conflict of Interest Disclosures: The Authors have no conflicts of interest to disclose.

Author Contributions:

Conception and design: Sears, Schellhammer, Wassersug.

Critical revision of the manuscript for scientific and factual content:

Watson, Sears, Schellhammer, Wassersug.

Drafting the manuscript: Wassersug.

Data analysis and interpretation: Watson.

Supervision: Watson, Schellhammer.

Corresponding Author: Richard Wassersug, PhD, Department of Cellular and Physiological Sciences, Faculty of Medicine, University of British Columbia, 2350 Health Sciences Mall, Vancouver, British Columbia BC V6T 1Z3, Canada (Richard.wassersug@ubc.ca).

References

1. McKay RR, Hong A, Razo JF, et al. Adherence and persistence on relugolix for the treatment of prostate cancer in the United States Medicare fee-for-service population. *Urol Pract.* 2025;12(6):691-699. doi:10.1097/UPJ.0000000000000886
2. Tombal B, Collins S, Morgans AK, et al. Impact of relugolix versus leuprolide on the quality of life of men with advanced prostate cancer: results from the phase 3 HERO study. *Eur Urol.* 2023;84(6):579-587. doi:10.1016/j.eururo.2023.09.007
3. Tutrone R, Saad F, George DJ, et al. Testosterone recovery for relugolix versus leuprolide in men with advanced prostate cancer: results from the phase 3 HERO study. *Eur Urol Oncol.* 2024;7(4):906-913. doi:10.1016/j.euo.2023.11.024
4. Estradiol Initiative Key findings from the 2025 survey of prostate cancer patients' interest in alternative forms of ADT. Accessed December 15, 2025. <https://estradiolinitiative.org/2025-survey-of-opinions/>
5. Russell N, Hoermann R, Cheung AS, Zajac JD, Grossmann M. Effects of oestradiol treatment on hot flushes in men undergoing androgen deprivation therapy for prostate cancer: a randomised placebo-controlled trial. *Eur J Endocrinol.* 2022;187(5):617-627. doi:10.1530/EJE-22-0318
6. Wibowo E, Wassersug RJ, Robinson JW, et al. An educational program to help patients manage androgen deprivation therapy side effects: feasibility, acceptability, and preliminary outcomes. *Am J Mens Health.* 2020;14(1):1557988319898991. doi:10.1177/1557988319898991

Submitted December 15, 2025; Accepted January 3, 2026; Published February 23, 2026.