

Navigating PSMA-RLT for Prostate Cancer: What Clinicians Need to Know Now

Written by The Life Science Feed Editorial Team · Published 27 August 2026 · Edited by Mara Voss

Prostate-specific membrane antigen (PSMA)-targeted radioligand therapy (RLT) has become an established treatment option for metastatic castration-resistant prostate cancer (mCRPC). With its inclusion in international guidelines, understanding the practical aspects of integrating PSMA-RLT into clinical practice is crucial for oncologists and healthcare professionals managing prostate cancer patients.

KEY TAKEAWAYS

- **The Pivot:** PSMA-RLT is now an established treatment for mCRPC, with expanding evidence for earlier use in other prostate cancer settings.
- **The Data:** Landmark trials (VISION, TheraP, PSMAfore) have demonstrated improved survival, progression-free survival, and biochemical response rates with [177Lu] Lu-PSMA-617.
- **The Action:** Clinicians must prioritize appropriate patient selection via PSMA PET imaging and multidisciplinary evaluation, and understand practical treatment considerations and toxicity monitoring.

PSMA-RLT: An Evolving Treatment Landscape

Prostate-specific membrane antigen (PSMA)-targeted radioligand therapy (RLT) represents a significant advancement in the management of prostate cancer. Specifically, [177Lu] Lu-PSMA-617 has emerged as an established treatment for metastatic castration-resistant prostate cancer (mCRPC) and is now incorporated into international guidelines. This therapy has demonstrated improved oncologic outcomes, including enhanced survival, progression-free survival, and biochemical response rates, as evidenced by landmark clinical trials such as VISION, TheraP, and PSMAfore1.

Patient Selection and Imaging Biomarkers

Appropriate patient selection is a critical factor for optimizing the efficacy and safety of PSMA-RLT. The selection process primarily relies on PSMA positron emission tomography (PET) imaging to confirm PSMA expression in tumor lesions and assess the overall disease burden. This imaging helps identify patients who are most likely to benefit from PSMA-RLT. Beyond imaging, a comprehensive multidisciplinary evaluation is essential to consider the patient's overall health, prior treatments, and potential comorbidities. While current selection criteria are well-defined, emerging imaging biomarkers are under investigation and may further refine patient selection in the future1.

Expanding Indications for PSMA-RLT

Initially established for heavily pretreated mCRPC, the evidence base for PSMA-RLT is expanding to include earlier stages of prostate cancer. Research is exploring its utility in taxane-naïve disease, metastatic hormone-sensitive prostate cancer (mHSPC), and even in neoadjuvant settings. This expansion suggests a broader potential role for PSMA-RLT

across the prostate cancer treatment continuum, potentially offering new therapeutic avenues for patients at different disease stages¹.

Practical Treatment Considerations and Toxicity Monitoring

Integrating PSMA-RLT into clinical practice requires careful attention to practical considerations. These include the logistical aspects of radionuclide administration, patient preparation, and post-treatment care. Given the nature of radioligand therapy, robust toxicity monitoring protocols are essential. Clinicians must be prepared to manage potential adverse events, which may include hematologic toxicities, xerostomia, and renal impairment, among others. Regular monitoring of blood counts, renal function, and salivary gland function is typically part of the treatment regimen to ensure patient safety and manage side effects proactively¹.

Clinical Implications: Why this matters for clinical practice today

The growing evidence supporting PSMA-RLT underscores the need for oncologists to be well-versed in its application. For clinicians managing prostate cancer, understanding the nuances of patient selection, the practicalities of treatment delivery, and effective toxicity management is paramount. The shift towards considering PSMA-RLT in earlier disease stages means that referring oncologists should proactively identify suitable candidates and collaborate closely with nuclear medicine specialists. Establishing clear referral pathways and multidisciplinary team discussions will be key to ensuring patients receive timely and appropriate access to this evolving therapy, ultimately optimizing their treatment outcomes.

Limitations and Future Directions

While PSMA-RLT has demonstrated significant benefits, ongoing research continues to refine its application. Current limitations include the need for further investigation into optimal dosing schedules, combination therapies, and the long-term management of potential toxicities. Future directions for PSMA-RLT involve exploring its efficacy in combination with other systemic therapies, identifying predictive biomarkers beyond PSMA expression to further personalize treatment, and evaluating its role in very early-stage disease or as a consolidative therapy. Continued research will help to fully integrate PSMA-RLT into a comprehensive, individualized prostate cancer management strategy¹.

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REFERENCES

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