



Editorial

The Role of Theranostics

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Theranostics is a field of medicine that combines therapy and diagnostics to create a tailored approach to treating diseases, particularly cancer. It involves the use of specific diagnostic tests to determine the most effective treatment for a patient. The concept typically includes diagnostic and therapeutic parts. The therapeutic part involves developing targeted therapies based on the diagnostic findings. Therapeutic strategies can include the use of specific drugs, radiation, or other interventions according to the individual's condition. This approach aims to improve treatment outcomes by ensuring that patients receive therapies that are most likely to work for their specific disease profile, leading to more effective and efficient healthcare. Theragnostic in men with metastatic castration-resistant prostate cancer (mCRPC) has been developed to target bone and the tumor itself. Currently, bone-directed (TAT) targeted alpha therapy with radium-223 (223Ra) is the only theragnostic agent proven to prolong survival in men with mCRPC who have symptomatic bone metastases and no known visceral metastases. The clinical utility and therapeutic success of 223Ra has encouraged the development of other tumor-targeting theragnostic agents in mCRPC, primarily targeting Prostate-Specific Membrane Antigen (PSMA) with Radioligand Therapy (RLT). There is increasing evidence of promising response rates and a low toxicity profile with 177Lu-labeled PSMA RLT in patients with mCRPC. A phase III randomized study of 177Lu-labeled PSMA RLT has completed buildup and is awaiting results as to whether the drug improves radiographic progression-free survival and overall survival in men with mCRPC receiving standard of care treatments. Additional early clinical trials are investigating the role of tumor-directed targeted alpha therapy with radiotracers such as 225Ac [1].

Controlled therapy and immunotherapy have become up-to-date in cancer treatment. However, only few patients benefit from these expensive therapies, and often responses are short-lived or coincide with side effects. There is growing sense in oncology, which is the development of theranostics. This enables patient selection, treatment, and monitoring. In this approach, labeled compounds and imaging technology are used to diagnose patients and select

the best treatment option. whereas for therapy, related compounds are used to target cancer cells or the tumor stroma. In this context, nanobodies and nanobody-directed therapeutics have gained interest. This interest slows from their high antigen specificity, small size, ease of labeling and engineering, allowing specific imaging and design of therapies targeting antigens on tumor cells, immune cells as well as proteins in the tumor environment [2]. In recent years, a model shift from single-photon-emitting radionuclide radiotracers toward Positron-Emission Tomography (PET) radiotracers has occurred in nuclear oncology. Although PET-based molecular imaging of the kidneys is still in its infancy, such a trend has emerged in the field of functional renal radionuclide imaging. Potentially allowing for precise and thorough evaluation of renal radiotracer urodynamics, PET radionuclide imaging has numerous advantages including precise anatomical co-registration with CT images and dynamic three-dimensional imaging capability. In addition, relative to scintigraphic approaches, PET can allow for significantly reduced scan time enabling high-throughput in a busy PET practice and further reducing radiation exposure, which may have a clinical impact in pediatric populations. In recent years, multiple renal PET radiotracers labeled with 11C, 68Ga, and 18F have been utilized in clinical studies. Beyond providing a precise non-invasive read-out of renal function, such radiotracers may also be used to assess renal inflammation. In addition, future applications will be introduced, e.g. by transferring the concept of molecular **image-guided diagnostics and therapy (theranostics)** to the field of nephrology [3].

Merging targets collectively signals the next phase of PCa theranostics, defined not by a single antigen but by a portfolio of complementary tools tailored to diverse biological contexts. The future lies in integration: using multiple tracers to capture tumor heterogeneity, combining theranostics with systemic therapies, and applying biomarker-guided algorithms to match patients with optimal targets. Key challenges include developing robust biomarker assays, standardizing imaging and dosimetry, and aligning regulatory and commercial efforts with scientific progress. As new targets advance, thoughtful sequencing and combination

strategies will be essential. This evolution moves the field closer to personalized radiotheranostics that match the right patient at the right time [4].

The rapid evolution of radiotheranostics has transformed advanced PCa management, with PSMA as its cornerstone. However, variable expressions, therapy-induced downregulation, and absence in subsets such as NEPC (neuroendocrine prostate cancer) highlight the need. Another study introduced ²²⁵Ac-Macropa-PEG4-YS5, an innovative radioimmunoconjugate utilizing optimized chelation chemistry and improved linker technology linked to a specific cancer-specific antibody with low background tissue binding. Compared to the previously described ²²⁵Ac-DOTA-YS5, it demonstrated remarkable stability, improved tumor-to-background ratios, and treatment efficacy in the prostate cancer 22Rv1 xenografts. While there was mild to moderate renal toxicity at the highest dose levels, it also highlighted the potential for significant antitumor responses, emphasizing the importance of optimizing short PEG linkers for a balanced therapeutic efficacy and nephrotoxicity profile. Additionally, it was demonstrated the feasibility of theranostic matched pair imaging, and using ¹³⁴Ce/¹³⁹La for imaging alongside ²²⁵Ac. Ongoing research efforts aim to ease toxicities and maximize clinical utility, underscoring the promising future of this approach in cancer therapy [5].

To summarize, Theragnostics combines therapy and diagnostics to treat cancer. It involves the use of specific diagnostic tests to determine the most effective treatment for a patient. It includes diagnostic and therapeutic parts.

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