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Q1 You are recognised internationally for your work in advanced prostate cancer. What defining principles or philosophies guide your work as a clinician-scientist?

My approach is grounded in three core principles: a strong commitment to patient-centred medicine, scientific rigour and intellectual curiosity, and the promotion of guideline-driven, value-based care across health systems.

Patient-centred decision-making involves placing shared decision-making at the centre of care by integrating patient values, comorbidities, and life goals with high-level evidence and multidisciplinary expertise.

Scientific rigour and curiosity mean designing and contributing to clinical trials that address clinically meaningful, real-world questions, including toxicity, quality of life, and cost-effectiveness, rather than focusing on efficacy alone.

Finally, guideline-driven, value-based care is about ensuring that innovations, particularly costly new drugs and technologies, are used judiciously, targeted at patients most likely to benefit, and implemented in a way that minimises unnecessary resource utilisation.

Q2 How has the management of advanced and metastatic prostate cancer evolved during your career, and which shift do you believe has been the most transformative for patient outcomes?

I have been privileged to witness and actively participate in the development of androgen receptor pathway inhibition in prostate cancer. I recall a time when, beyond androgen deprivation therapy (ADT), treatment options were limited to first-generation antiandrogens such as bicalutamide and flutamide. The introduction of abiraterone and enzalutamide in the late stages of disease fundamentally transformed the management of advanced prostate cancer. This was followed by substantial efforts to move these agents, along with apalutamide and darolutamide, into earlier disease settings to improve overall survival, delaying disease progression, and preserving quality of life.

More recently, the field has entered a new and auspicious phase, shifting from largely biology-agnostic treatment strategies towards biologically-informed care. The widespread adoption of genomic profiling, prostate-specific membrane antigen (PSMA) PET imaging, and the use of poly-ADP ribose polymerase (PARP) inhibitors in homologous recombination repair-altered disease now enables a more personalised, tailored therapeutic approach, moving decisively away from a one-size-fits-all paradigm.

Q3 Many patients remain on long-term ADT. What strategies do you advocate for to mitigate its long-term toxicity and improve patients' quality of life?

My guiding principle for minimising the adverse effects of ADT has always been simple: "Do not use it if it is not truly needed." I firmly believe that ADT is substantially overused, particularly in earlier

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disease stages when combined with radiotherapy. Similarly, in the metastatic setting, systemic treatments could likely be interrupted more often in carefully selected exceptional responders, specifically patients who achieve a deep biochemical response, such as a prostate-specific antigen level below 0.2 ng/mL.

Prevention of cardiovascular complications is another critical priority. All patients should be systematically screened for pre-existing cardiovascular disease, and when treatment options are available, therapies with a more favourable cardiovascular safety profile should be preferred.

Beyond treatment selection, supportive care interventions are essential. I consistently advocate for the early initiation of structured exercise programmes combining aerobic and resistance training, which have been shown to improve body composition, muscle strength, and physical function in men receiving ADT. In parallel, bone, metabolic, and cardiovascular health should be addressed proactively through regular dual-energy X-ray absorptiometry surveillance and the use of bone-protective agents when indicated; optimisation of blood pressure, lipid profiles, and glycaemic control; and comprehensive lifestyle counselling encompassing diet, smoking cessation, and alcohol moderation.

Q4 How do you approach discussions about sexual health, fertility preservation, and masculine identity with patients starting lifelong hormonal therapy?

Discussions start before therapy, using clear language about expected changes in libido, erectile function, body composition, and mood, and offering early referral for sexual medicine support, devices, or penile rehabilitation where appropriate.

For men with potential future parenthood, sperm cryopreservation is presented as standard, and conversations explicitly acknowledge the impact on masculine identity, inviting partners when possible and normalising psychological support and peer groups.

Q5 PSMA-targeted radioligand therapy (RLT) has generated considerable momentum. What patient characteristics or disease features predict the best response in your experience?

I must admit that I have some concerns regarding the rapid dissemination of PSMA-based RLTs. Conceptually, these agents represent a form of targeted therapy, and I find it difficult to justify their use in situations where target expression is low or absent, or when they are co-administered with treatments known to downregulate PSMA expression. This concern directly echoes my broader commitment to guideline-driven, value-based care, a principle that I am surprised remains insufficiently emphasised in many discussions surrounding RLT.

Evidence consistently shows that the best responses to ^177Lu-PSMA-617 occur in carefully selected patients: those with high and homogeneous PSMA expression on PET imaging, minimal or absent PSMA-negative/fluorodeoxyglucose-positive disease, and adequate bone marrow and renal reserve, as demonstrated in the VISION and TheraP trials and confirmed in subsequent analyses.

Moreover, lower baseline disease burden, preserved performance status, and favourable biochemical profiles, such as lower alkaline phosphatase and lactate dehydrogenase levels, are independently associated with deeper prostate-specific antigen responses and improved survival in multivariable models.

Q6 What major research questions remain unanswered before RLT can move earlier in the treatment pathway?

The optimal timing and number of cycles of PSMA-based RLT remain poorly defined. Dedicated clinical trials are still needed to determine when RLT should be administered and how it should be integrated with ADT, androgen receptor signalling inhibitors, chemotherapy, or PARP inhibitors, both in the hormone-sensitive setting and in earlier stages of metastatic castration-resistant prostate cancer.

If we are candid, RLT has thus far demonstrated its greatest efficacy in late-stage disease, whereas studies exploring its use at earlier stages have reported more modest benefits. We may never obtain a clear answer regarding optimal timing without trials specifically designed to compare early versus late administration of RLT, incorporate treatment re-challenge, and allow systematic cross-over.

Moreover, too many RLT trials have been drug-centred rather than patient-centred, with designs optimised primarily to demonstrate benefit for the investigational agent. A notable example is PSMAfore, in which docetaxel, the most widely accepted standard comparator, was excluded. What is urgently needed is patient-oriented trials

to define the most effective sequencing and combinations for individual patients.

The optimal number of RLT cycles also remains a critical unresolved issue. The blanket approach of administering six cycles to all patients, simply because this was done in clinical trials, is inconsistent with the drug's mechanism of action and risks unnecessary overexposure. Dose adaptation guided by serial imaging and treatment response should, in my view, become the standard of care.

Finally, several key questions remain unanswered, including the risk of long-term bone marrow toxicity, cumulative dose limits, optimal sequencing with other radiopharmaceuticals, and whether earlier use of RLT influences clonal evolution or promotes PSMA-negative escape.

Q7 How can health systems ensure equitable access to precision oncology tools, particularly in resource-limited settings?

This is a challenging issue. At a minimum, diagnostic tests should be recommended only when there is robust, evidence-based justification that their results will meaningfully influence clinical management. Too often, this is not the case, particularly with modern imaging. The use of PSMA PET has expanded rapidly and is vastly uncontrolled, despite limited evidence defining the clinical scenarios in which it truly alters disease trajectory or patient outcomes.

To address this, health systems should adopt tiered diagnostic pathways that prioritise high-value investigations, such as targeted germline and somatic testing or PSMA PET imaging in clearly defined indications. Health-technology assessment frameworks can help guide reimbursement decisions and ensure that resources are allocated where clinical benefit is demonstrable.

At a system level, the development of regional diagnostic hubs, shared image-reading platforms, and cross-border referral networks can help consolidate expertise and infrastructure. Such models allow patients who are treated in resource-limited centres to access molecular diagnostics and advanced imaging through structured referral pathways or clinical trials, promoting equity while maintaining efficiency and quality.

Q8 How can we better include patients who are older, frailer, or comorbid, and who represent much of the real-world population, in clinical trials?

This represents my primary commitment for the years ahead. The systematic exclusion of patients who are older, frailer, and comorbid is one of the most critical limitations of drug-centred randomised clinical trials. I am consistently struck by how broadly these trial results are disseminated, even though they ultimately reflect the benefit of an intervention in a highly selected population. The problem is further amplified when the same trials are repeatedly incorporated into multiple meta-analyses, leading to an expanding body of evidence that remains largely unaware of the extent of patient selection.

This issue is particularly concerning in prostate cancer, where approximately one-quarter of diagnoses occur in men older than 75 years, the majority of whom have at least one significant comorbidity, and frequently multimorbidity. Trials should therefore adopt more pragmatic inclusion criteria, relying on geriatric assessment and functional status rather than chronological age alone, and incorporate endpoints that meaningfully capture functional independence and quality of life.

In parallel, trial designs must evolve to better reflect real-world care. Decentralised visits, simplified treatment regimens, and caregiver-friendly protocols, together with dedicated studies specifically designed for frail populations, are essential to ensure that clinical trial results are applicable to the patients we actually treat, rather than to a highly selected minority.

Q9 How do you foresee workforce training in urologic oncology changing to keep pace with increasingly complex systemic therapies?

Urologic oncology, as a medico-surgical specialty, is confronted with a fundamental question: do we aspire to train 'skilled and safe technicians', or 'coordinators of multiprofessional urological cancer care'? There is a real risk that, if urologists fail to embrace the full biological and systemic dimensions of the disease, they may function like factory workers, operating complex machines by pushing buttons and pulling levers without understanding the mechanisms that drive them. Such an approach undermines the ability to justify surgical interventions on sound scientific grounds or to articulate why, based on evolving insights from genomics, proteomics, and metabolomics, imposing surgical stress represents the most appropriate therapeutic choice.

I strongly oppose this narrow vision. Training in urologic oncology must instead integrate formal education in systemic therapies, molecular oncology, and theranostics, supported by structured, joint rotations across urology, medical oncology, radiation oncology, and nuclear medicine.

Looking forward, competency frameworks should increasingly emphasise proficiency in trial interpretation; the management of complex treatment-related toxicities, including those associated with PARP inhibitors and RLTs; and the effective use of digital decision-support tools and multidisciplinary tumour boards. This broader skill set is essential if urologic oncologists are to remain central, informed leaders in the care of patients with urological cancers.

Q10 What do you believe will be the single biggest change in advanced prostate cancer management over the next decade?

AI is emerging as both the most exciting opportunity and the most complex challenge in prostate cancer care. In diagnostics, AI already rivals expert radiologists and pathologists in interpreting MRI and digital pathology, creating the prospect of faster, more consistent detection and grading worldwide. By integrating imaging, pathology, genomics, and routine clinical data, AI models can generate far more granular risk profiles, helping to individualise active surveillance, choose between local and systemic options, and time treatment intensification or de escalation. In advanced disease, decision support systems built on trial and real world datasets may soon help optimise combinations and sequences of androgen receptor signalling inhibitors, chemotherapy, PARP inhibitors, and RLTs for each patient. At the same time, workflow tools for automatic contouring, PSMA-PET quantification, toxicity prediction, and report generation could release precious clinician time for conversations and shared decision making rather than data administration. The central challenge is that many AI tools are trained on narrow, often homogeneous datasets, risking loss of performance and amplification of existing disparities when deployed in more diverse real world populations. Their black box nature raises legitimate concerns about explainability, accountability, and how to obtain meaningful informed consent when an opaque algorithm influences life-changing decisions. Regulatory frameworks and reporting standards in urologic oncology are only beginning to catch up, leaving uncertainty about validation requirements, post marketing surveillance, and liability when things go wrong. There is also a human challenge: clinicians must acquire new skills to critically interrogate AI outputs, understand their limitations, and avoid automation bias while still embracing tools that can genuinely augment judgment. For health systems, particularly in Europe, a key question is how to deploy AI in a way that narrows rather than widens the gap between highly resourced centres and hospitals with limited digital infrastructure. In the coming decade, the task will be to ensure that AI becomes an ethically governed partner in prostate cancer care, enhancing precision, efficiency, and equity, without undermining the trust and human connection at the heart of the clinician-patient relationship.