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Theranostics comes of age

This month's *CUAJ* features a Canadian, multidisciplinary expert consensus that provides guidance on prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) interpretation, prostate cancer staging and restaging, and the use of PSMA-targeted radioligand therapy (RLT).[1]

An important theme running through the consensus is a conservative approach to PSMA PET/CT when changing standard-of-care management. The limited sensitivity for low-volume nodal or prostate bed disease is recognized in statements discouraging omission of treatment to potential pelvic disease sites on the basis of a negative PSMA PET/CT when treatment is otherwise indicated. This guidance is supported by the POP-RT trial,[2] in which randomization between prostate-only and prostate-plus-pelvic-nodal radiotherapy was contingent on negative nodal PET imaging, yet demonstrated a disease-free survival benefit in the pelvic radiotherapy arm. It was further supported by Emmett et al, who reported high rates of biochemical response to salvage prostate-bed radiotherapy with either a prostate bed-confined or negative PSMA PET/CT, suggesting a negative scan may enrich for prostate bed-only disease.[3]

The document likewise emphasizes sources of false-positive uptake (non-specific bone lesions, benign processes, physiologic activity, and temporal responses to treatment). Solitary lesions receive particular attention, given the considerable prognostic and therapeutic implications of metastatic vs. non-metastatic classification, and radiographic and clinical correlation is appropriately encouraged.

In the ongoing Canadian PATRON trial (NCT04557501), all men have standard-of-care treatment, with PSMA PET/CT findings used only to escalate, never de-escalate, therapy. This approach ensures that men still receive standard-of-care radical therapy. in addition to lesion-directed intensification. PATRON endpoints, when reported, will be instrumental in further shaping appropriate use of PSMA PET/CT in high-risk primary and recurrent disease.

Finally, recommendations restricting RLT in earlier-stage metastatic disease to clinical trials are appropriately conservative. The contrasting results of PR.21 and PSMAddition,[4] and pending Health Canada review of the latter indication, reinforce that earlier use of RLT will require nuanced decision-making, particularly in oligometastatic disease, where integration of PSMA PET-enabled lesion-directed stereotactic radiotherapy with hormone intensification, chemotherapy, and RLT remains to be defined.

One caveat to the report is that while Health Canada approvals of diagnostic and therapeutic radioligands, together with provincial funding decisions, are now allowing Canadian men to benefit from these advances, panelists voted assuming unrestricted access to PSMA PET/CT and RLT; timely, equitable access across provinces remains an implementation challenge.

Lalani et al are to be congratulated on providing a snapshot of Canadian practice and appropriate-use criteria among expert practitioners. The strong consensus within our community bodes well for the ongoing rigorous, evidence-informed deployment of these exciting innovations.

COMPETING INTERESTS: Dr. Bauman has given talk on PSMA PET/CT for Novartis and is participating in a trial of ^{18}F-PSMA 1007 PET/CT for the Centre for Probe Development and Commercialization. He is also involved in a prospective PSMA PET/CT registry study supported by Ontario Health.

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