What is the best PET target for early biochemical recurrence of prostate cancer?

Following their retrospective case series[1] of patients undergoing ^{18}F-fluciclovine and ^{68}Ga-PSMA-11 PET imaging and subsequent commentaries,[2,3] Calais and colleagues[4] have attempted to do a formal head-to-head comparative study of the two agents; however, some limitations of the study conduct and analysis are apparent. First, of 143 screened patients, only 50 (35%) were enrolled. Second, the study is not single centre because 12 (24%) of 50 ^{18}F-fluciclovine scans were done outside the University of California, Los Angeles, potentially confounding the objective of comparing imaging tracers. Third, ^{18}F-fluciclovine readers were substantially less experienced (150–400 scans) than ^{68}GaPSMA-11 readers (1000–3000 scans). Fourth, image quality assessment was the first item in the PET reading spreadsheet guidelines, yet this information is not reported. Finally, the Article states, "All patients had standard-of-care ^{18}F-fluciclovine and investigational PSMA PET–CT according to guidelines"; however, the reported median uptake time of 2 min (IQR 1–3) does not follow US Food and Drug Administration (FDA)-recommended image acquisition guidelines to begin PET scanning 3–5 min after injection, which would have affected image quality.[5]

Concurrent with Calais and colleagues' publication, Pemthaler and colleagues[6] reported their prospective, head-to-head comparison of ^{18}F-fluciclovine and ^{68}Ga-PSMA-11. They scanned 58 patients with biochemical recurrence after definitive primary prostate cancer therapy at one institution on one of two scanners, ensuring that each patient had both scans done on the same scanner. ^{18}F-Fluciclovine image acquisition followed the US FDA-recommended protocol. Both ^{68}Ga-PSMA and ^{18}F-fluciclovine scans were evaluated by masked readers applying standardised interpretation criteria.[6] This cohort had a mean prostate-specific antigen (PSA) concentration of 14·9 ng/mL (median 4·1 ng/mL). Per-patient detection rates in patients with a PSA level of 2 ng/mL or less calculated from the data in table 2 were ten (53%) of 19 patients for ^{68}Ga-PSMA and eight (42%) of 19 patients for ^{18}F-fluciclovine.

Pemthaler and colleagues and Calais and colleagues used similar ^{68}Ga-PSMA acquisition parameters and, consequently, report similar ^{68}Ga-PSMA detection rates at a PSA value of 2 ng/mL or less. However, the ^{18}F-fluciclovine detection rate was higher in Pemthaler and colleagues' cohort (42%) than Calais and colleagues' cohort (26%), where greater variability in scanning was evident. The ^{18}F-fluciclovine detection rate at a PSA of 2 ng/mL or less calculated from Pemthaler and colleagues' data is consistent with findings from LOCATE[7] (57 [42%] of 136), a US multicentre trial using the same standardised acquisition and interpretation criteria. This supports the idea that ^{18}F-fluciclovine detection rates are not overestimated by Pemthaler and colleagues and highlights the potential negative effect of the inconsistencies in ^{18}F-fluciclovine scanning by Calais and colleagues.

Pemthaler and colleagues' study addresses many limitations of Calais and colleagues' study, representing a "reliable and robust head-to-head comparison". Calais and colleagues' conclusion that "PSMA should be the PET tracer of choice" is somewhat premature, given they studied only one PSMA agent when multiple ligands, labelled with ^{68}Ga or ^{18}F, are currently under investigation.

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