Impact of Clinical Factors on ^{18}F-Piflufolastat and ^{18}F-Flotufolastat Detection Rates in Participants with Recurrent Prostate Cancer Post-prostatectomy: Results from an Intra-patient Head-to-head Phase 4 Study

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Introduction and overall goal: Prostate-specific membrane antigen (PSMA)-targeted positron emission tomography (PET) has become the mainstay of prostate cancer imaging. BED-PSMA-411 (NCT06604442) was the first intra-patient head-to-head comparator study of two ^{18}F-labeled PSMA-PET radiopharmaceuticals, ^{18}F-piflufolastat and ^{18}F-flotufolastat, in participants with biochemical recurrence (BCR) of prostate cancer.

Specific aims: To evaluate intra-patient comparator data; to understand the impact of clinical factors on both^{18}F-piflufolastat and ^{18}F-flotufolastat detection rates (DR).

Rationale and background: PSMA-PET focused studies of radiopharmaceuticals including ^{18}F-piflufolastat have reported increases in clinicopathologic factors such as prostate specific antigen (PSA) levels, PSA kinetics and Gleason scores to have an association with DR in men with BCR.[1,2] A recent study showed that ^{18}F-flotufolastat DR increased with PSA levels but remained uniformly high across International Society of Urological Pathology (ISUP) Grade Group (GG) and regardless of prior treatment.[3]

Methods and materials: Men ≥ 18 years with low PSA (≤ 0.5 ng/mL) BCR of prostate cancer ≥ 6 months after radical prostatectomy (RP) with undetectable PSA post-surgery were enrolled. Participants underwent PET 60 minutes after IV administration of 333 MBq ^{18}F-piflufolastat. After 1–10 days, the participants had a second PET on the same scanner, 60 minutes after receiving IV ^{18}F-flotufolastat (296 MBq). Images were interpreted by two blinded central readers, with a third to resolve disagreements, allowing majority read results (reported throughout). DR were stratified by baseline PSA, time since RP, initial disease stage, and ISUP GG.

Results: In total, 55 men (median PSA, 0.28 ng/mL) had evaluable scans with both radiopharmaceuticals.

The overall participant-level DR was 27% (15/55) for ^{18}F-piflufolastat and 45% (25/55) for ^{18}F-flotufolastat. Although low numbers of participants in some categories limit practice-changing conclusions, ^{18}F-flotufolastat showed higher overall DR in every PSA stratification. This included participants in the ≤ 0.1, > 0.1–0.2, and > 0.2–0.3 ng/mL groups (0% [0/2], 42% [8/19], and 25% [4/16] for ^{18}F-piflufolastat and 100% [2/2], 47% [9/19], and 44% [7/16] for ^{18}F-flotufolastat, respectively). In the prostate bed, the DR was 14% (3/21) for both ^{18}F-piflufolastat and ^{18}F-flotufolastat at PSA levels ≤ 0.2 ng/mL, and 8.8% (3/34) and 21% (7/34), respectively, at PSA levels > 0.2–0.5 ng/mL.

Participants with < 5 years between RP and BCR (31% [13/42] for ^{18}F-piflufolastat and 50% [21/42] for ^{18}F-flotufolastat) had higher DR compared with those with ≥ 5 years between RP and BCR (15% [2/13] for ^{18}F-piflufolastat and 31% [4/13] for ^{18}F-flotufolastat).

^{18}F-Piflufolastat and ^{18}F-flotufolastat DR were 21% (6/28) and 43% (12/28), respectively, among participants who were N0 at initial diagnosis, and 0% (0/2) and 50% (1/2) for participants who were N1. The DR for both radiopharmaceuticals increased with increasing ISUP GG. The DR was 0% (0/3) for both ^{18}F-piflufolastat and ^{18}F-flotufolastat for ISUP GG 1, 28% (11/39) and 46% (18/39), respectively, for GG 2–3, and 31% (4/13) and 54% (7/13) for GG 4–5.

Discussion and conclusion: This intra-patient comparator study demonstrates the suitability of both ^{18}F-piflufolastat and ^{18}F-flotufolastat PET for imaging a broad range of participants with BCR of prostate cancer, with ^{18}F-flotufolastat consistently offering higher DR among this low PSA population.

References: 1. Cerci et al. *J Nucl Med*. 2022;63(2):240–247. 2. Mena et al. *J Nucl Med.* 2022;63(8):1184–1190. 3. Lowentritt et al. *Adv Radiat Oncol*. 2024;9(8):101532.