True positive ^{18}F-rhPSMA-7.3 lesions in patients with prostate cancer recurrence with negative conventional imaging: Results from the prospective, phase 3, multicenter, SPOTLIGHT study

Andrei Purysko[1], on behalf of the SPOTLIGHT Study Group

1. Cleveland Clinic, Cleveland OH, USA. Email: PURYSKA@ccf.org

Introduction and overall goal:

^{18}F-rhPSMA-7.3 represents a new class of radiohybrid (rh) high affinity prostate-specific membrane antigen (PSMA)-targeted positron emission tomography (PET) radiopharmaceuticals with potential for low bladder activity and scope for theranostic development. SPOTLIGHT (NCT04186845) assessed the diagnostic efficacy of ^{18}F-rhPSMA-7.3 in men with biochemical recurrence (BCR) of prostate cancer.

Specific aims:

Here, we report the rates of true positive (TP) ^{18}F-rhPSMA-7.3 lesions in patients with negative baseline conventional imaging.

Rationale and background: Despite improvements in prostate cancer primary therapy, BCR remains common. Accurate localization of recurrent lesions can help direct optimal salvage therapy, however, localization of recurrence with conventional imaging remains challenging, especially when prostate-specific antigen (PSA) levels are low.

Methods and materials:

Men with suspected BCR underwent PET 50–70 min after intravenous administration of 296 MBq ^{18}F-rhPSMA-7.3. PET findings were validated using histopathology or confirmatory imaging. Image guided biopsies of PET lesions took place ≤60 days post-PET and confirmatory imaging took place ≤90 days. Three blinded central readers evaluated the ^{18}F-rhPSMA-7.3 PET scans.

A verified detection rate (VDR; proportion of all patients with ≥1 true positive (TP) lesion as confirmed by the SoT, regardless of any coexisting false positive lesions) was documented for patients with negative baseline conventional imaging (performed ≤118 days before PET) and the results were stratified according to the patients' prior therapy.

Results:

In total, 366 men (mean [range] PSA 3.95 [0.03–134.60] ng/mL) were enrolled across 27 US/European sites, underwent ^{18}F-rhPSMA-7.3 PET, and had sufficient data to determine a SoT ("Efficacy Analysis Population" [EAP]). The overall detection rate in the EAP was 88% by majority read. The overall VDR ranged from 51-54% across the 3 readers and was seen to increase with increasing baseline PSA, ranging from 24-30% at PSA <0.5 ng/mL to 77-84% at PSA ≥10 ng/mL.

In total, 250 (68%) of the 366 patients in the EAP had negative baseline conventional imaging. Depending on the reader, between 113 and 117 of these patients had at least one TP ^{18}F-rhPSMA-7.3 lesion (VDR, 45-47%).

According to the three readers, among the patients in the EAP with negative baseline conventional imaging who had undergone prostatectomy, between 3.5 and 8.0% of ^{18}F-rhPSMA-7.3 positive scans showed TP lesions in the prostate bed region, 18-21% in pelvic lymph nodes, and 21-26% in other sites. Among those who had received radiotherapy, the TP rates were 39-41% in the prostate region, 6.5% in pelvic lymph nodes and 20-30% in other sites.

Discussion and conclusion:

^{18}F-rhPSMA-7.3 showed a positive VDR across a wide range of PSA levels and frequently identified TP lesions in patients with negative baseline conventional imaging. The use of ^{18}F-rhPSMA-7.3 PET may help to better define sites of disease recurrence and inform salvage therapy decisions.