BERLIN 2025 ESMO congress

LBA90

Prospective randomized phase II trial of 177Lutetium-PSMA therapy neoadjuvant to stereotactic ablative radiotherapy for recurrent oligo-metastatic hormone-sensitive prostate cancer (LUNAR NCT05496959)

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Background

We hypothesized that adding prostate-specific membrane antigen (PSMA)-targeting radioligand therapy (RLT) to metastasis-directed stereotactic body radiotherapy (SBRT) will improve progression-free survival (PFS) in patients with oligometastatic hormone sensitive prostate cancer (omHSPC).

Methods

This was a single-center investigator-iniated trial conducted at UCLA. Patients with recurrent omHSPC by PSMA PET/CT (1-5 lesions outside the prostate or prostate bed) were randomized in a 1:1 fashion to receive either SBRT to all metastatic lesions vs. 2 cycles of neoadjuvant 177Lu-PSMA PNT2002 (6.8 GBq/cycle) 6-8 weeks apart followed by SBRT to all metastatic lesions. Stratification was based on number of lesions (1 vs. 2-3 vs. 4-5) and PSMA-PET based stage (N1/M1a vs. M1b vs.M1c). The primary endpoint was PFS, with progression defined as PSMA-PET positive lesions seen at the time of biochemical progression or on a scheduled PSMA PET/CT performed 12 months after SBRT completion, initiation of salvage therapy, or death. We used a randomized phase 2 design with a one-sided alpha of 0.1 and a power of 0.80, yielding a target accrual of 90 patients.

Results

From September 2022 to November 2023, 92 patients were randomized (n=47 SBRT alone, n=45 177Lu-PSMA+SBRT); 5 patients randomized to SBRT alone dropped out prior to therapy. Median PSA was 1.1 ng/mL (IQR 0.5-3.1). The median number of lesions per patient was 2: 37 (43%) had a solitary lesion, 36 (41%) 2-3 lesions, and 14 (16%) had 4-5 lesions. 54 (62%) and 33 (38%) had had N1/M1a and M1b disease, respectively. At a median followup of 22 months, the addition of 177Lu-PSMA to SBRT significantly prolonged PFS (17.6 months [95%CI 15 months - not reached)] *versus* 7.4 months (95%CI 6.0-13.5 months); HR 0.37 [95%CI 0.22-0.61], p<0.0001). 64/65 progression events (98%) were due to new lesions. The only grade 3 adverse events were lymphopenia: 2 patients [4.8%] in the SBRT group and 3 patients [6.7%] in the ^{177}Lu+SBRT group.

Conclusions

In this randomized trial, administering 2 cycles of 177Lu-PSMA prior to SBRT improved PFS in men with omHSPC, without increasing toxicity.

Clinical trial identification

NCT05496959.

Legal entity responsible for the study

The authors.

Funding

POINT Biopharma / Lantheus.

Disclosure

J. Calais: Financial Interests, Personal, Advisory Board: Astellas, Blue Earth Diagnostics, Curium, Fibrogen, GE Healthcare, Novartis, Nucleus Radiopharma, Radiomedix, Telix; Financial Interests, Personal, Steering Committee Member: Novartis, Lantheus; Financial Interests, Institutional, Research Grant: Novartis, Lantheus; Financial Interests, Institutional, Local PI: Novartis, POINT Biopharma, Lantheus, Telix, Janssen, Fusion Pharma; Non-Financial Interests, Advisory Role: Oncidium Foundation; Non-Financial Interests, Other, Associate Editor: The Journal of Nuclear Medicine; Non-Financial Interests, Member: SNMMI, ARS, ASCO, SWOG. All other authors have declared no conflicts of interest.