Preliminary efficacy and safety results from the TATCIST trial: A PSMA-directed targeted alpha therapy with FPI-2265 (225Ac-PSMA-I&T) for the treatment of metastatic castration-resistant prostate cancer

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Abstract

Introduction

Targeted radionuclide approaches are designed to deliver radiation specifically to cancer cells by combining a radiolabeled small molecule with a targeting moiety (e.g., a monoclonal antibody or radionuclide-labeled PSMA-binding peptide). Some studies have shown that alpha-emitting radionuclides, such as lutetium (177Lu), FPI-2265 (225Ac-PSMA-I&T), or lutetium (177Lu)-PSMA-617 have potential therapeutic advantages over palladium (103Pd) or radionuclide-labeled PSMA-binding peptides. The TATCIST trial (NCT02650590) evaluated the preliminary efficacy and safety results of FPI-2265 (225Ac-PSMA-I&T) in participants enrolled in the TATCIST trial (TATCIST open label trial) who had previously received prior Lu treatment.

Methods

The TATCIST open-label trial is an extension of the TATCIST trial (NCT02650590). Participants were evaluated in this subset of the TATCIST trial (TATCIST open label trial) who had previously received prior Lu treatment. Participants were included in the efficacy analysis if they had a baseline PET/CT scan between October 2020 and May 2021 (24 weeks before study drug administration) and had a post-treatment PET/CT scan within 12 weeks after the last dose of radiotherapy. All post-treatment PET/CT scans were performed approximately 12 weeks after administration of at least one dose of FPI-2265 (225Ac-PSMA-I&T). Data were analyzed by an independent radiologist according to Response Evaluation Criteria In Solid Tumors (RECIST) v1.1 criteria. Key Exclusion Criteria: Participants were excluded from the efficacy analysis if they had a prior history of noncompliance; required use of prohibited treatment; sponsor/investigator decision; or death. The treatment was continued until disease progression by PCWG3 or unacceptable toxicity or patient withdrawal. For survival outcomes, data were censored at the date of the last confirmed vital status or last contact. Data were last updated on November 14, 2022.

Results

By August 2022, 20 participants had achieved an PSA response by week 24 and 8 participants had a superscan at week 24 (32%). The majority of TRAEs were grade 1 or 2. In the safety analysis, safety was evaluated in 29 of 35 participants. The median duration of follow-up for participants included in the safety analysis was 20.1 weeks (range: 11-28.2 weeks). No participant discontinued treatment because of the radionuclide-related toxicity. Safety and efficacy results are summarized in Table 3.

Conclusion

This study showed that FPI-2265 (225Ac-PSMA-I&T) had an acceptable safety profile and preliminary efficacy results in participants with prior Lu treatment. Data are awaited from a larger trial to confirm the clinical benefit of FPI-2265 (225Ac-PSMA-I&T). Additional randomized studies are needed to further evaluate the safety and efficacy of FPI-2265 (225Ac-PSMA-I&T) in participants with metastatic castration-resistant prostate cancer.

Disclosure

The authors declare no conflicts of interest.

References

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