TPS5125 Poster Session

SECuRE: A dose escalation/expansion study to assess the anti-tumor efficacy of ^{67}Cu-SAR-bisPSMA in patients with metastatic castrate resistant prostate cancer.

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Background: Prostate cancer (PC) is common and despite recent advances in treatment options, patients with metastatic disease still have poor outcomes. The double PSMA binding moiety of SAR-bisPSMA in ^{64}Cu-SAR-bisPSMA (imaging) and ^{67}Cu-SAR-bisPSMA (therapy) may offer advantages compared to currently used single-target PSMA agents. Clinical evidence demonstrated 2-3 times higher uptake of ^{64}Cu-SAR-bisPSMA compared to the single-target PSMA agent, ^{68}Ga-PSMA-11. Pre-clinical efficacy data of ^{67}Cu-SAR-bisPSMA in mice showed statistically significant tumor growth inhibition and increased survival in a PC xenograft study. These results led to the development of the SECuRE trial, which aims to assess the safety and anti-tumor efficacy of ^{67}Cu-SAR-bisPSMA in patients with metastatic castrate resistant PC (mCRPC). **Methods:** SECuRE is a Phase I/IIa multi-center, open-label, non-randomized, dose-escalation and cohort expansion study of ^{64}Cu-SAR-bisPSMA and ^{67}Cu-SAR-bisPSMA in patients with mCRPC. The target population is patients who have progressed despite having at least one androgen receptor pathway inhibitor and demonstrate positivity on ^{64}Cu-SAR-bisPSMA PET. The study comprises 3 phases: Dosimetry (N=6), Dose Escalation (N~24) and Cohort Expansion (N=24). The ^{67}Cu-SAR-bisPSMA dose levels investigated in the Dose Escalation Phase are: 4 GBq (cohort 1, single dose), 8 GBq (cohort 2, single dose), 12 GBq (cohort 3, single dose) and 24 GBq across two doses (cohort 4, two doses at the maximum tolerated dose or maximum feasible dose [MTD/MFD] established in cohorts 1-3; two additional doses may be offered in case of radiological non-progression). In the Cohort Expansion phase, participants will receive 2 doses of ^{67}Cu-SAR-bisPSMA at the recommended dose determined in the Dose Escalation Phase (those with radiological non-progression may be offered up to 2 additional doses). A recent protocol amendment increased the number of participants from 14 to 24 in the Cohort Expansion phase, in which 8 will receive combination therapy of ^{67}Cu-SAR-bisPSMA with enzalutamide. The primary and key secondary objectives include assessment of ^{64}Cu- and ^{67}Cu-SAR-bisPSMA's safety and dosimetry and determining the anti-tumor efficacy of ^{67}Cu-SAR-bisPSMA. Response to ^{67}Cu-SAR-bisPSMA will be assessed biochemically ($\geq$50% decline in prostate-specific antigen) and radiographically (by RECIST V1.1 and PCWG3). Clinical trial information: NCT04868604. Research Sponsor: Clarity Pharmaceuticals.