Safety & dosimetry of ^{177}Lu-rosopatamab tetraxetan plus SoC in patients with metastatic castration-resistant prostate cancer: preliminary results from Part 1 of Phase 3 ProstACT Global study

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Background: ProstACT Global is a Phase 3 study of ^{177}Lu-rosopatamab + standard of care (SoC) for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). We present preliminary safety, dosimetry, & pharmacokinetics results from Part 1 (Lead-In).

Methods: Eligible pts had PSMA+ mCRPC (confirmed on ^{68}Ga-PSMA-11 PET/CT) with disease progression on ≥12w prior therapy on their 1st androgen receptor pathway inhibitor in metastatic castration-sensitive PCa, non-mCRPC, or mCRPC setting. Pts may have received docetaxel in mCSPC setting if ≥6 months prior.

Pts received 2 single IV injections ^{177}Lu-rosopatamab (76 mCi each), 14d apart, with assigned SoC (Cohort 1, +abiraterone; Cohort 2, +enzalutamide; Cohort 3, followed by docetaxel; planned n=10 each).

Pts were monitored for treatment-emergent adverse events (TEAEs; onset on or after initiation of study treatment). Pts underwent serial SPECT/CT imaging after ^{177}Lu-rosopatamab administration (4, 24, 96, 168, 360h) for dosimetry & blood sampling for pharmacokinetics (PK).

Co-primary endpoints were safety & dosimetry of ^{177}Lu-rosopatamab + SoC. Analyses were preplanned, descriptive, & overseen by IDMC. No formal statistics were performed. Dosimetry & biodistribution were evaluated using observed values without formal hypothesis testing.

Results: Data from 36 pts (baseline median PSA: 18.18 ng/mL) who received any study treatment was included (Cohorts 1, 2, 3: n=11, 11, 14, resp.). 55.6% pts had Gleason score 8-10, 72% pts were 2L mCRPC, & 25% pts had previous taxane exposure.

No new safety signals were identified; TEAEs were predominantly transient & manageable hematologic events. Hematologic TEAEs (% pts any grade; Grade ≥3) included thrombocytopenia (77.8%; 44.4%), neutropenia (63.9%; 47.2%), & lymphopenia (55.6%;41.7%). Non-hematologic TEAEs were all Grade ≤2, except for 1 Grade 3 dizziness. Fatigue (19 events) was most common. Only 9 xerostomia events reported (all Grade 1). No Grade 5 treatment-related TEAEs reported.

Blood activity concentration over time demonstrated bi-exponential clearance kinetics. Liver received highest absorbed radiation (range, 1.62-5.08 mGy/MBq), with lower doses received by kidneys (0.336-0.961 mGy/MBq) & salivary glands (0.001-0.104 mGy/MBq). Lesion activity concentrations were higher than in normal tissues & detectable at last imaging timepoint (15d).

Conclusions: ^{177}Lu-rosopatamab + SoC for pts with mCRPC demonstrates a manageable safety & tolerability profile; predictable PK profile with prolonged tumor residence; & organ radiation exposure below recommended thresholds. Radiation absorbed dose was highest for liver (clearance organ), which is comparatively radioresistant. Data support continued investigation in Part 2.

Disclosure: This study is sponsored by Telix Pharmaceuticals.