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Preliminary safety and efficacy data of [212Pb]VMT-α-NET in somatostatin receptor 2 (SSTR2) expressing neuroendocrine tumors (NETs)

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BACKGROUND

Despite the introduction of Lutathera, there remains an unmet medical need for new front-line therapies for advanced NETs. In this Phase I study, [^{212}Pb]VMT-α-NET, a novel targeted alpha radionuclide therapy (TAT) to SSTR2, is being investigated for safety and efficacy in PRRT-naïve patients with SSTR2 expressing tumors. Here we present initial results from the first two dose escalation cohorts.

METHODS

This is a first-in-human dose-escalation study to determine the safety, pharmacokinetics, and preliminary efficacy of [^{212}Pb]VMT-α-NET in adult NETs of any grade, Small Cell Lung Cancer, Pheochromocytoma and Paraganglioma with progressive disease as assessed by RECIST 1.1. (NCT05636618).

The Phase 1 of the trial includes four escalating cohorts and follows a Bayesian modified toxicity probability interval (mTPI-2) design. The first two cohorts incorporate dosimetry evaluations with the therapeutic surrogate [203Pb]VMT-α-NET prior to receiving up to 4 treatment cycles of [^{212}Pb]VMT-α-NET with injected activity of 92.5 MBq (2.5 mCi) or 185 MBq (5 mCi) for Cohort 1 or 2, respectively. Reno-protective amino acids are co-administered with [^{212}Pb]VMT-α-NET. DLT assessment period is defined as the first 6 weeks of cycle 1. Safety is assessed weekly during cycle 1 and bi-weekly for subsequent cycles. The total in-trial follow-up period will be 18 months following the final administration. Efficacy will be assessed by RECIST 1.1 criteria. The primary objective is to evaluate the tolerability of [^{212}Pb]VMT-α-NET, collection and measurement of radioactive blood and urine PK samples at specific timepoints, and determination of the recommended phase 2 dose of [^{212}Pb]VMT-α-NET in PRRT naïve participants with NETs.

RESULTS

A total of 9 patients were enrolled (2 in cohort 1 and 7 cohort in 2). There were no DLTs or grade 3 AEs for Cohort 1 (92.5 MBq (2.5 mCi). 4/33 TEAEs were grade 2 AEs (elevated Amylase, fatigue, nausea and urinary tract infection). Cohort 2 Safety Monitoring Committee (SMC) meeting was held on July 17th, 2024, with no DLTs. There were 2 grade 3 AEs (diarrhea, syncope), 4 grade 2 AEs (fatigue, nausea, presyncope and weight loss). The most frequent TEAE were in descending order: nausea, alopecia, diarrhea and fatigue. No nephrotoxicity was reported in either cohort. One patient discontinued due to progressive disease.

CONCLUSIONS

[212Pb]VMT-α-NET is safe up to 185 MBq (5 mCi) dose level, and the SMC supported dose escalate to cohort 3 at 277.5 MBq (7.5 mCi) following a mandatory FDA review in fall. Cohort 2 remains open for dose level expansion.

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