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Phase 1 Trial of Pb-212-VMT-alpha-NET in Select Metastatic or Inoperable Somatostatin Receptor Positive Tumors

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BACKGROUND

Somatostatin receptors (SSTR) is overexpressed in a number of different tumors, including GI Neuroendocrine Tumors (GI-NET), Pheochromocytoma/Paraganglioma (PPGL), small cell lung cancer (SCLC), renal cell carcinoma (RCC), and certain head and neck cancers (H&N) such as olfactory neuroblastoma. It has been demonstrated that these SSTR-expressing tumors can be treated with beta-emitting radioligand therapy (RLT) that binds to SSTR such as Lu-177-DOTATATE. However, there are known limitations of beta emitting radionuclides such as Lu-177-DOTATATE, such as having low objective response rates and lack of durable responses. As alpha particle emitters such as Pb-212 have significantly higher tumor-kill potential compared to beta particles due to their larger physical size and higher linear energy transfer (LET), it is hypothesized that SSTR-targeting alpha emitters will have greater efficacy than betas. Early clinical trial data of other similar SSTR-targeting alpha emitters such as of Pb-212-DOTAMTATE have already shown good clinical efficacy. This phase 1 trial will evaluate the efficacy of a novel agent Pb-212-VMT-alpha-NET in patients with SSTR+ tumors who are naïve to prior RLT.

METHODS

This is an open-label, single arm, single-center, phase 1 study evaluating the safety, tolerability, and pharmacokinetic properties of the alpha-emitting, systemic radioligand therapy agent Pb-212-VMT-α-NET in five different SSTR+ tumors: GI-NET, PPGL, SCLC, RCC, and H&N. The phase 1 dose escalation will be using a standard 3+3 design, with the dose regimen being 4 cycles of fixed dose Pb-212-VMT-α-NET starting at 2.5 mCi and increasing by 2.5 mCi per dose level until a maximum dose of 10.0 mCi or MTD is reached. Pb-203-VMT-α-NET will be used as an imaging agent is a selected dosimetry cohort. Urine and blood will be collected for pharmacokinetic analysis. Both FDG and DOTATATE PET scans will be acquired at baseline and in follow-up. The primary objective is to determine the RECIST 1.1 response rate in treated patients. Secondary objectives includes identifying Progression Free Surival (PFS), Overall Survival (OS), as well as imaging and biochemical correlatives. At the MTD, there will be an expansion cohort so that at least 6 patients per histology will be treated on study.

RESULTS

The study will open for enrollment in Q3 of 2023.

CONCLUSIONS

This phase 1 trial in progress with Pb-212-VMT-α-NET in SSTR+ tumors is a promising new treatment protocol which can improvement management of patients naïve to prior RLT in a variety of histologies.

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