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Phase 1/2 Trial of Pb-212-VMT-alpha-NET in GI Neuroendocrine Tumors and Pheochromocytoma/ Paraganglioma Previously Treated with Radioligand Therapy

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BACKGROUND

Metastatic GI Neuroendocrine Tumors (GI-NET) and pheochromocytoma/paraganglioma (PPGL) are are tumors which overexpresses somatostatin receptors (SSTR) and can be treated with targeted radioligand therapy (RLT) such as Lu-177-DOTATATE. However, despite demonstrated clinical efficacy at stabilizing tumor growth, durable response is very rare and almost all patients inevitably progresses at some time after treatment. Good systemic therapy options after beta-emiting RLT are limited. Alpha emitters such as Pb-212 can be effective treatments in patients who have progressed on beta emitter therapy such as Lu-177-DOTATATE. This phase 1/2 trial will find the maximum tolerated dose of a novel alpha-emiting, SSTR-targeting agent Pb-212-VMT-alpha-NET and evalute its preliminary efficacy is GI-NET and PPGL patients who have previously been treated with RLT.

METHODS

This is an open-label, single arm, single-center, phase 1/2 study evaluating the safety, tolerability, and pharmacokinetic properties of the alpha-emitting, systemic radioligand therapy agent Pb-212-VMT-α-NET in SSTR+ GI-NET and PPGL. The phase 1 dose escalation portion will be standard 3+3 design, and there will be 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 phase 2 primary objective will be to determine the RECIST 1.1 best overall response rate (ORR). Secondary objectives includes identifying Progression Free Surival (PFS), Overall Survival (OS), as well as imaging and biochemical correlatives. The statistical analysis will employ an optimal Simon 2-stage design with the goal of improving the ORR from 13% (historical response rate of Lu-177-DOTATATE) to at least 38%. Total number of patients needed to complete the study is 53 patients.

RESULTS

The study will open for enrollment in Q3 of 2023.

CONCLUSIONS

This phase 1/2 trial in progress with Pb-212-VMT-α-NET in SSTR+ GI-NET and PPGL is a promising new treatment protocol which can improvement management of patients refractory or who have progressed on beta-emitting RLT.

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