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Phase 1/2 study of Lu-177-DOTATATE in combination with olaparib in metastatic or inoperable GI neuroendocrine tumors - first results

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BACKGROUND

GI neuroendocrine tumors express somatostatin (SSTR) receptors, and the radioloabeled SSTR analog Lu-177-DOTATATE is an FDA-approved systemic treatment for those with metastatic disease. Olaparib is a poly (ADP-ribose) polymerase inhibitor (PARPi) which inhibits cells from repairing damaged DNA, especially single-stranded DNA breaks caused by beta particle emissions from the radioactive decay of Lu-177. We report the first results of a phase 1/2 study evaluating the safety and efficacy of Lu-177-DOTATATE in combination with olaparib.

METHODS

This is an open-label, single-arm, single-center phase 1/2 study being conducted at the National Institutes of Health (NCT04086485). Phase 1 is a standard 3+3 design where Lu-177-DOTATATE is being given at the FDA-approved fixed dose of 200 mCi x 4 cycles 8 weeks apart and the olaparib undergoes escalation at the 50mg bid, 100mg bid, 200mg bid, and 300mg bid levels. Olaparib is given daily starting 2 days prior to the administration of each Lu-177-DOTATATE until 28 days post, for a total of 30 days for each Lu-177-DOTATATE administration. Eligibility criteria includes SSTR+ tumors, histologically confirmed diagnosis, and progressive disease by RECIST 1.1 within 36 prior to enrollment. As part of the study, both FDG and DOTATATE PETs are acquired at baseline and at the completion of treatment. The study opened for enrollment in September 2022 and will require 33 patients for full accrual.

RESULTS

One patient with metastatic neuroendocrine tumor of the pancreas has been enrolled and completed treatment on study, at the 50mg bid olaparib dose level. First set of restaging scans at 4 weeks after the second cycle of Lu-177-DOTATATE shows decrease in some tumors up to 17% but overall stable disease by RECIST 1.1, while restaging at end of 4 cycles showed continued decrease in tumor size but still RECIST SD. The combination was well-tolerated with AE profile similar to previous reported. Only grade 1 hematotoxcity was seen. Transient grade 3 hyperglycemia was noted but likely due to dietary non-compliance over the holidays, although causal relationship to treatment cannot be completed ruled out. Baseline WBC, Hgb, and platelets were 6.77k, 15.7, and 608k, respectively, and were 5.99k, 14.7, and 459k, respectively (all values within normal range) at 4 weeks after the second cycle of Lu-177-DOTATATE, and 3.77k, 13.8, and 401k by end of therapy.

CONCLUSIONS

The combination of Lu-177-DOTATATE and olaparib shows early evidence of efficacy and is well-tolerated in this limited data set. More data is needed to confirm and refine these findings.

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