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ETCTN 10558: A Phase II Randomized Control Trial of Triapine Plus Lutetium 177 Dotatate Versus Lutetium 177 Dotatate Alone for Well-Differentiated Somatostatin Receptor-Positive Neuroendocrine Tumors.

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BACKGROUND

Radiolabeled somatostatin analogues provide a means of delivering targeted radiation with a high therapeutic index to NETs that express somatostatin receptors (SSTRs). Radiolabeled somatostatin analogue Lutetium 177 DOTATATE (Lutathera) is a beta-emitting radionuclide, FDA approved for use in SSTR positive gastroenteropancreatic neuroendocrine tumors (GEPNETS) in the US based on the NETTER-1 Phase III trial. Despite favorable PFS and safety profile, the drug has limited cytoreductive capability with a 14% ORR. Peptide receptor radionuclide therapy (PRRT) also doesn't seem to be very effective in treating peritoneal disease. We hypothesize that addition of an effective radiation sensitizer could help improve antitumor activity of Lutathera. Radiation is a potent inducer of DNA double-strand breaks, and ribonucleotide reductase (RNR) is the rate-limiting enzyme in the synthesis and repair of DNA, making RNR-targeted therapy a rationale therapeutic strategy for radiosensitization. ETCTN 10388 (NCT04234568) evaluated safety and efficacy of the combination of lutetium 177 DOTATATE, a beta-emitting radionuclide in combination with triapine, a ribonucleotide reductase (RNR) inhibitor. The combination of triapine and Lu-177 DOTATATE was safe with preliminary efficacy signals.

METHODS

This study is an investigator initiated, NCI sponsored, multicenter randomized phase 2 trial of triapine and lutetium Lu 177 DOTATATE in well-differentiated somatostatin receptor-positive neuroendocrine tumor. A total of 94 patients will be equally randomized to either Lu-177 dotatate or Triapine + Lu-177 dotatate arm. The study will be open through the NCI ETCTN (National Cancer Institute Experimental Therapeutics Clinical Trials Network) program. Triapine will be administered orally from D1-14 with each dose of PRRT [200 mCi]. Primary endpoint is to evaluate overall response rate (ORR). Secondary endpoint is to evaluate median PFS. We are also evaluating triapine PK, plasma deoxyribonucleosides, circulating DNA and plasma hPG80, a novel blood based diagnostic biomarker. NCT05724108

RESULTS

N/A

CONCLUSIONS

N/A

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