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Surgical Debulking Prior to Peptide Receptor Radionuclide Therapy in Patients with Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND

Gastroenteropancreatic Neuroendocrine Tumors (GEPNETs) are among the most prevalent NETs in the US, with metastatic involvement in 50-75% of the cases. Liver failure secondary to metastatic disease is the leading cause of death in patients with GEPNETs. Although to Peptide Receptor Radionuclide Therapy (PRRT) with ^{177}Lu-DOTATATE has become a transformative therapy for patients with GEPNETs, the cytoreductive potential of the treatment is modest. The post-hoc analysis from the NETTER-1 study identified a subset of patients with GEPNETs with one or more tumors >3 cm reduced progression-free survival (PFS). Surgical debulking is an established treatment for patients with metastatic GEPNETs with hepatic involvement with some series showing improved survival. However, complete surgical debulking is not always technically feasible. This pilot study aims to assess the feasibility and clinical impact of surgical debulking of tumors >3 cm prior to PRRT with ^{177}Lu-DOTATATE in patients with GEPNETs. Additionally, we will explore mechanistic impact of surgical debulking in changes in somatostatin receptor 2 (SSTR2) expression based on ^{64}Cu-DOTATATE PET/CT.

METHODS

This is a single institution pilot study to assess the objective response rate of the combination of standard of care treatment in GEPNET by first surgical debulking of tumors >3 cm followed by PRRT with ^{177}Lu-DOTATATE within 90 days of surgery. The study will enroll six patients with metastatic well-differentiated, grade 1-2 GEPNETs with adequate SSTR avidity defined as ≥ liver SSTR uptake confirmed on a ^{64}Cu DOTATATE PET/CT. Only patients with hepatic metastases, and at least one large tumor >3 cm which is accessible for surgical resection, will be enrolled. All patients will be reviewed for study candidacy at a multidisciplinary neuroendocrine tumor board. Following surgery, patients will undergo a ^{64}Cu DOTATATE PET/CT within 12 weeks. All patients will then receive standard treatment with up to 4 cycles of ^{177}Lu-DOTATATE. The primary objective is to measure objective response rate of a combination of surgical debulking followed by PRRT. The secondary objective is to assess the radiomic profile including SSTR standardized uptake values of large (>3 cm) and non-large (<3 cm) tumors.

RESULTS

This study is open and enrolling

CONCLUSIONS

Trial in progress.

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