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Intra-Arterial Peptide Receptor Radionuclide Therapy Using Y-90 DOTATOC for Hepatic Metastases of Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND: Intravenous Lu-177 DOTATATE (a form of peptide receptor radionuclide therapy, PRRT) delays progression in metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Up to 75% of GEP-NET patients have liver metastases. We aimed to determine whether direct intra-arterial (IA) injection of 90Y-based PRRT into the liver would achieve higher intratumoral concentrations of PRRT, thus maintaining efficacy while reducing systemic toxicity.

METHODS: PRRT-naïve GEP-NET patients with liver-predominant metastases involving <70% of the liver were enrolled in this pilot, single-center, open-label study. Patients underwent baseline PET/CT imaging using intravenous 68Ga-DOTATOC. On a subsequent date, 94.7 ± 5.4 mCi 90Y-DOTATOC was administered into the proper hepatic artery over 30 minutes. The first five patients concurrently received IA 68Ga DOTATOC and underwent PET imaging within 1 hour. All patients were followed for response (RECIST1.1) and toxicity (CTCAE v4.0) (median 44 weeks, range 24 to 52).

RESULTS: Of 10 enrolled patients, 30% (3/10) pts experienced grade 3 adverse events (AEs) (2/10 bilirubin, 1/10 anemia). During the follow-up period, best response was SD in 70% (7/10) and PD in 30% (n=3/10). No PR or CR was observed. Patients who received IA 68Ga DOTATOC failed to demonstrate increased uptake by hepatic metastases compared to IV, with average IA:IV

SUVmax ratio 0.86 +/- 0.24. However, extrahepatic metastases and background demonstrated expected decreased uptake between IA and IV (ratio 0.68 +/- 0.19).

CONCLUSION: Our study demonstrated that administration of PRRT via the proper hepatic artery is generally safe and well tolerated. However, a single treatment resulted in minimal disease response. In addition, in contrast to previous reports, there was no increased uptake of 68Ga DOTATOC in hepatic metastases when delivered IA compared to IV. One possible reason is somatostatin receptor saturation, as the imaged 68Ga-DOTATOC was administered alongside a much larger dose of 90Y-DOTATOC than diagnostic doses of somatostatin receptor agonists used in prior studies.