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Tumor and Normal Tissue Uptake of ^{68}Ga-DOTA-tyr^3-Octreotide after Treatment with Unlabeled Octreotide in Patients with Carcinoid Tumors and Pancreatic Neuroendocrine Tumors

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Rationale: Octreotide therapy is routinely discontinued prior to imaging or therapy with radiolabeled somatostatin analogues. Lower doses of octreotide (50 mcg) however may increase the tumor uptake of ^{68}Ga-DOTA-tyr^3-Octreotide (^{68}Ga-DOTATOC) and/or decrease the uptake in normal tissues, improving the visualization of tumors (Velikyan et al. Nucl Med Biol 2010: 37: 265-275). The primary objective of this study is to identify the dose of pretreatment subcutaneous Octreotide that will provide the optimal ratio of tumor to normal tissue (kidney) uptake of Ga-68 DOTATOC. If octreotide administration improves the tumor to kidney uptake ratio, this paradigm will be tested in a therapeutic trial using Y-90 DOTATOC.

Aims: 1. To determine the optimal dose of subcutaneous octreotide that will increase the ratio of tumor to normal tissue uptake of Ga-68 DOTATOC in patients with carcinoid and pancreatic neuroendocrine tumors (NETs). 2. To analyze the effects of octreotide on the pharmacokinetics of Ga-68 DOTATOC uptake in the tumor. 3. Determine the effect of octreotide on the renal uptake of Ga-68 DOTATOC.

Methods: Subjects with histological diagnosis of carcinoid or pancreatic neuroendocrine tumor, with at least one lesion (primary or metastatic) identified on CT, MRI or OctreoScan, will undergo two Ga-68 DOTATOC PET scans, one at baseline and one after the administration of subcutaneous octreotide. The dose of subcutaneous octreotide will be started at 25 micrograms in Cohort 1, escalating to 50, 100, 150 and 200 micrograms, 3 subjects per cohort. If 1/3 subjects in any cohort demonstrate reduction of ratio of tumor to normal kidney uptake (T/K) of Ga-68 DOTATOC compared to baseline, 3 additional subjects will be entered in the

cohort. If 2/6 subjects in the cohort show reduction of T/K, no further subjects will be enrolled in that dose cohort and the dose in the previous cohort will be considered as the optimal dose of octreotide.

Ga-68 DOTATOC dynamic PET images will be obtained for 60 min followed by whole body PET-CT images. Dynamic images will be analyzed using a 2-compartment tissue model to evaluate the changes in the pharmacokinetics, i.e. receptor binding and cellular internalization of Ga-68 DOTATOC accumulation in the tumor after octreotide. Standardized uptake values (SUV) of tumor lesions and kidneys and other normal organs will be measured on whole body images and compared between the baseline scan and the post octreotide scan.