TPS4226 Poster Session

NCI 10479: A phase I dose escalation-expansion trial of sunitinib malate plus lutetium (Lu-177) dotatate in somatostatin receptor positive pancreatic neuroendocrine tumors.

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Background: Patients with metastatic or unresectable pancreatic neuroendocrine tumors (PanNETs) have a poor prognosis, even with currently available treatments, with a 5-year overall survival (OS) of less than 20%. Lutetium Dotatate (Lu-177) is a radiopharmaceutical that consists of the somatostatin analogue DOTA-Tyr3-Octreotate, coupled to the metal-ion chelating moiety, DOTA, and radiolabeled with lutetium-177. Lu-177 was approved by the FDA in 2018 for treatment of somatostatin receptor (SSTR)-positive gastroenterohepatic NETs, but it is limited in its efficacy to achieve cytoreduction and provide durable responses. Sunitinib malate is an oral small-molecule tyrosine kinase inhibitor targeting VEGFRs, PDGFRs, and KIT and is also FDA approved as a monotherapy for the treatment of metastatic unresectable PanNETs. There is preclinical, as well as clinical evidence of sunitinib being used as a radiosensitizer with classic radiation, but it has never been combined with a radiolabeled analogue in patients with PanNETs. **Methods:** This is a Phase I dose escalation/expansion study aiming to enroll up to 24 patients across several sites. Eligible patients will be offered fixed dose Lu-177 at 200 mCi for 4 fractions with concurrent oral sunitinib administration initiating on C1D1 and concluding 28 days after the last Lu-177 infusion. Dose escalation applies to sunitinib and will be guided by a 3+3 design to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D). Once the RP2D has been established, up to 12 more patients will be offered participation in the expansion phase in an attempt to further record antitumor activity and correlation with imaging, tumor markers, as well as Lu-177 dosimetry. Treatment will continue until disease recurrence/progression, unacceptable toxicity, or completion of planned protocol. Key eligibility criteria include age $>=$ 18 years, ECOG performance status $<=$ 2, histologic diagnosis of metastatic, unresectable well- or moderately-differentiated SSTR-positive PanNETs of any grade, up to 1 prior treatment except for somatostatin analogues and appropriate baseline hematological parameters. Key exclusion criteria are prior use of sunitinib, Lu-177 or other radiopharmaceuticals, myocardial or cerebrovascular accident within the prior 12 months and left ventricular ejection fraction of $<=$ 50%. The study uses an 8-week safety window to determine its primary endpoint, which is DLTs during administration of the combination. Secondary endpoints are objective response (ORR), duration of response (DOR), progression-free survival (PFS) and overall survival (OS), intensity of tumor uptake on pre-treatment SSTR PET and post Lu-177, chromogranin A level response as well as optional dosimetry imaging. Enrollment is ongoing. Clinical trial information: NCT05687123. Research Sponsor: National Cancer Institute.