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Randomized, parallel arm, Phase II Study of Telotristat in combination with Lutetium Lu 177 Dotatate (Lutathera) in Well-Differentiated Neuroendocrine Tumors (NETs)

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BACKGROUND: Telotristat ethyl (TE) inhibits tryptophan hydroxylase, the rate-limiting enzyme in serotonin biosynthesis. TE is indicated for carcinoid syndrome diarrhea and results in a reduction of urinary 5-HIAA. Preclinical data in cell lines of typical (NCI-H727), atypical (NCI-H720) bronchopulmonary NET, small intestinal NET (KRJ-I), and human pancreatic carcinoid cell line (BON) has demonstrated a serotonin proliferative effect on tumor cell growth. This growth stimulation occurs in an autocrine manner. These observations of TE's anti-neoplastic activity extend to other solid tumors including cholangiocarcinoma (NCT03790111). We hypothesize that inhibition of serotonin production will complement the anti-tumor activity of Lu-177 dotatate.

METHODS: This is an investigator initiated, single center, open label, randomized, parallel arm, phase II study evaluating two dose levels of TE (250 mg PO TID and 500 mg PO TID) in combination with Lu-177 dotatate in well-differentiated neuroendocrine tumors. The primary endpoint is 20-month PFS for each arm and assesing non-inferiority compared to historical control (NETTER-1). Secondary endpoint includes ORR by RECIST v1.1 at 6, and 12-months. To establish additional efficacy and safety profiles of the combination of TE and Lu-177 dotatate, median progression-free survival (mPFS) and quality of life as measured by the QLQ-C30 and QLQ-GI.NET21 will be measured.

RESULTS: Protocol is expected to open for accrual in Sept 2020

CONCLUSION: Trials in progress.

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