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NET RETREAT: a Phase II Study of 177Lutetium-Dotatate Retreatment vs. Everolimus in Metastatic/Unresectable Midgut NET

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BACKGROUND

177Lu-DOTATATE is an FDA and Health Canada-approved treatment option for metastatic, progressive GEPNET patients. 177Lu-DOTATATE is now often considered the treatment of choice for small bowel/midgut patients who have progressed on somatostatin analogs (SSA). Despite 177Lu- DOTATATE's impressive disease stabilization, many patients will eventually progress. Progression after prior use of PRRT does not necessarily render these tumors resistant to future PRRT treatments. PRRT retreatment strategies have been tested in various European centers where PRRT has been available for the past two decades. Several studies report single institute, non-randomized, retrospective data on PRRT retreatment with varying degrees of efficacy and relatively safe toxicity profiles. Despite a growing body of evidence favoring limited dose PRRT retreatment, prospective randomized data is lacking in support of a PRRT retreatment strategy. Prior studies also suffer from a heterogenous patient population and inconsistent PRRT regimens. Many times, Y-90-based PRRT treatment is incorporated either during the initial treatment or PRRT retreatment. Y-90 based PRRT is known to have a preponderance of nephrotoxicity. Currently, Y-90 based PRRT is not available commercially in the US. Hence, NET-RETREAT fulfills an unmet medical need by exclusively studying limited dose retreatment of 177Lu-DOTATATE PRRT in midgut NET patients who have previously benefitted from PRRT.

RATIONALE

This multi-center prospective randomized study will evaluate the efficacy of the PRRT retreatment strategy and will also confirm the safety profile of a limited dose PRRT re-challenge. PRRT retreatment strategy builds on the fact that SSTR receptor expression remains intact in most patients post-initial PRRT progression.

METHODS

This CCTG-SWOG, international multi-center, open-label, randomized phase II trial will evaluate the efficacy and safety of limited dose 177Lu-DOTATATE as compared to everolimus in metastatic/unresectable well-differentiated midgut neuroendocrine tumor patients who have previously experienced durable response (12 months of stable disease per RECIST 1.1) to 177Lu- DOTATATE.

One hundred (100) midgut unresectable/metastatic NET patients will be randomized 2:1 in favor of the experimental arm. The primary objective is to evaluate progression-free survival (PFS) while secondary and correlative objectives include assessment for safety, objective responses, quality of life metrics, and evaluation of novel blood-based predictive and diagnostic markers (NETEST, PPQ, and hPG80)

ClinicalTrials.gov Identifier: NCT 05773274

RESULTS

NA

CONCLUSIONS

NA

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