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Netter-1: First Pivotal Multicenter Phase III Study Evaluating ^{177}Lu-dotatate in Midgut Neuroendocrine Tumors

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Background: The unmet medical need for an effective treatment of inoperable, advanced neuroendocrine tumors (NETs) is well known. There are limited therapeutic options for patients with midgut NETs (30-45% of NETs): somatostatin analogues are approved for symptomatic treatment. Other treatments are either investigational or off-label.

Since 2000, thousands of patients have been treated with tumor-targeted peptide receptor radionuclide therapy (PRRT) with ^{177}Lu-DOTA0-Tyr3-Octreotate (^{177}Lu-DOTATATE) showing promising results in terms of tumor response, safety and quality of life improvement. NETTER-1 is the first Phase III multicentric, stratified, open, randomized, controlled, parallel-group study, comparing 177Lu-DOTATATE with Octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive midgut carcinoid tumors.

Methods: The protocol consists of treatment with a cumulative dose of 29.6 GBq of 177Lu-DOTATATE (4x7.4 GBq every 8 weeks) plus supportive care with 30 mg Octreotide LAR compared to 60 mg Octreotide LAR every 4-weeks.

The primary endpoint is Progression Free Survival (PFS) as per RECIST 1.1 criteria. Objective tumor assessment is performed every 12 weeks until progression is documented using an independent image reading center.Main secondary objectives are determination of Objective Response Rate (ORR), Overall Survival (OS), Time To Progression (TTP), safety, tolerability and health-related quality of life. Dosimetry, pharmacokinetics and ECG evaluations are also performed in a subset of patients.

Results: Enrollment began in July 2012 with a target of 230 patients. PFS primary analysis point occurs at 74 evaluable and centrally confirmed disease progression or death events. The OS period includes 18-months accrual plus a 5-year follow-up.
36 European and 15 American sites are involved. An independent Data Safety Monitoring Board is supervising the conduct of the study and regularly assesses the safety outcome.

Conclusions: NETTER-1 shall provide important efficacy and safety information on PRRT with ^{177}Lu-DOTATATE in patients with advanced midgut neuroendocrine tumors.