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## NETTER-1 Phase III: Progression-Free Survival, Radiographic Response, and Preliminary Overall Survival Results in Patients with Midgut Neuroendocrine Tumors Treated with 177-Lu-Dotatate

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**Background:** Currently, there are limited therapeutic options for patients with advanced midgut neuroendocrine tumors progressing on first-line somatostatin analog therapy.

**Methods:** NETTER-1 is the first Phase III multicentric, randomized, controlled trial evaluating $^{177}$Lu-DOTA$^{0}$-Tyr$^{3}$-Octreotate (Lutathera®) in patients with inoperable, progressive, somatostatin receptor positive midgut NETs. 230 patients with Grade 1-2 metastatic midgut NETs were randomized to receive Lutathera 7.4 GBq every 8 weeks (x4 administrations) versus Octreotide LAR 60 mg every 4-weeks. The primary endpoint was PFS per RECIST 1.1 criteria, with objective tumor assessment performed by an independent reading center every 12 weeks. Secondary objectives included objective response rate, overall survival, toxicity, and health-related quality of life.

**Results:** Enrolment was completed in February 2015, with a target of 230 patients randomized (1:1) in 35 European and 15 sites in the United States. At the time of statistical analysis, the number of centrally confirmed disease progressions or deaths was 23 in the Lutathera group and 67 in the Octreotide LAR 60 mg group. The median PFS was not reached for Lutathera and was 8.4 months with 60 mg Octreotide LAR [95% CI: 5.8-11.0 months], $p<0.0001$, with a hazard ratio of 0.21 [95% CI: 0.13-0.34]. Within the current evaluable patient dataset for tumor responses (n=201), the number of CR+PR was 19 (18.8%) in the Lutathera group and 3 (3.0%) in the Octreotide LAR 60 mg group ($p<0.0004$). Although the OS data are not mature enough for a definitive analysis, the number of deaths was 13 in the Lutathera group and 22 in the Octreotide LAR 60 mg group ($p<0.019$ at interim analysis) which suggests an improvement in overall survival.

**Conclusions:** The Phase III NETTER-1 trial provides evidence for a clinically meaningful and statistically significant increase in PFS and ORR, and also suggests a survival benefit in patients with advanced midgut NETs treated with Lutathera.