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The Phase 3 NETTER-1 Study of ^{177}Lu -DOTATATE in Patients with Midgut Neuroendocrine Tumors: Updated Progression-free Survival Analyses

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BACKGROUND: In NETTER-1, primary analysis of centrally-assessed progression-free survival (PFS; primary endpoint: HR, 0.18 [95% CI, 0.11, 0.29]; $p < 0.0001$, data cut-off [DCO] 24-July-2015), median PFS (mPFS) was not reached in the ^{177}Lu -DOTATATE arm.

METHODS: 231 patients were randomized to four cycles of ^{177}Lu -DOTATATE 7.4 GBq (200 mCi) Q8W plus long-acting octreotide 30 mg or long-acting octreotide 60 mg Q4W. After required PFS events for primary analysis, central assessment continued until disease progression (PD) or 18 months after randomization. Exploratory analyses of updated PFS (post hoc) and time from randomization to second investigator-assessed progression or death (PFS2; pre-specified) were performed.

RESULTS: At 31-August-2017 DCO, updated, centrally-assessed mPFS was 28.4 months (95% CI: 28.4, NE) and 8.5 months (95% CI: 5.8, 11.0) in the ^{177}Lu -

DOTATATE and control arms (HR, 0.21 [95% CI: 0.14, 0.33]); investigator-assessed mPFS was 26.0 months (95% CI: 19.4, 31.0) versus 8.5 months (95% CI: 6.0, 11.2; HR, 0.31 [95% CI: 0.21, 0.45]). At final analysis (18-January-2021 DCO), there were 54/117 (46.2%; PD: 41/117) and 73/114 (64.0%; PD: 63/114) investigator-assessed PFS events in ¹⁷⁷Lu-DOTATATE and control arms; mPFS was 25.0 months (95% CI: 17.8, 28.4) and 8.5 months (95% CI: 6.0, 11.2; HR, 0.30 [95% CI: 0.21, 0.44]). Similar numbers in each arm received everolimus and more patients in the control arm received PRRT as first subsequent treatment (Table). Median PFS2 was 45.0 months (95% CI: 39.6, 50.4) and 23.2 months (95% CI: 18.5, 28.4) in the ¹⁷⁷Lu-DOTATATE and control arms (HR, 0.42 [95% CI: 0.29, 0.60]).

CONCLUSION: Updated PFS results by central and investigator assessment were consistent and clinically remarkable. The benefit with ¹⁷⁷Lu-DOTATATE was sustained into the subsequent line of therapy. First subsequent systemic anti-cancer treatment during long-term follow-up.

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