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Objective

This randomized, controlled trial evaluated the efficacy and safety of lutetium-177 (¹⁷⁷Lu)-Dotatate in patients with advanced, progressive, somatostatin-receptor-positive midgut neuroendocrine tumours.

Background

Patients with advanced midgut neuroendocrine tumours who have had disease progression during first-line somatostatin analogue therapy have limited therapeutic options.

Methods

We randomly assigned 229 patients who had well-differentiated, metastatic midgut neuroendocrine tumours to receive either ¹⁷⁷Lu-Dotatate (116 patients) at a dose of 7.4 GBq every 8 weeks (four intravenous infusions, plus best supportive care including octreotide long-acting repeatable [LAR] administered intramuscularly at a dose of 30 mg) (¹⁷⁷Lu-Dotatate group) or octreotide LAR alone (113 patients) administered intramuscularly at a dose of 60 mg every 4 weeks (control group). The primary end point was progression-free survival. Secondary end points included the objective response rate, overall survival, safety, and the side-effect profile. The final analysis of overall survival will be conducted in the future as specified in the protocol; a prespecified interim analysis of overall survival was conducted and is reported here.

Results

At the data-cutoff date for the primary analysis, the estimated rate of progression-free survival at month 20 was 65.2% (95% confidence interval [CI], 50.0 to 76.8) in the ¹⁷⁷Lu-Dotatate group and 10.8% (95% CI, 3.5 to 23.0) in the control group. The response rate was 18% in the ¹⁷⁷Lu-Dotatate group versus 3% in the control group (P<0.001). In the planned interim analysis of overall survival, 14 deaths occurred in the ¹⁷⁷Lu-Dotatate group and 26 in the control group (P=0.004). Grade 3 or 4 neutropenia, thrombocytopenia, and lymphopenia occurred in 1%, 2%, and 9%, respectively, of patients in the ¹⁷⁷Lu-Dotatate group as compared with no patients in the control group, with no evidence of renal toxic effects during the observed time frame.

Conclusions

Treatment with ¹⁷⁷Lu-Dotatate resulted in markedly longer progression-free survival and a significantly higher response rate than high-dose octreotide LAR among patients with advanced midgut neuroendocrine tumours. Preliminary evidence of an overall survival benefit was seen in an interim analysis; confirmation will be required in the planned final analysis. Clinically significant myelosuppression occurred in less than 10% of patients in the ¹⁷⁷Lu-Dotatate group. (Funded by Advanced Accelerator Applications; NETTER-1 ClinicalTrials.gov number,

