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Phase 3 LEVEL trial of 177Lu-edotreotide versus everolimus in patients with advanced neuroendocrine tumors of lung or thymic origin (GETNE-T2217)

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BACKGROUND

Everolimus is the only approved drug for patients with advanced bronchopulmonary neuroendocrine tumors (NET), and there is an urgent unmet need for alternative treatments. Retrospective data for peptide receptor radionuclide therapy (PRRT) have demonstrated promising activity in somatostatin receptor (SST)-positive lung NET. This study aims to investigate the clinical efficacy, safety, and patient-reported outcomes when ^{177}Lu-edotreotide is used to treat advanced lung and thymic NET, as compared to everolimus.

METHODS

The LEVEL trial is a randomized, open-label, phase 3 international trial of ^{177}Lu-edotreotide versus everolimus in patients with confirmed advanced, well/moderately differentiated NET of lung or thymic origin. Participants (target sample N=120) must have WHO grade 1 or 2 disease (typical/atypical), SST-positive lesions and radiological evidence of disease progression in the last 12 months according to RECIST v1.1. They can be systemic treatment naïve or have experienced progression on somatostatin analogues and/or ≤2 additional systemic treatments (e.g., chemotherapy, targeted agents, immunotherapy). Prior PRRT or mammalian target of rapamycin (mTOR) inhibitor treatment is not permitted. Eligible participants will be randomly assigned 3:2 to 6 cycles of ^{177}Lu-edotreotide (total dose 7.5±0.7 GBq) or to oral everolimus 10 mg once daily until progressive disease (PD) or intolerable toxicity. CT or MRI scans will be performed every 12 weeks until PD. Blood samples will be analyzed at baseline, at the time of administration of the first dose of study drug, and at PD for pharmacodynamics and to identify potential predictive biomarkers of treatment response. Archival tumor tissue samples will be analyzed for ancillary studies. The primary endpoint is progression-free survival (PFS) according to RECIST v1.1. The sample size provides at least 80% power to demonstrate statistical significance of treatment differences on PFS based on the protocol assumption. The study uses an event-driven analysis, where the analysis will be performed once the prespecified number of events is reached. Secondary outcome measures include overall response rate, overall survival, safety (adverse events [AEs] and treatment-related AEs], and quality of life (assessed using the EORTC QLQ-C30).

RESULTS

The LEVEL trial has received institutional review board/ethics committee approval, and site start-up is ongoing.

CONCLUSIONS

The results of this trial are anticipated to provide evidence regarding the efficacy, safety and effect on quality of life of ^{177}Lu-edotreotide in patients with advanced lung and thymic NET. The study is designed to demonstrate superiority of ^{177}Lu-edotreotide compared to everolimus and may emerge as a new treatment option for this underserved patient population.

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