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Genetic profiling in the randomized controlled phase 3 COMPOSE trial of 177Lu-edotreotide for well-differentiated aggressive grade 2/3 gastroenteropancreatic neuroendocrine tumors

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BACKGROUND

Targeted radionuclide therapies (TRTs) have changed the treatment paradigm of neuroendocrine tumors (NET) and are expected to be widely available for patients with various gastroenteropancreatic (GEP)-NET phenotypes. However, while they have great potential, TRT-based therapeutic strategies for high-grade GEP-NET demonstrate variable outcomes, and there is a current lack of tools to identify patients who are likely to respond to TRT. To address this need, the randomized, controlled, open-label, phase 3 COMPOSE trial of ^{177}Lu-edotreotide TRT versus best standard of care (CAPTEM, FOLFOX, or everolimus; chosen by the investigator) in patients with well-differentiated, aggressive, G2/G3 (Ki-67 index 15–55%), somatostatin receptor-positive GEP-NET will include a genetic profiling analysis. By applying an integrative, systemic multiomics approach, we aim to identify predictive and prognostic genetic markers to improve understanding of tumor progression and TRT responses and to guide individualized treatment of NET.

METHODS

Participation in the genetic profiling analysis will be optional for COMPOSE trial participants and will not affect disease management or trial procedures. The genetic signatures of GEP-NET at the time of diagnosis will be analyzed by whole exome sequencing to understand predisposition and mutational drivers of oncogenesis. In addition, tumor biopsies and blood samples (the latter collected before treatment, during treatment, and at disease progression) will be analyzed to identify relevant genomic and gene expression signatures, with a focus on suppressive/activating genetic traits.

RESULTS

We plan to create a bioinformatic pipeline for predicting TRT efficacy and disease progression. The pipeline will integrate genomic and gene expression signatures with structural and functional imaging data, histopathology, and patients' clinical characteristics.

CONCLUSIONS

Data from this study are expected to contribute to individualized management of GEP-NET by making it easier to predict which treatment(s) individual patients are likely to respond to.

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