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Investigator-Assessed Disease Progression in a Phase 2 Study of Paltusotine in Patients with Neuroendocrine Tumors and Carcinoid Syndrome

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BACKGROUND

Paltusotine is an oral, nonpeptide, selective SST2 receptor agonist. In a phase 2 study, treatment with once-daily paltusotine reduced the frequency and severity of carcinoid syndrome (CS) symptoms and was well tolerated. The anti-tumor effects of paltusotine were further explored.

METHODS

This study included an 8-week randomized treatment phase and a 102-week open-label extension phase (OLE; currently ongoing). Enrolled patients were adults with a stable documented grade 1 or 2 NET and CS. These patients were actively symptomatic and either untreated with somatostatin receptor ligand (SRL) therapy (average of ≥4 bowel movements [BMs] per day or >2 flushing episodes per day in ≥2 days over 2-week period) or washed out of SRL therapy (symptoms previously controlled on SRL), with demonstrated symptom worsening after washout. Patients had stable disease in the 6 months prior to study entry. Patients were randomized to once-daily paltusotine 40 mg or 80 mg; one optional uptitration of 40 mg (to 80 mg or 120 mg) was permitted. Patients who completed the randomized treatment phase were eligible to enter the OLE. Radiographic tumor assessments (CT or MRI) were conducted pretrial, at week 10, week 36, week 70, week 110, and at end of treatment. At each assessment, investigators reported (yes/no) whether imaging represented disease progression, and "investigator-assessed progression-free survival (PFS)" was based on the overall impression of imaging results. This preliminary analysis (data cutoff: May 21, 2025) assessed tumor progression per investigator's assessment; the Kaplan-Meier method was used to calculate the PFS.

RESULTS

The patient in this case demonstrated a deep partial response with minimal side effects attributable to D/T. The patient experienced progression of disease after 17 months of treatment and proceeded to next-line therapy. The patient remains alive at the time of this report, over 21 months from the date of diagnosis. Available cohorts suggest a prevalence of BRAF V600E mutations in GEP-NENs to be between 5-15%. Other reported targetable alterations in GEP-NENs include *KRAS, ALK, BRCA1/2, ATM, NTRK, FGFR*, and *RET*.

CONCLUSIONS

The observed PFS rate (74%) after 1 year of treatment with paltusotine, in this preliminary analysis of a phase 2 study, is encouraging data and warrants further investigation in the ongoing CAREFNDR Phase 3 study.

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