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CAREFNDR: Phase 3, Randomized, Placebo-Controlled Study of Paltusotine in Adults With Carcinoid Syndrome Due to Well-Differentiated Neuroendocrine Tumors

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BACKGROUND

Paltusotine is a once-daily, oral, nonpeptide, selective SST2 receptor agonist in development for the treatment of acromegaly and carcinoid syndrome (CS). In a phase 2, open-label, dose-ranging study, paltusotine reduced the frequency and severity of CS symptoms and was well tolerated (NCT05361668).

METHODS

CAREFNDR is a phase 3, multicenter, randomized, parallel-group, placebo-controlled trial to evaluate the symptom control and safety of paltusotine in patients with CS due to well-differentiated neuroendocrine tumors (NETs). The study will enroll patients with documented, grade 1-2 NETs with CS who exhibit symptoms of flushing with or without frequent bowel movements (BMs). Patients naïve to somatostatin receptor ligands (SRLs) or untreated for ≥4 months must have >1 flushing episode/day (14-day average) and plasma 5HIAA or serotonin ≥2× ULN. Patients who had symptom control on SRLs (average ≤2 flushing episodes/day and ≤3 BMs/day in first 2-week injection cycle) must demonstrate symptom worsening after SRL washout (increase in average flushing episodes/day and >1 flushing episode/day [14-day average]). More than 50% of enrolled patients must meet eligibility criteria for flushing and >3 BMs/day. Patients with significant disease progression within the previous 6 months will be excluded. Approximately 141 patients will be randomized 2:1 to receive paltusotine 80 mg or placebo. The 16-week randomized controlled period will be followed by an open-label extension (OLE) of paltusotine treatment for up to 104 weeks. Antidiarrheal medications and short-acting octreotide are permitted, based on protocol-standardized criteria. A CS Symptom Diary of 7 of the most impactful CS symptoms will be completed daily during screening and the randomized controlled period, and periodically throughout the OLE. The primary endpoint will be the change from baseline to Week 12 in the number of flushing episodes/day (14-day average) for paltusotine versus placebo. The key secondary endpoint will be change from baseline in the number of BMs/day. Other secondary

endpoints will include flushing severity, BM urgency episodes, and percentage of days with short-acting octreotide use. Safety and tolerability assessments will include the incidence of treatment-emergent adverse events and changes in safety parameters.
The antitumor effect of paltusotine will also be explored. Global enrollment in CAREFNDR is ongoing.

RESULTS

N/A

CONCLUSIONS

N/A

ABSTRACT ID 33408