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Once-daily Oral Paltusotine in the Treatment of Patients With Carcinoid Syndrome: Results From a Phase 2, Randomized, Parallel-Group Study

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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).

METHODS

This open-label, multicenter, dose-ranging study examined the safety, tolerability, pharmacokinetics, and exploratory efficacy of paltusotine in patients with CS. Eligible patients had documented, well-differentiated, grade I or II NETs (eg, GEP-NETs, bronchial NETs) with CS. Patients who were somatostatin receptor ligand (SRL) treatment naïve or currently untreated and actively symptomatic (average of ≥4 bowel movement [BMs] per day or >2 flushing episodes per day in ≥2 days over 2-week period) and patients with symptom control on SRLs who demonstrated symptom worsening after SRL washout were randomly assigned to receive once-daily oral paltusotine 40 mg or 80 mg for 8 weeks. Exploratory efficacy was assessed using a daily symptom diary. Meaningful within-patient change (MPWC) thresholds were derived using FDA-recommended methods: for daily BM frequency -0.90 to -1.10 (single threshold: -0.90) and for daily flushing frequency -1.70 to -1.85 (single threshold: -1.80).

RESULTS

Thirty-six patients (n=9 treatment naïve or currently untreated; n=27 SRL washout) were enrolled. Entry criteria were met by 22 patients for flushing and 25 patients for BM. Among Week 8 completers (n=30), mean reduction from baseline in daily BM frequency was -1.1, and in daily flushing frequency it was -1.7. In patients with >3 BMs per day at baseline, mean excess daily BM frequency decreased from 2.0 to 0.8 (-60%). In patients with >1 flushing episode per day at baseline, mean daily flushing frequency decreased from 3.2 to 1.2 (-63%). Mean daily frequency of urgent BM episodes decreased from 1.1 to 0.4 (-64%); mean abdominal pain severity (worst pain score, scale from 0-10) decreased from 2.5 to 1.2 (-52%); and mean flushing severity (worst flushing score, scale from 0-10) decreased from 3.7 to 1.5 (-59%). During treatment, paltusotine dose was increased (per protocol) in 9 patients. Among patients meeting entry criteria for the corresponding symptom, 40% (10/25) met the daily BM frequency MWPC threshold of -0.90 and 59% (13/22) the daily flushing frequency MWPC threshold of -1.80. No severe or

serious adverse events (AEs) were considered treatment related. Two patients discontinued the study due to AEs (encephalopathy and bowel obstruction; not drug related). No new safety signals were identified.

CONCLUSIONS

In this phase 2 study, treatment with once-daily, oral paltusotine reduced the frequency and severity of CS symptoms and was well tolerated, justifying further clinical development.

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