Longer-Term Paltusotine Treatment in Patients With Carcinoid Syndrome: Safety and Exploratory Efficacy Results From a 2-Year Open-Label Extension Study

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BACKGROUND

- Paltusotine (PALSONIFY®) is an oral, once-daily, nonpeptide, selective somatostatin 2 receptor agonist approved in the United States and Europe for the medical treatment of adults with acromegaly[1,2]
- Paltusotine is currently being investigated for the treatment of carcinoid syndrome (CS), a common paraneoplastic syndrome in patients with neuroendocrine tumors (NETs). The safety and efficacy for use in this new indication have not been fully evaluated by regulatory authorities

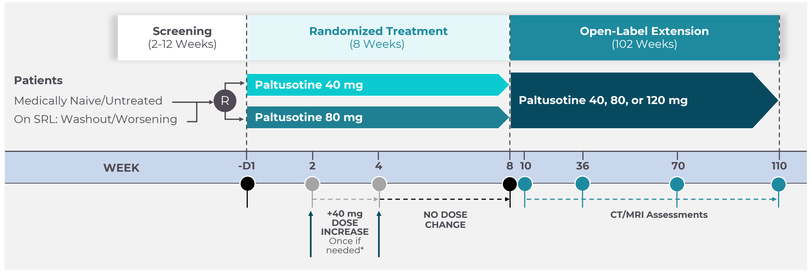
OBJECTIVE

- To evaluate the longer-term safety and exploratory efficacy of paltusotine in the treatment of patients with CS

METHODS

- This phase 2, multicenter study (NCT05361668) included an 8-week randomized treatment phase (RTP) and a 102-week open-label extension (OLE)
- The study enrolled adults with a locally advanced or metastatic, well-differentiated, grade 1 or 2 NET (stable disease in the 6 months prior to study entry) and actively symptomatic CS, either
  - Untreated with somatostatin receptor ligand (SRL) therapy (average of ≥4 bowel movements/day or >2 flushing episodes/day on ≥2 days over a 2-week period) *or*
  - Washed out of SRL (symptoms and tumor previously controlled on SRL) with demonstrated CS symptom worsening after washout
- Exploratory efficacy was assessed using a daily diary
- Utilizing radiographic tumor assessments, 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 analysis evaluated the effects of paltusotine treatment through the end of the 2-year OLE

Study Design



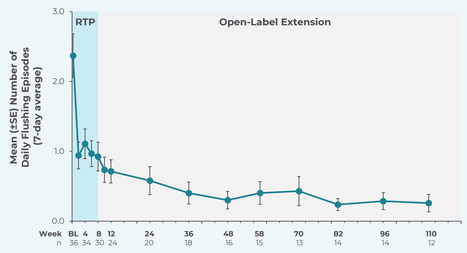
*Criteria for uptitration were CS symptoms that required treatment with short-acting injected octreotide at least once within the previous 7 days.
CS = carcinoid syndrome; CT = computed tomography; D = day; MRI = magnetic resonance imaging; R = randomization; SRL = somatostatin receptor ligand.

RESULTS

Patient Characteristics

- Thirty-six patients (n=9 untreated; n=27 SRL washout) were enrolled
  - Mean age was 60.8 years (range, 35-83 years), 52.8% were female, and 47.2% had a grade 2 NET
  - Of 30 RTP completers, 26 continued into the OLE
- The final paltusotine dose (at the last available assessment: end of RTP, end of OLE, or early discontinuation) was 40 mg/day in 11 patients, 80 mg/day in 18 patients, and 120 mg/day in 7 patients

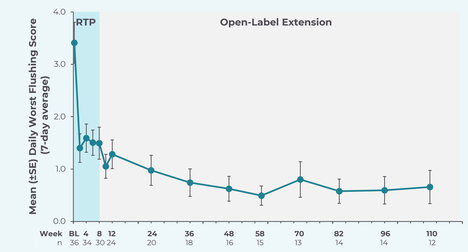
Daily Flushing Frequency



RTP = randomized treatment phase.

- The mean number of flushing episodes per day decreased from 2.4 at baseline to 0.9 at week 8 (end of RTP), 0.4 at week 58, and 0.3 at week 110 (end of OLE)

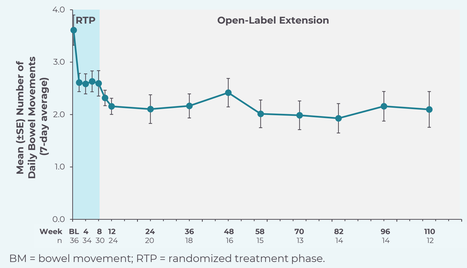
Flushing Severity



Flushing severity was rated using a numeric rating scale of 0 to 10.
RTP = randomized treatment phase.

- The mean daily worst flushing severity score (numeric rating scale from 0-10) decreased from 3.4 at baseline to 1.5 at week 8 (end of RTP), 0.5 at week 58, and 0.7 at week 110 (end of OLE)

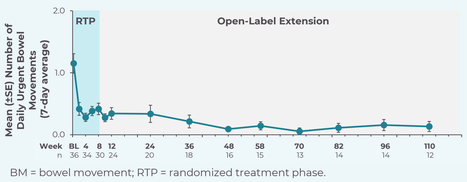
Daily Bowel Movement Frequency



BM = bowel movement; RTP = randomized treatment phase.

- The mean number of bowel movements per day decreased from 3.6 at baseline to 2.6 at week 8 (end of RTP), 2.0 at week 58, and 2.1 at week 110 (end of OLE)

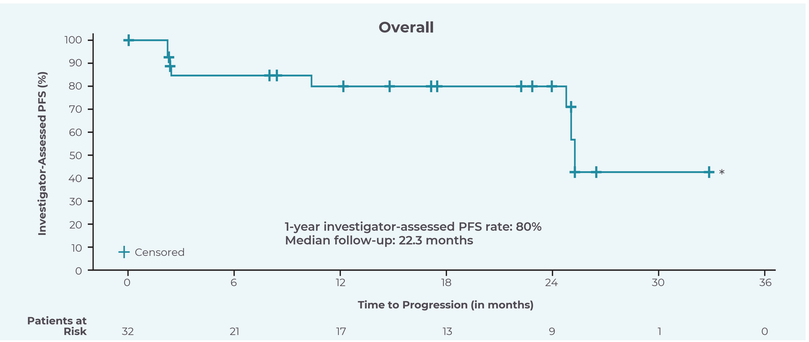
Daily Urgent Bowel Movement Frequency



BM = bowel movement; RTP = randomized treatment phase.

- The mean number of urgent bowel movements per day decreased from 1.2 at baseline to 0.4 at week 8 (end of RTP), 0.1 at week 58, and 0.1 at week 110 (end of OLE)

Investigator-Assessed Progression-Free Survival



This analysis included 32 patients (naive/untreated, n=8; SRL washout, n=24); 4 patients were excluded due to not having a post-baseline CT/MRI scan and electing not to enroll in the OLE. The Kaplan-Meier method was used to calculate PFS, which was defined as the time from baseline to the date when the investigator reported "yes" for disease progression.
*The last observation is censored. This patient initially completed the original protocol, which included 50 weeks of OLE. Following a protocol amendment extending the OLE to 110 weeks, the patient was re-enrolled. PFS for this patient includes the entire period, as no disease progression was observed during the time off protocol. The final tumor assessment for this patient occurred at 33 months after randomization in the original protocol.
CT = computed tomography; MRI = magnetic resonance imaging; OLE = open-label extension; PFS = progression-free survival.

Summary of Adverse Events

Adverse Events, n (%)	Randomized Treatment Period (n=36)	Open-Label Extension (n=26)
AE leading to treatment discontinuation*	1 (2.8)	2 (7.7)
Treatment-related serious AE	0	0
Most common treatment-related AEs†		
Diarrhea	9 (25.0)	2 (7.7)
Abdominal pain	6 (16.7)	1 (3.8)
Nausea	4 (11.1)	3 (11.5)
Headache	4 (11.1)	1 (3.8)

*Large intestinal obstruction (n=1) in RTP, and carcinoid crisis (n=1) and transverse myelitis (n=1) in OLE; none were considered treatment-related.
†Incidence >10% in either treatment period (RTP or OLE).
AE = adverse event; OLE = open-label extension; RTP = randomized treatment phase.

CONCLUSIONS

- In this phase 2 study, once-daily oral paltusotine reduced the frequency and severity of CS symptoms, and improvements were sustained during longer-term (up to 2 years) treatment
- The investigator-assessed PFS rate was 80% after 1 year of treatment
- Paltusotine was well tolerated; the incidence of most treatment-related AEs decreased over the study period, and no new safety signals were identified
- The safety and exploratory efficacy of paltusotine in the treatment of patients with CS support further development through a phase 3, randomized, placebo-controlled trial (CAREFNDR; carefndr.com)

References
1. PALSONIFY® (paltusotine) tablets, for oral use. Package insert. Crinetics Pharmaceuticals, Inc.; 2025.
2. Palsonify (paltusotine) tablets. Summary of product characteristics. Crinetics Pharmaceuticals Europe GmbH; 2026.

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For author affiliations, disclosures, and additional acknowledgments, please use the QR code.

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