CAREFNDR: a Phase 3, Randomized, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Paltusotine in Adults With Carcinoid Syndrome Due to Well-Differentiated Neuroendocrine Tumors

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Background

- Paltusotine is a once-daily, selective, non-peptide, somatostatin receptor type 2 agonist in development as an oral treatment for acromegaly and carcinoid syndrome (CS)[1,2]
- In a phase 2, open-label, dose-ranging study (NCT05361668), paltusotine reduced the frequency and severity of CS symptoms and was well tolerated (please see poster with those study findings)

Objective

- To evaluate the efficacy and safety of paltusotine for the treatment of patients with CS in a randomized controlled trial

Methods

- Phase 3, multicenter, randomized, parallel-group double-blind, placebo-controlled trial
- ~140 adults with CS to be randomized in a 2:1 ratio to once-daily paltusotine 80 mg or matching placebo
- Electronic carcinoid symptom diary to be completed daily
- Antidiarrheal medications (eg, loperamide, diphenoxylate atropine) and rescue medications (eg, short-acting octreotide) are permitted
- OLE to include assessment of anti-tumor effects (eg, progression-free survival)

Efficacy Endpoints

Primary Endpoint

- Flushing episodes per day: change from baseline to Week 12 (14-day average)

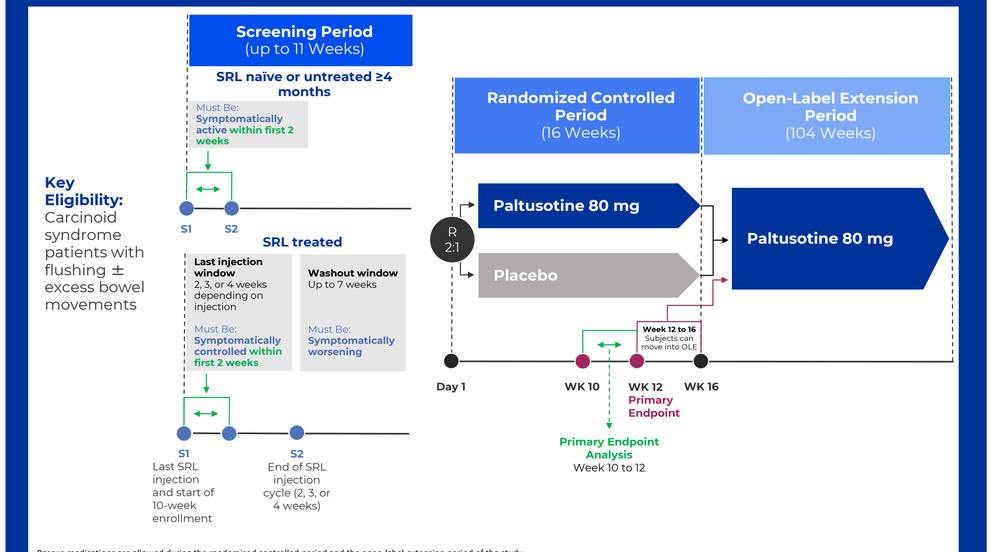
Key Secondary Endpoint

- BMs per day: change from baseline to Week 12 (14-day average)

Other Secondary Endpoints

- BMs per day: change from baseline to Week 12 (14-day average) in patients with >3 BMs per day at baseline
- Flushing severity: change from baseline to Week 12 (14-day average)
- BM urgency episodes per day: change from baseline to Week 12 (14-day average) in patients with >1 BM urgency episode per day at baseline

Study Design



Rescue medications are allowed during the randomized controlled period and the open-label extension period of the study.

Key Inclusion Criteria

- Male or female ≥18 years of age
- Well-differentiated Grade 1 or Grade 2 NET(s)
  - Positive SST receptor tumor status (previously documented or established during screening)
- Carcinoid syndrome: flushing with or without frequent BMs
- SRL naïve or untreated for ≥4 months *or* currently treated with SRL and agree to washout
- If SRL naïve or untreated for ≥4 months
  - >1 flushing episode/day (14-day average)
  - 5-HIAA or serotonin ≥2x ULN
- If SRL washout
  - Symptom control on SRL
  - Increase in flushing frequency to >1 flushing episode/day (14-day average)
  - History of elevated 5-HIAA or serotonin (in urine or blood sample)

Key Exclusion Criteria

- Diarrhea attributed to any condition(s) other than CS
- Need second-line treatment (eg, telotristat) for control of CS symptoms
- Treatment with specific NET therapy (eg, everolimus, hepatic embolization, radiotherapy, PRRT, debulking) during the past 4 weeks
- Documented prior nonresponse to SRL

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Efficacy Endpoints Cont'd

Other Secondary Endpoints Cont'd

- Percentage of treatment days with short-acting octreotide use
- Total number of treatment days with ≤3 BMs in participants with >3 BMs per day at baseline
- Percentage of treatment days with antidiarrheal medication use
- Total number of treatment days with zero flushing episodes; proportion of patients with zero flushing episodes (14-day average)

Exploratory Biomarkers

- Plasma 5-HIAA and serum serotonin

Safety Endpoint

- Incidence of AEs, including serious AEs and AEs leading to treatment discontinuation
- Clinical laboratory tests, vital signs, electrocardiogram

Pharmacokinetic Endpoint

- Plasma paltusotine concentration

Summary

- Results from the phase 2 study of paltusotine in patients with CS has supported the design of this phase 3 study
- This phase 3 trial will begin enrolling patients soon in ~100 sites (15 countries) to evaluate the efficacy and safety of paltusotine in the treatment of CS
- More information about this study is available at www.carefndr.com

REFERENCES

1. Zhao J, et al. *ACS Med Chem Lett*. 2023;14(1):66-74. **2.** Madan A, et al. *Pituitary*. 2022;25(2):328-339.

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DISCLOSURES

All authors are employees of Crinetics and may hold company stock and shares.