Long-Term Safety and Efficacy of Once-Daily Oral Paltusotine in the Treatment of Patients With Acromegaly: Update From ACROBAT Advance

MON-695

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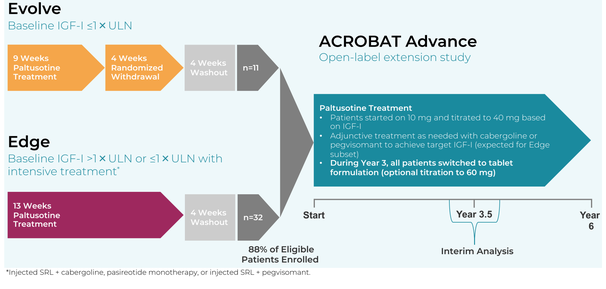
BACKGROUND

- Paltusotine is the first once-daily, non-peptide, selective SST2 receptor agonist in development as oral treatment for patients with acromegaly or carcinoid syndrome[1]
- Positive phase 3 data from PATHFNDR-1 and PATHFNDR-2 studies have recently been reported[2,3]
- Here we report long-term data from the phase 2 ACROBAT program, evaluating durability of safety and efficacy of paltusotine in acromegaly

METHODS

- Interim results from ACROBAT Advance, an ongoing, 6-year, open-label extension study
- Eligible patients completing phase 2 ACROBAT Edge or Evolve entered ACROBAT Advance immediately (on completion of washout period) or after a delay (during which they reverted to standard of care treatment)
- Paltusotine therapy: initiated at 10 mg/day and titrated to maximum dose of 60 mg/day based on IGF-I and tolerability
  - Capsule formulation (dose range, 10-40 mg) at study initiation, changed to tablet (dose range, 20-60 mg) during Year 3
  - This analysis: all patients with ≥2 assessments after switching to tablet
- Combination therapy allowed for patients not reaching therapeutic targets with paltusotine monotherapy
- IGF-I measured centrally using IDS iSYS immunoassay

Study Design: ACROBAT Advance



*Injected SRL + cabergoline, pasireotide monotherapy, or injected SRL + pegvisomant.

REFERENCES
1. Zhao J, et al. *ACS Med Chem Lett.* 2023;14(1):66-74. **2.** Gadelha MR, et al. Presented at ENDO 2024; June 1-4, 2024; Boston, MA. **3.** Biller BMK, et al. Presented at ENDO 2024; June 1-4; Boston, MA.

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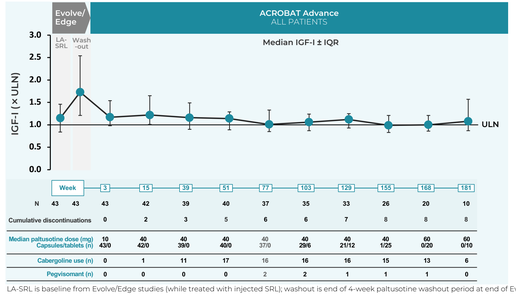
RESULTS

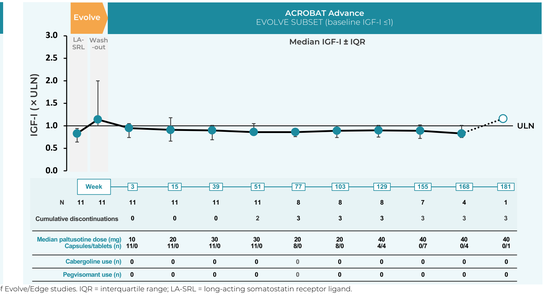
Patient Characteristics at Enrollment

Parameters	All Patients (n=43)
Age, years, mean (SD)	53.0 (11.6)
Female, n (%)	24 (55.8)
Time since diagnosis, months, mean (SD)	129.4 (78.4)
Prior pituitary surgery, n (%)	37 (86.0)
Pre-trial medical treatment*	
Lanreotide 60/90/120 mg/month, n	1/2/4
Octreotide 20/30/40 mg/month, n	3/17/3
Pasireotide (Edge) 40/60 mg/month, n	1/1
SRL + cabergoline (Edge), n	10
Pegvisomant (Edge) 20 mg/week, n	1

*Defined as prior to parent trial for direct rollovers and prior to ACROBAT Advance for delayed rollovers. SRL = somatostatin receptor ligand.

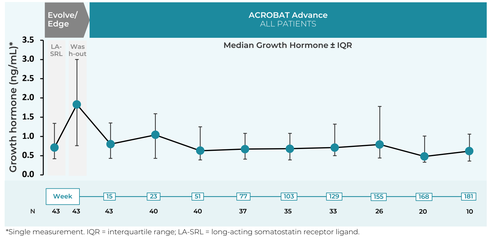
IGF-I Maintained at Injected SRL Baseline Levels





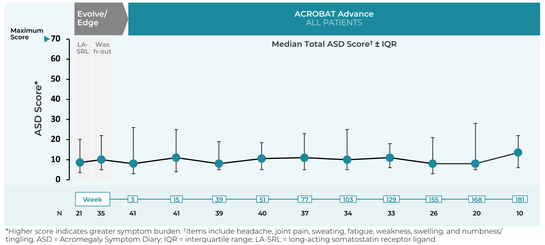
LA-SRL is baseline from Evolve/Edge studies (while treated with injected SRL); washout is end of 4-week paltusotine washout period at end of Evolve/Edge studies. IQR = interquartile range; LA-SRL = long-acting somatostatin receptor ligand.

Growth Hormone Levels Remained Stable



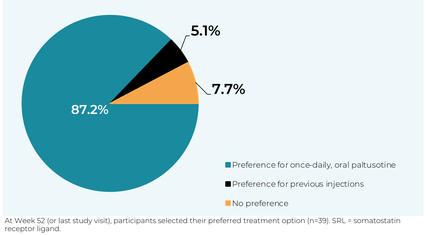
*Single measurement. IQR = interquartile range; LA-SRL = long-acting somatostatin receptor ligand.

Acromegaly Symptoms Stably Controlled (ASD)



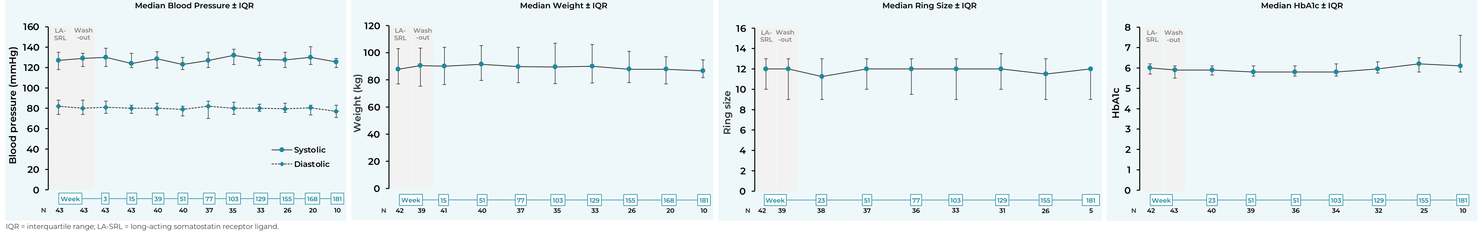
*Higher score indicates greater symptom burden. †Items include headache, joint pain, sweating, fatigue, weakness, swelling, and numbness/tingling. ASD = Acromegaly Symptom Diary; IQR = interquartile range; LA-SRL = long-acting somatostatin receptor ligand.

Paltusotine Preferred Over Injected SRLs



At Week 52 (or last study visit), participants selected their preferred treatment option (n=39). SRL = somatostatin receptor ligand.

Clinical Outcomes Stable Over Time

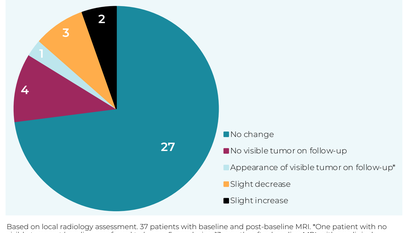


IQR = interquartile range; LA-SRL = long-acting somatostatin receptor ligand.

CONCLUSIONS

- Once-daily, oral paltusotine demonstrated durable IGF-I and GH levels for more than 3 years, comparable to levels attained on paltusotine at 3 weeks and on prior injected SRL therapy
- Signs and symptoms associated with acromegaly remained stable over time
- Paltusotine was well tolerated; no new safety signals were observed during longer-term treatment

Pituitary MRI Findings



Based on local radiology assessment. 37 patients with baseline and post-baseline MRI. *One patient with no visible tumor at baseline was found to have a 5-mm lesion 13 months after baseline MRI, with no clinical sequelae.

Summary of Adverse Events

- Most common AEs: arthralgia (27.3%), headache (30.2%), and fatigue (2.3.%)
- 1 treatment-related serious AE: cholelithiasis
- 2 discontinuations due to AEs: 1 patient with mild thyroid hormone increase, 1 patient with moderate headache and mild anxiety
- No safety signals seen in clinical laboratory tests or ECG; no amylase/lipase elevations >3 × ULN

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

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ACKNOWLEDGMENTS

The authors thank the site investigators, study coordinators/nurses, clinical staff, and patients who participated in the study. This study was funded by Crinetics Pharmaceuticals, Inc. The authors thank Michael Keeley, PhD, and Michael Monahan, MBA, Crinetics Pharmaceuticals, for their contributions. Technical editorial and medical writing assistance were provided under the direction of the authors by Janetricks Okeyo, PhD, Crinetics Pharmaceuticals, and Synchrony Medical Communications, LLC, West Chester, PA, USA; funding for this support was provided by Crinetics Pharmaceuticals, Inc.

DISCLOSURES

MRG reports being a PI of research grants from Crinetics and Recordati; occasional consultant for Crinetics, Ipsen, Novo Nordisk, and Recordati; and speaker for Ipsen, Novo Nordisk, and Recordati. HR reports no conflicts of interest. MBG reports receiving research support from Ascendis, Camurus, Chiasma, Corcept, Crinetics, Ipsen, Novartis, Novo Nordisk, Opko, Pfizer, and Strongbridge; and serving as a scientific consultant for Crinetics, HRA Pharma, Novo Nordisk, and Recordati Rare Diseases. MD reports being a PI of a research grant from Crinetics; and advisory board member for Pfizer in CEE. EM reports being a PI for a research grant from Crinetics. MT reports being a PI of a research grant from Crinetics; and speaker and consultant for Ipsen, Lilly, Novartis, and Recordati. CLB reports receiving consulting fees, honoraria, and meeting support from Ipsen, Novo Nordisk, and Recordati; and serving on advisory boards for Novo Nordisk and Recordati. CD, CTFC, AC, and AK are employees of Crinetics Pharmaceuticals.