ACROBAT Advance: long-term safety and efficacy results of paltusotine for the treatment of acromegaly

P80

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INTRODUCTION

- Paltusotine is an oral, once-daily, nonpeptide somatostatin receptor type 2 (SST2) agonist
- Phase 2 (ACROBAT Evolve & Edge) studies in patients with acromegaly involved switching from long-acting Somatostatin Receptor Ligands (SRLs) to 13 weeks of paltusotine monotherapy
- ACROBAT Advance is an ongoing open-label, long-term (5 year) safety and efficacy study of paltusotine in patients rolling-over from the ACROBAT Evolve & Edge studies. Interim results from a data snapshot as of August 31, 2021 are presented

METHODS

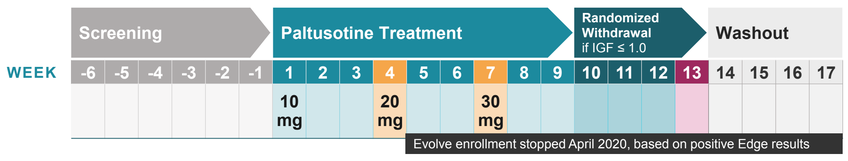
- Eligible patients completing ACROBAT Edge and Evolve entered ACROBAT Advance either immediately on completion of a washout period in the parent study or after a gap during which they reverted to their routine standard of care treatment
- Paltusotine therapy: initiated at 10 mg/day and titrated up to maximum dose of 40 mg/day based on IGF-1 and tolerability. Combination therapy allowed for patients not reaching therapeutic targets with 40 mg/day of paltusotine monotherapy
- IGF-1 measured centrally with IDS-ISYS assay calibrated to WHO recombinant reference standard

CONCLUSIONS

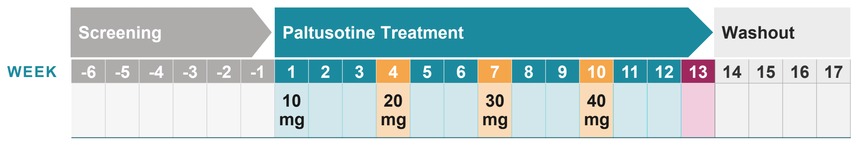
- Once daily, oral paltusotine lowered and maintains IGF-1 at levels comparable to prior injected SRL therapy for up to 51 weeks. This was seen in all subsets of patients representing a wide range of baseline disease control.
- Paltusotine is well tolerated with a safety profile similar to that of SRLs, including when used in combination with cabergoline
- The phase 3 program for paltusotine has been initiated, as ACROBAT Advance continues to accumulate long-term safety and efficacy data

DESIGN OF PARENT STUDIES

Evolve—Median Dose 10 mg/day
Primary Population
Patients treated with octreotide or lanreotide & baseline **IGF-1 ≤1x ULN**



Edge—Median Dose 40 mg/day*
Primary Population
Patients treated with octreotide or lanreotide & baseline **IGF-1 >1x ULN**



EDGE Results - ENDO 2021 Presentation

RESULTS

N=41

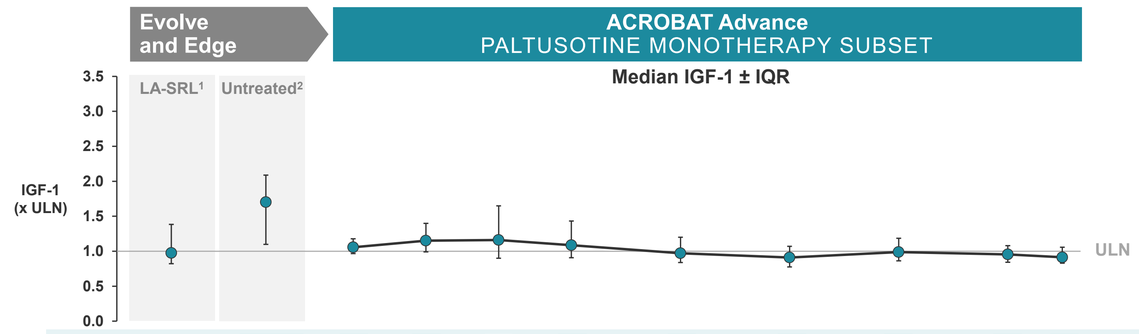
To date, the study has enrolled 41 of 49 eligible patients (84%)

Baseline characteristics ACROBAT Advance Patients

	All Patients N=41
Age, Mean (SD)	53.2 (11.5)
Sex, Female, n (%)	23 (56.1)
Months since diagnosis, Mean (SD)	129.7 (79.8)
Prior pituitary surgery, n (%)	35 (85.4)
Pre-trial medical treatment[1]	
Lanreotide, n - 60/90/120 mg/month	1/2/13
Octreotide, n - 20/30/40 mg/month	3/16/3
Pasireotide, n - 40/60 mg/month	1/1
SRL + Cabergoline, n	10
Pegvisomant, n - 20 mg/week	1

1. Pre-trial is defined as prior to parent trial for direct rollovers and prior to ACROBAT Advance for delayed rollovers.

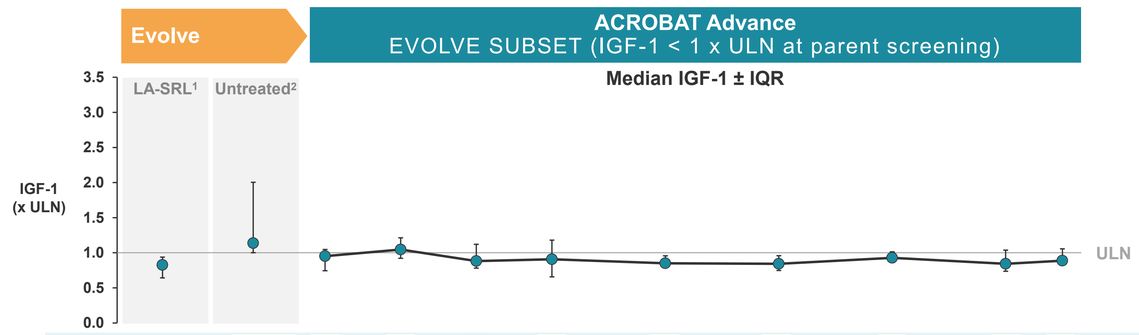
FIGURE 1. **Paltusotine lowered IGF-1 levels and maintained long-term IGF-1 at levels previously achieved with injected SRLs**



Week	3	7	11	15	23	31	39	47	51
N 29 29	29	27	26	26	22	20	19	14	13
Cumulative Discontinuations	0	0	0	0	2	2	3	3	3
Median Paltusotine Dose (mg)	10	10	20	20	40	40	40	35	40
Cabergoline added (n)	0	0	0	0	0	0	0	0	0

1. Baseline (screening) from Evolve/Edge studies while on injected SRL therapy.
2. End of 4-week wash-out from paltusotine at end of Evolve/Edge studies.
ACROBAT Advance DATA-through August 31, 2021

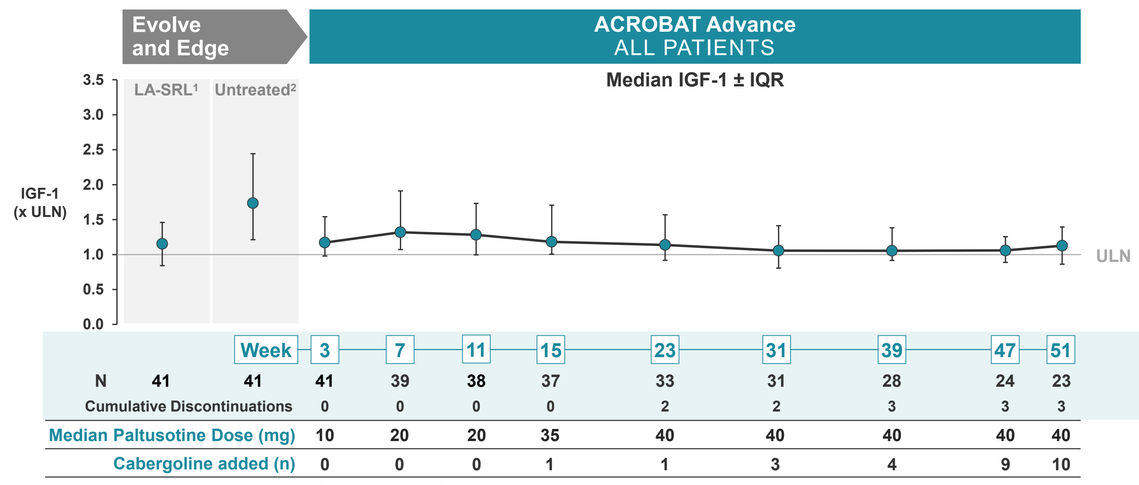
FIGURE 2. **Paltusotine lowered IGF-1 and maintained long-term IGF-1 control at levels previously achieved with injected SRLs**



Week	3	7	11	15	23	31	39	47	51
N 11 11	11	11	11	11	9	10	9	7	6
Cumulative Discontinuations	0	0	0	0	0	0	0	0	0
Median Paltusotine Dose (mg)	10	10	20	20	20	25	30	30	30
Cabergoline added (n)	0	0	0	0	0	0	0	0	0

1. Baseline (screening) from Evolve study while on injected SRL therapy.
2. End of 4-week wash-out from paltusotine at end of Evolve study.
ACROBAT Advance DATA -through August 31, 2021

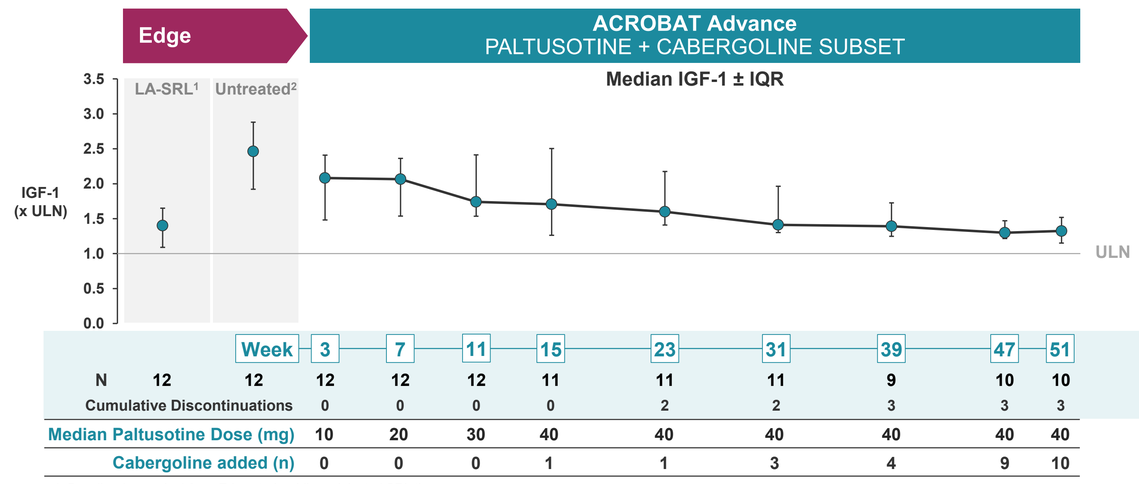
FIGURE 3. **Paltusotine lowered IGF-1 levels and maintained long-term IGF-1 at levels previously achieved with injected SRLs**



Week	3	7	11	15	23	31	39	47	51
N 41 41	41	39	38	37	33	31	28	24	23
Cumulative Discontinuations	0	0	0	0	2	2	3	3	3
Median Paltusotine Dose (mg)	10	20	20	35	40	40	40	40	40
Cabergoline added (n)	0	0	0	1	1	3	4	9	10

1. Baseline (screening) from Evolve/Edge studies while on injected SRL therapy.
2. End of 4-week wash-out from paltusotine at end of Evolve/Edge studies.
ACROBAT Advance DATA through August 31, 2021

FIGURE 4. **Paltusotine lowered IGF-1 levels and maintained long-term IGF-1 at levels previously achieved with injected SRLs**



Week	3	7	11	15	23	31	39	47	51
N 12 12	12	12	12	11	11	11	9	10	10
Cumulative Discontinuations	0	0	0	0	2	2	3	3	3
Median Paltusotine Dose (mg)	10	20	30	40	40	40	40	40	40
Cabergoline added (n)	0	0	0	1	1	3	4	9	10

1. Baseline (screening) from Edge study while on injected SRL therapy.
2. End of 4-week wash-out from paltusotine at end of Edge study.
ACROBAT Advance DATA through August 31, 2021

SAFETY

The safety population is comprised of all patients who have received at least one dose in ACROBAT Advance

n = The number of unique patients per preferred term

m = The number of occurrences for each preferred term

TEAE= treatment emergent adverse events

TEAEs occurring in ≥ 3 patients

TEAEs	Any Dose N=41 n (%) m
Headache	12 (29.3) 17
Arthralgia	9 (22.0) 19
Fatigue	6 (14.6) 11
Paresthesia	5 (12.2) 8
Hyperhidrosis	5 (12.2) 7
Diarrhea	5 (12.2) 5
Peripheral swelling	4 (9.8) 9
Corona virus infection	4 (9.8) 4
Apnea	3 (7.3) 5
Anxiety	3 (7.3) 3
Dizziness	3 (7.3) 3
Hypoglycemia	3 (7.3) 3
Hypotension	3 (7.3) 3

- No safety signals seen in clinical laboratories, including no amylase/lipase elevations >3x ULN, HbA1c, LFTs, ECGs
- 3 non-treatment related SAEs in 2 patients: gallstone pancreatitis and worsening of coronary artery disease followed by sinus arrest post coronary artery bypass surgery
- There were 4 discontinuations: 1 adverse event (headache), 1 pregnancy, 1 withdrawn consent, 1 patient preference (who discontinued after the Week 51 IGF-1 measurement)
- Of 22 patients who had pituitary MRIs performed during the study, 16 had no visible residual tumor. Of those who had visible tumor, 5 had pituitary tumor size reductions (range 1-8 mm), 3 had no change. One patient with no visible tumor at baseline was found to have a 5 mm lesion 13 months following the baseline MRI.
- No AEs related to combination therapy with paltusotine and cabergoline were identified

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