Safety and Effectiveness of Lonapegsomatropin in the SkybriGHt Registry Study: Analysis of the First 100 Patients Enrolled With 1 Year of Follow-Up

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Background

Lonapegsomatropin (SKYTROFA®; TransCon® hGH), a prodrug of somatropin, is approved for the once-weekly treatment of pediatric growth hormone deficiency (GHD) by the Food and Drug Administration (pediatric patients 1 year or older and weighing at least 11.5 kg),[1] and by the European Commission (pediatric patients aged 3 years to 18 years).[2]

The lonapegsomatropin phase 3 clinical trial program evaluated efficacy and safety outcomes in children with GHD.[3,4,5]

- Lonapegsomatropin demonstrated efficacy and safety in children with GHD who were treatment-naive in the 52-week heiGHt trial[3] and treatment-experienced in the 26-week fliGHt trial[4]
- The enliGHten open-label extension trial enrolled children from heiGHt and fliGHt to further evaluate long-term efficacy, safety, and tolerability, including children transitioning into puberty (more advanced pubertal stages)[5,6]

Real-world data extend our understanding of clinical trial findings by providing insights into disease management, treatment utilization, and long-term outcomes in routine clinical practice.

Aims

The objectives of the SkybriGHt study are to assess the safety and effectiveness of lonapegsomatropin in the post-marketing setting. We report outcomes in the first 100 enrolled patients who have reached 1-year follow-up.

Conclusions

This is the first prospective study evaluating real-world clinical experience with lonapegsomatropin treatment for pediatric GHD.

Among the first 100 patients enrolled with 12 months follow-up, the median and maximum lonapegsomatropin treatment duration at 1 year was 1.75 and 7.8 years, respectively.

Patient demographics reflected:

- A diverse age distribution
- 82% male, consistent with growth hormone (GH) prescription patterns[7]
- 59% of patients were previously treated with daily GH

Median height standard deviation score (SDS) increased over time and exceeded zero (CDC population mean height for age and sex)[8] at month 12 (0.207); median annualized height velocity (AHV) at month 12 was 7.82 cm/year.

IGF-I SDS remained stable over the 12 months analyzed (median change from enrollment at months 6 and 12 was 0).

There were no serious, serious related, severe, or severe related treatment-emergent adverse events (TEAEs), and none leading to treatment discontinuation.

Clinical Implication

At 1 year, data for the first 100 patients enrolled in the SkybriGHt registry demonstrated safety and effectiveness aligned with prior trial reports of lonapegsomatropin treatment for pediatric GHD.

Methods

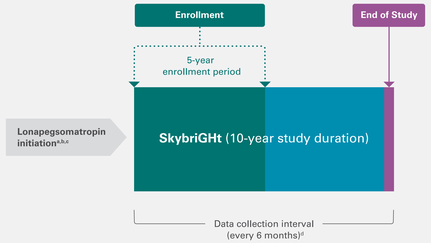
SkybriGHt Registry Study

- SkybriGHt aims to enroll 900 participants from the United States
- Patients who are prescribed lonapegsomatropin consistent with routine clinical practice are eligible
- Decision to treat with lonapegsomatropin is made prior to, and independently of, any potential study participation
- Enrollment will occur over a 5-year period with the study intended to conclude after a total of 10 years
- Clinical outcomes are evaluated through height SDS, annualized height velocity (AHV), and insulin-like growth factor I (IGF-I) SDS
- Safety is evaluated through adverse event (AE) reporting and laboratory test results

Statistical Analyses

- Data cut-off: October 15, 2024
- Analyses were based on the first 100 patients who had reached 12 months of follow-up after enrollment
  - Patients had to have the date of 1st dose entered in the electronic data capture (EDC) system
  - First 100 patients based on the chronological order of consent date
- Descriptive statistics were summarized for:
  - Demographics and baseline disease characteristics, prior GH therapy, and lonapegsomatropin treatment
  - Clinical outcomes assessed at enrollment and at 6 and 12 months following enrollment, with a 3-month window applied for the 6- and 12-month time points
  - AEs, including those that were serious, treatment-related, severe, or resulted in treatment discontinuation

Figure 1. **SkybriGHt Registry Study Design**



[a]Lonapegsomatropin initiaion

- Lonapegsomatropin treatment may have been initiated at varying times and of varying duration prior to enrollment
- Patients may have participated in lonapegsomatropin clinical trials prior to SkybriGHt
- Initiation of lonapegsomatropin may have been preceded by other GH therapies such as daily somatropin or another long-acting growth hormone

[b]Data collection interval

- Included baseline and medical history at enrollment and data entry for outcomes and AEs every 6 months following enrollment

Results

Table 1. **Disposition**

Variable	Number of Patients (%)
All patients enrolled	100
Initiated lonapegsomatropin > 60 days prior to enrollment	86 (86)
Participated in heiGHt, fliGHt, and/or enliGHten clinical trial(s)	17 (17)
Withdrew from treatment[a]	17 (17)

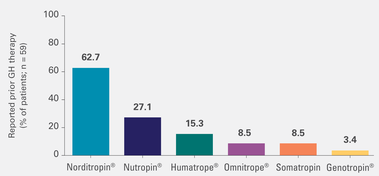
[a]Reasons included: reached adult height/bone age maturation, change in insurance coverage, withdrawal by patient, other.

Table 2. **Demographics**

Variable	Category	Total (N = 100%)
Sex, n (%)	Male	82 (82)
	Female	18 (18)
Age, years	Median	10.0
	Q1, Q3	8.0, 12.0
Age category, n (%)	< 3 years	0
	≥ 3 and < 6 years	5 (5)
	≥ 6 to < 11 years for girls, ≥ 6 to < 12 years for boys	47 (47)
	≥ 11 years for girls, ≥ 12 years for boys	48 (48)
Race, n (%)	White	86 (86)
	Asian	6 (6)
	Not reported	4 (4)
	Black or African American	3 (3)
	Other	1 (1)
Ethnicity, n (%)	Not Hispanic or Latino	88 (88)
	Hispanic or Latino	9 (9)
	Unknown	2 (2)
	Not reported	1 (1)
Peak stimulated GH at diagnosis, n (%)[a]	≤ 3 ng/mL	4 (6)
	> 3 ng/mL to ≤ 7 ng/mL	37 (56)
	> 7 ng/mL[b]	25 (38)

All 100 participants in the analysis set had a diagnosis of pediatric GHD.
[a]Percentages were calculated based on patients with available test results (n = 66).
[b]All participants were < 10 ng/mL except for 1 patient at 10.2 ng/mL.

Figure 2. **Prior Growth Hormone Therapy**



- 59% of participants had been previously treated with daily GH
  - The median (Q1, Q3) prior daily GH dose at SkybriGHt enrollment was 0.31 (0.30, 0.31) mg hGH/kg/week and the median (Q1, Q3) duration of prior treatment was 9.1 (4.3, 13.5) months
- No participants had been previously treated with another long-acting GH

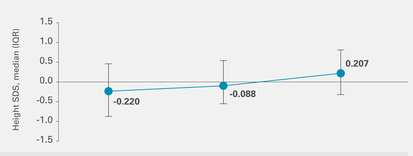
Somatropin indicates brand not specified. Patients could have received multiple brands of GH, and therefore, the summed percentages exceed 100%.

Table 3. **Lonapegsomatropin Exposure**

Variable	Category	Total (N = 100)
Duration of treatment[a] (weeks)	n	100
	Median	91.0
	Min, Max	56.0, 408.0
Initial prescribed[b] dose (mg hGH/kg/week)	n	77
	Median	0.23
	Min, Max	0.12, 0.36
Prescribed[c] dose at Month 6 (mg hGH/kg/week)	n	54
	Median	0.24
	Min, Max	0.15, 0.37
Prescribed[c] dose at Month 12 (mg hGH/kg/week)	n	28
	Median	0.26
	Min, Max	0.12, 0.37

[a]Total duration of treatment since first dose of lonapegsomatropin.
[b]Dose as recorded in patient's chart at time of first dose of lonapegsomatropin.
[c]Average prescribed dose within ±3-month window of each timepoint.

Figure 3. **Height SDS**



Months	0	6	12
n[a]	100	89	73
Δ height SDS[b]		0.105	0.204

[a]At each post-enrollment visit, n is the number of patients with available measurement.
[b]Δ height SDS is the change from enrollment, presented as median.

Table 4. **Annualized Height Velocity at 12 Months Following Enrollment**

Variable	Category	Total (N = 100)
AHV at month 12 (cm/year)	n	73
	Median	7.82
	Q1, Q3	6.54, 8.81

Table 5. **IGF-I SDS**

Variable	Category	Total (N = 100)
Enrollment IGF-I SDS[a]	n	67
	Median	1.30
	Q1, Q3	0.80, 1.70
Month 6 IGF-I SDS	n	57
	Median	1.30
	Q1, Q3	0.80, 1.90
Month 12 IGF-I SDS	n	43
	Median	1.20
	Q1, Q3	0.50, 1.70
Median (Q1, Q3) IGF-I SDS change from enrollment	Month 6	0 (-0.60, 0.60)
	Month 12	0 (-0.80, 0.30)

[a]Timing of IGF-I sample collection was variable and may not always represent the average weekly IGF-I. IGF-I SDS reflects value reported at the site in EDC.

Table 6. **Adverse Event Summary**

Variable	Total (N = 100)
Treatment-Emergent Adverse Events (TEAEs), n (%)	26 (26)
Related TEAEs,[a] n (%)	10 (10)
Serious TEAEs, n (%)	0
Serious related TEAEs, n (%)	0
Severe TEAEs, n (%)	0
Severe related TEAEs, n (%)	0
TEAEs leading to discontinuation of study drug, n (%)	0

[a]Related TEAEs included: insulin-like growth factor increased, injection site pain, and pain in extremity.

Table 7. **Adverse Events by System Organ Class**

Variable	Total (N = 100)
Patients with at least one TEAE, n (%)	26 (26)
Infections and infestations	10 (10)
Investigations	9 (9)
Injury, poisoning, and procedural complications	5 (5)
Nervous system disorders	4 (4)
General disorders and administration site conditions	2 (2)
Musculoskeletal and connective tissue disorders	1 (1)
Respiratory, thoracic and mediastinal disorders	1 (1)

TEAEs occurring in ≥ 5% of patients by system organ class included: Infections and infestations (bronchitis, otitis media, upper respiratory tract infection, cellulitis, conjunctivitis, gastroenteritis, nasopharyngitis, and pneumonia); Investigations (insulin-like growth factor increased); Injury, poisoning, and procedural complications (head injury, limb injury, skin laceration, torus fracture, wrist fracture).

Abbreviations

AE = adverse event; **AHV** = annualized height velocity; **CDC** = Centers for Disease Control and Prevention; **EDC** = electronic data capture; **GH** = growth hormone; **GHD** = growth hormone deficiency; **hGH** = human growth hormone; **IGF-I** = insulin-like growth factor I; **IQR** = interquartile range; **SDS** = standard deviation score; **TEAE** = treatment emergent adverse event

References

1. SKYTROFA. US Prescribing Information (USPI). Ascendis Pharma; 2024. Accessed May 30, 2024. https://ascendispharma.us/products/pi/skytrofa/skytrofa_pi.pdf; **2.** SKYTROFA. SmPC. EPAR product information. EMA. https://www.ema.europa.eu/en/documents/product-information/skytrofa-previously-lonapegsomatropin ascendis-pharma-epar-product-information_en.pdf. Accessed March 29, 2023; **3.** Thornton PS, Maniatis AK, Aghajanova E, et al. Weekly Lonapegsomatropin in Treatment-Naive Children With Growth Hormone Deficiency: The Phase 3 heiGHt Trial. *J Clin Endocrinol Metab*. 2021;106(11):3184-3195; **4.** Maniatis AK, Nadgir UJ, Saenger P, et al. Switching to Weekly Lonapegsomatropin from Daily Somatropin in Children with Growth Hormone Deficiency: The fliGHt Trial. *Horm Res Paediatr*. 2022;95(3):233-243; **5.** Maniatis AK, Casella SJ, Nadgir UM, et al. Safety and Efficacy of Lonapegsomatropin in Children With Growth Hormone Deficiency: enliGHten Trial 2-Year Results. *J Clin Endocrinol Metab*. 2022;107(7):e2680-e2689; **6.** Maniatis AK, Thornton PS, Nadgir UM, et al. Children with Growth Hormone Deficiency Treated With Lonapegsomatropin Demonstrated Sustained Height Improvements for up to 6 Years: enliGHten Trial Final Results. *Horm Res Paediatr*. 2025. Online ahead of print; **7.** Grimberg A, Huerta-Saenz L, Grundmeier R, et al. Gender Bias in U.S. Pediatric Growth Hormone Treatment. *Sci Rep*. 2015;9:5:10199. **8.** Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: Methods and Development. *Vital Health Stat 11*. May 2002;(246):1-190.

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