Poster 6600

Phase 3 Study Evaluating Once Weekly Somatrogon Compared to Daily Genotropin in Japanese Patients With Pediatric Growth Hormone Deficiency (pGHD)

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Objective

- Assess the efficacy and safety of somatrogon administered once weekly compared with Genotropin administered once daily in prepubertal Japanese children with GHD.

Conclusions

- The study met its primary objective: somatrogon administered once weekly was comparable to Genotropin administered once daily with regard to annual HV after 12 months of treatment.
- The mean HV and height SDS were numerically higher in the somatrogon group across all post-baseline visits in comparison with the Genotropin group.
- Both treatment groups showed similar changes in bone maturation; advancement in bone age did not exceed advancement in chronological age.
- Somatrogon administered once weekly was generally well-tolerated in children with GHD.
- The results of this Japanese phase 3 study are consistent with those reported from the global phase 3 study that met its primary endpoint of non-inferiority to Genotropin administered once daily.

Background

- Somatrogon is a long-acting recombinant human growth hormone (rhGH) comprising the amino acid sequence of human growth hormone and 3 copies of the carboxy-terminal peptide of human chorionic gonadotropin, with a half-life that permits once weekly (QW) administration.
- Somatrogon is currently in development as QW treatment for pediatric patients with growth hormone deficiency (GHD).
- A phase 3, open-label, randomized study was conducted to compare somatrogon administered QW with Genotropin® administered once daily (QD) in Japanese children with GHD (NCT03874013).

Methods

- This was a 12-month, open-label, randomized, active controlled, parallel-group study.
- After a 4-week screening period to confirm GHD, subjects were randomized 1:1 to receive either QW somatrogon or QD Genotropin via subcutaneous injection.
- QW Somatrogon was administered in 3 escalating doses (0.25, 0.48, and 0.66 mg/kg/wk; 2 weeks at each dose) for 6 weeks, after which subjects continued to receive somatrogon at a dose of 0.66 mg/kg/wk for 46 weeks.
- QW Somatrogon was administered using a single, patient use, multidose, disposable, prefilled pen.
- QD Genotropin was administered (0.025 mg/kg/d) using previously approved commercial pen presentations.
- Prepubertal boys (ages 3 to <11 y) or girls (ages 3 to <10 y) with a confirmed diagnosis of GHD were eligible for enrollment if they had impaired height and height velocity (HV), baseline IGF-1 standard deviation score (SDS) ≤ –1, and had not received prior rhGH therapy.

ASSESSMENTS AND ENDPOINTS

- Height measurements were performed at screening, baseline, and Weeks 13, 26, 39, and 52 (end of treatment).
- Adverse events (AEs), including injection site reactions, were assessed at each study visit, with the exception of injection site reactions, which were not assessed at predose visits; subjects were also trained to record injection site reactions in a diary.
- The primary efficacy endpoint was annual HV after 12 months. Comparability of somatrogon administered QW and Genotropin administered QD was demonstrated for the primary efficacy endpoint if the point estimate of the mean treatment difference (somatrogon–Genotropin) was ≥ –1.8 cm/y.
- Secondary efficacy endpoints included annualized HV at 6 months of treatment, change in height SDS at 6 and 12 months, and change in bone maturation at 12 months.
- Least squares (LS) mean was based on ANCOVA model, with classification terms for treatment and gender; baseline height SDS and peak GH were included as covariates.

Results

STUDY PARTICIPANTS

- 65 subjects were screened and 44 subjects randomized at 24 sites in Japan; of the 44 dosed subjects, 43 completed the 12-month main study, and 1 subject in the Genotropin group discontinued from the study due to an AE (craniopharyngioma).
- Demographic and baseline characteristics were similar between the 2 treatment groups (somatrogon and Genotropin), with most (70%) subjects aged between 3 and 7 years.

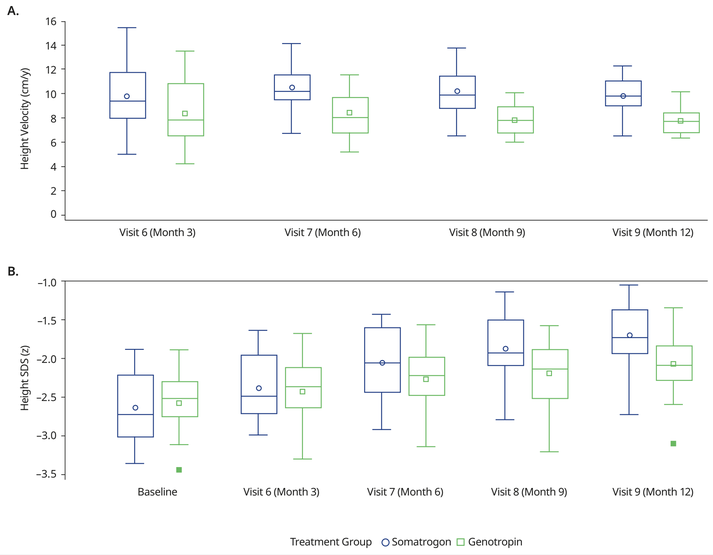
EFFICACY

- The LS mean of HV at Month 12 was 9.65 cm/y in the somatrogon group and 7.87 cm/y in the Genotropin group (**Figure 1A**); similar results were observed for annualized HV at Month 6.
- LS mean treatment difference of +1.79 cm/y (95% CI: 0.97–2.61) in HV at Month 12 was greater than the pre-established margin of –1.8 cm/y, demonstrating QW somatrogon was comparable to QD Genotropin.
- At 6 and 12 months, respectively, mean height SDS was higher in the somatrogon group (–2.02 and –1.64) compared with the Genotropin group (–2.23 and –2.03) (**Figure 1B**).
- The LS mean change from baseline in height SDS at 6 and 12 months, respectively, was higher in the somatrogon group (0.58 and 0.94) compared with the Genotropin group (0.31 and 0.52).
- Advancement in bone age (BA) did not exceed advancement in chronological age (CA); mean bone maturation (defined as the ratio of BA to CA) at 12 months was <1.0 in both treatment groups (somatrogon: 0.80; Genotropin: 0.80).

SAFETY

- The number of subjects with all-causality treatment-emergent AEs (TEAEs) were similar between treatment groups (**Table 1**).
- Subjects in the somatrogon group had a higher incidence of TEAEs vs the Genotropin group (362 vs 108 events); TEAE of injection site pain was the primary cause for the difference in the incidence of TEAEs between groups (205 vs 8 events).
- The most common all-causality TEAEs were nasopharyngitis, injection site pain, and influenza (**Table 1**); the majority of TEAEs were mild to moderate in severity.
- The most common treatment-related TEAE was injection site pain: somatrogon: 16/22 (72.7%), Genotropin: 3/22 (13.6%).
- The incidence of serious AEs was low in both treatment groups; treatment-emergent serious AEs were reported by 2 (9.1%) subjects in the somatrogon group (hypoparathyroidism, influenza, traumatic fracture, and febrile convulsion) and 2 (9.1%) subjects in the Genotropin group (craniopharyngioma and asthma).

Figure 1. Box plot of (A) height velocity and (B) height SDS over time



Outliers shown as filled squares.

Table 1. All-causality treatment-emergent adverse events reported in ≥10% of subjects in either treatment group

n (%)	Somatrogon n=22	Genotropin n=22	Total N=44
With any adverse event	22 (100.0)	17 (77.3)	39 (88.6)
Nasopharyngitis	12 (54.5)	11 (50.0)	23 (52.3)
Injection site pain	16 (72.7)	3 (13.6)	19 (43.2)
Influenza	6 (27.3)	6 (27.3)	12 (27.3)
Pyrexia	4 (18.2)	3 (13.6)	7 (15.9)
Pharyngitis	3 (13.6)	4 (18.2)	7 (15.9)
Conjunctivitis	1 (4.5)	5 (22.7)	6 (13.6)
Gastroenteritis	4 (18.2)	2 (9.1)	6 (13.6)
Bronchitis	4 (18.2)	1 (4.5)	5 (11.4)
Vomiting	3 (13.6)	1 (4.5)	4 (9.1)
Eczema asteatotic	0	3 (13.6)	3 (6.8)

Subjects were counted once per treatment per event.

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