Poster 6887

Results From an Open-Label Extension of the Phase 2 Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in Pediatric Patients With Growth Hormone Deficiency (GHD)

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Objective

- Assess the efficacy and safety of long-term exposure to somatrogon once weekly in pediatric subjects with GHD who continued in the OLE.

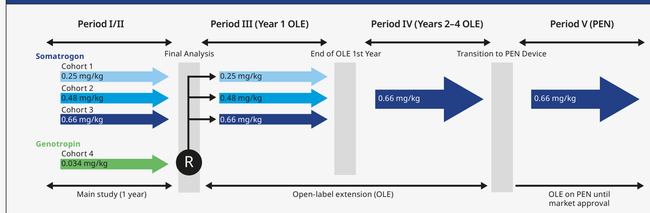
Conclusions

- Subjects treated with somatrogon once weekly for up to 5 years in the OLE study showed sustained improvement in annual HV, height SDS, and change in height SDS.
- Once weekly administration of somatrogon for an extended period was well tolerated in pediatric subjects with GHD.

Background

- Somatrogon is a long-acting recombinant human growth hormone (rhGH) consisting of the amino acid sequence of human growth hormone and 3 copies of the carboxy-terminal peptide of human chorionic gonadotropin.
- Somatrogon is currently being developed as a once-weekly (QW) treatment for pediatric patients with growth hormone deficiency (GHD).
- This open-label extension (OLE) phase 2 study was a continuation of a randomized 12-month study that investigated the safety, efficacy, and tolerability of 3 dose levels of somatrogon QW (0.25, 0.48, or 0.66 mg/kg/wk) compared with daily rhGH (Genotropin® 0.034 mg/kg/d) in initially rhGH-naïve prepubertal pediatric subjects with GHD.[1]
- This global phase 2 study (NCT01592500) is comprised of 5 treatment periods (**Figure 1**).

Figure 1. Study design



OLE=open-label extension; PEN=somatrogon delivery via prefilled pen device; R=randomization

- The main study (Period I and II) found that subjects in all 3 somatrogon dose cohorts achieved adequate catch-up growth, with the highest dose cohort (0.66 mg/kg/wk) achieving the highest mean growth rate and an annualized height velocity (HV) closest to that of Genotropin recipients.[1]
- The OLE phase of the study (Periods III, IV, and V) followed patients for up to 5 additional years of exposure to somatrogon.

Methods

- The study design and treatment arms of the main phase 2, open-label, randomized, dose-finding study have been described in detail previously.[1]
- Subjects who completed the main study (Periods I and II) and provided consent were eligible to be enrolled in the OLE study, which consisted of 3 periods (**Figure 1**):
  - **Period III**: an additional 12 months at the original somatrogon dose; Genotropin recipients were randomized to 1 of the 3 somatrogon dose regimens.
  - **Period IV**: Years 2–4 of the OLE, where all subjects received somatrogon at 0.66 mg/kg/wk.
  - **Period V**: currently ongoing until marketing approval; subjects transitioned from single-use vials of somatrogon (subcutaneous injection via needle and syringe) to a prefilled pen device at the same somatrogon dose (0.66 mg/kg/wk).
- Data up to 1 year of Period V are reported.

ASSESSMENTS AND ENDPOINTS

- Annual HV, change in height standard deviation score (SDS), and bone maturation were assessed every 12 months.
- Safety evaluations included monitoring of all adverse events (AEs), including serious AEs and local injection site reactions, as well as laboratory assessments, including IGF-1 levels and immunogenicity.
- Primary safety endpoints included the incidence of AEs and anti-drug antibody (ADA) formation, assessment of local site injections, IGF-1 levels, and IGF-1 SDS.
- Secondary endpoints included annual HV, change in height SDS, and annual bone maturation.
- All subjects were included in the full analysis set.

Results

STUDY PARTICIPANTS

- 48 of 53 subjects who completed the main study were randomized and entered Period III of the OLE.
- At the start of Period III, the majority (66.7%) of subjects were male and almost all (93.8%) of the subjects were White (**Table 1**).
- Completion rates for each OLE period (Periods III, IV, and Year 1 of Period V) ranged from 87.5 to 97.7%.

EFFICACY

- At the end of Period III, the mean (SD) annual HV for the 0.25 and 0.48 mg/kg/wk dose cohorts was similar (7.73 ± 1.89 and 7.54 ± 1.28 cm/y, respectively), but was higher in the 0.66 mg/kg/wk dose cohort (8.81 ± 1.12 cm/y), consistent with the results of the main study.[1]
- The HV in Periods IV and V indicated a sustained growth response that was independent of initial cohort assignment in the main study.
- Relative to the main study baseline (–3.98 ± 1.22),[1] mean (SD) height SDS improved progressively throughout the OLE and was within the normal range (–0.69 ± 0.87) at the end of the first year of Period V (**Figure 2**).

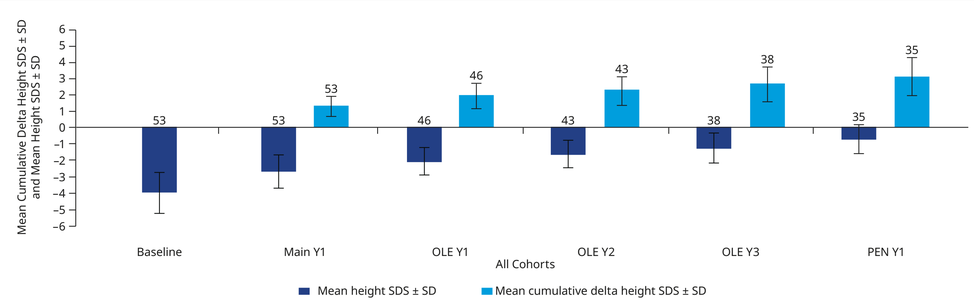
SAFETY

- Mean (SD) IGF-1 SDS values were similar at the end of Year 1 and 2 but increased at Year 3 (1.05 ± 0.82) and at the end of the first year of Period V (1.29 ± 0.81); mean IGF-1 SDS values were within the target therapeutic range and remained <2 SDS at all time points during the OLE.
- During the OLE, 39 (81.3%) subjects reported ≥1 treatment-emergent AE (TEAE) (**Table 2**); most TEAEs were mild or moderate in intensity and most were considered unrelated to study treatment.
- All reported serious TEAEs (in 3 subjects) were considered unlikely related to study treatment, with the exception of 1 instance of scoliosis, which the investigator considered unexpected and probably related to study treatment.
- During somatrogon administration with a needle and syringe (Period III and IV), no injection site reactions were reported; 3 (7.5%) subjects reported injection site reactions (bruising in 2 subjects and erythema in 1 subject) with the pen device, that were mild or moderate in intensity.

IMMUNOGENICITY

- ADAs were reported in 18 (37.5%) of 48 subjects during the OLE; 10 of these subjects also had ADAs in the main study.
- No clinically meaningful differences in annual HV or TEAEs were observed between ADA-positive and ADA-negative subjects.

Figure 2. Height SDS and cumulative delta height SDS for each year of the study (all cohorts combined)



OLE=open-label extension; SD=standard deviation; SDS=standard deviation score; Y=year

Table 1. Subject demographics and baseline characteristics at the beginning of Period III of the OLE

	Somatrogon Treatment Group[a]			
n (%)[b]	0.25 mg/kg/wk n=16	0.48 mg/kg/wk n=17	0.66 mg/kg/wk n=15	Total N=48
Age, mean (SD), y	7.98 (2.03)	7.55 (2.23)	7.49 (2.20)	7.67 (2.12)
Female	3 (18.8)	6 (35.3)	7 (46.7)	16 (33.3)
Race				
Black or African American	0 (0.0)	1 (5.9)	0 (0.0)	1 (2.1)
White	15 (93.8)	16 (94.1)	14 (93.3)	45 (93.8)
Other	1 (6.3)	0 (0.0)	1 (6.7)	2 (4.2)
Pubertal status				
Tanner I	16 (100.0)	17 (100.0)	14 (93.3)	47 (97.9)
Tanner II	0 (0.0)	0 (0.0)	1 (6.7)	1 (2.1)
Tanner III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tanner IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

[a] Includes subjects who received Genotropin during the main study and were re-randomized to receive somatrogon during the OLE period.
[b] Except where indicated.
OLE=open-label extension; SD=standard deviation

Table 2. Treatment-emergent adverse events observed in ≥3 subjects (full analysis set)

	All Subjects N=48		
n (%)	Treatment-related	Not related to treatment	Total
Any adverse event	7 (14.6)	32 (66.7)	39 (81.3)
Upper respiratory tract infection	0	13 (27.1)	13 (27.1)
Bronchitis	0	11 (22.9)	11 (22.9)
Nasopharyngitis	0	6 (12.5)	6 (12.5)
Rhinitis	0	6 (12.5)	6 (12.5)
Varicella	0	5 (10.4)	5 (10.4)
Ear infection	0	4 (8.3)	4 (8.3)
Pneumonia	0	3 (6.3)	3 (6.3)
Tonsillitis	0	3 (6.3)	3 (6.3)
Viral infections	0	3 (6.3)	3 (6.3)
Viral upper respiratory tract infection	0	3 (6.3)	3 (6.3)
Vomiting	0	3 (6.3)	3 (6.3)
Arthralgia	0	3 (6.3)	3 (6.3)
Pyrexia	0	3 (6.3)	3 (6.3)
Headache	0	3 (6.3)	3 (6.3)
Rhinitis allergic	0	3 (6.3)	3 (6.3)

Reference: 1. Zelinska N, et al. J Clin Endocrinol Metab 2017;102(5):1578-87.

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