Poster 7129

Switch Data From the Open-Label Extension of the Pivotal Phase 3 Study of Once Weekly Somatrogon Compared With Daily Somatropin in Pediatric Patients With Growth Hormone Deficiency (GHD)

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Objective

- Compare the efficacy and safety of the soma/soma regimen (somatrogon administered once weekly in both the main study and the OLE) vs the Geno/soma regimen (Genotropin administered once daily in the main study and somatrogon administered once weekly in the OLE).

Conclusions

- The soma/soma and Geno/soma treatment groups had similar HVs and change in height SDS after 12 months of the OLE.
- Results from the OLE demonstrated that 'catch-up' growth continued into the second year of treatment.
- Switching from Genotropin administered once daily to somatrogon administered once weekly in the second year of the study was shown to be noninferior to receiving somatrogon once weekly for 2 years.
- Metabolic (glycemic, lipid, and thyroid) parameters throughout the 12 months were similar to the levels observed at the OLE baseline, and levels were similar between treatment groups.

Background

- Somatrogon is a long-acting recombinant human growth hormone (rhGH) that consists of the amino acid sequence of human growth hormone and 3 copies of the carboxy-terminal peptide of human chorionic gonadotropin.
- Somatrogon is in development as a once weekly (QW) treatment for children with growth hormone deficiency (GHD).
- This open-label extension (OLE) phase 3 study was a continuation of a randomized 12-month main study (NCT02968004) that investigated the efficacy and safety of somatrogon, administered QW compared with rhGH (Genotropin®) administered once daily (QD) in initially rhGH-naïve prepubertal pediatric subjects with GHD.
- The main study showed that QW somatrogon is noninferior to QD Genotropin and that both treatments have a similar safety profile.
- After completing the main study, subjects were then eligible to be consented and enrolled into the (optional) OLE study, in which all subjects received QW somatrogon.

Methods

- The main study was an open-label, randomized, active controlled, parallel-group phase 3 study in which subjects were randomized 1:1 to receive QW subcutaneous (SC) doses of somatrogon (0.66 mg/kg/wk) or QD SC doses of Genotropin (0.034 mg/kg/d) for 12 months.
- Subjects who completed the main study and provided their consent were eligible to be enrolled in the single-arm OLE study.
- Subjects who received somatrogon in the main study continued to receive somatrogon QW at the same dose (0.66 mg/kg/wk) while subjects who received Genotropin in the main study were switched to somatrogon QW (0.66 mg/kg/wk).
- Due to COVID-19, a number of subject visits were delayed for Month 12, resulting in lower than anticipated subject numbers for several parameters.

ASSESSMENTS AND ENDPOINTS

- Clinical endpoints included annual height velocity (HV), change in height standard deviation score (SDS), and bone maturation, which were assessed every 12 months.
- Biochemical endpoints included IGF-1 levels, IGF-1 SDS, IGFBP-3 levels, and IGFBP-3 SDS, which were assessed on Day 4 after somatrogon dosing across study visits.

Results

STUDY PARTICIPANTS

- At the end of the main study, the least squares (LS) mean HV and the LS mean change in height SDS were similar between the somatrogon (10.10 cm/y and 0.92) and Genotropin groups (9.78 cm/y and 0.87).
- Of the 222 subjects who completed the main study, 212 subjects entered the OLE.
- At the beginning of the OLE, demographics and baseline characteristics were well balanced between soma/soma and Geno/soma treatment groups (**Table 1**).
  - The majority of subjects were male (70.75%) and most subjects were White (76.42%) (**Table 1**).
  - The soma/soma and Geno/soma treatment groups had similar mean height SDS (–2.01 vs –1.94), mean BMI (16.95 vs 15.53 kg/m^2), and bone age (6.39 vs 6.37 y) at baseline (**Table 2**).

EFFICACY

- The mean (SD) HV at Month 12 of the OLE was 7.98 (1.81) cm/y for the soma/soma treatment group and 8.23 (1.88) cm/y for the Geno/soma treatment group.
- The mean (SD) change in height SDS from the beginning of the OLE to Month 12 was +0.42 (0.33) for the soma/soma treatment group and +0.49 (0.33) for the Geno/soma treatment group.
- The soma/soma and Geno/soma treatment groups had similar mean height SDS (–1.46 vs –1.28), mean BMI (17.84 vs 17.58 kg/m^2), and mean bone age (8.29 vs 8.34 y) at Month 12 of the OLE (**Table 2**).
- An increase in bone maturation was observed from baseline to Month 12 for both the soma/soma and Geno/soma treatment groups, indicating continued bone maturation (**Table 2**).

SAFETY

- Mean IGF-1 SDS values were higher at Month 12 vs baseline, for both the soma/soma (1.14 vs 0.63) and Geno/soma (1.28 vs –0.70) treatment groups.
- Dose reductions due to IGF-1 SDS >2 were required in 19 (18.3%) of 104 subjects in the soma/soma treatment group and 25 (23.1%) of 108 subjects in the Geno/soma treatment group.
- Treatment-emergent adverse events (TEAEs) were reported in 71 (68.3%) and 87 (80.6%) subjects in the soma/soma and Geno/soma treatment groups, respectively; most (≥90%) TEAEs were mild to moderate in severity.
- The soma/soma treatment group had no discontinuations due to TEAEs whereas 6 discontinuations occurred in the Geno/soma treatment group.
- Across the 12 months of the OLE, mean glucose, HbA1c, FT4, TSH, and cholesterol (total, LDL, and HDL) values remained similar to baseline in both treatment groups.

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

	Soma/Soma Group[a] n=104	Geno/Soma Group[b] n=108	Total N=212
Age, mean (SD), y	8.89 (2.67)	8.69 (2.37)	8.79 (2.52)
Sex, n (%)			
Male	78 (75.00)	72 (66.67)	150 (70.75)
Female	26 (25.00)	36 (33.33)	62 (29.25)
Race, n (%)			
White	79 (75.96)	83 (76.85)	162 (76.42)
Black or African American	0	2 (1.85)	2 (0.94)
Asian	21 (20.19)	17 (15.74)	38 (17.92)
Other	4 (3.85)	6 (5.56)	10 (4.72)
Height, mean (SD), cm	119.87 (14.97)	119.44 (13.63)	119.65 (14.27)
Weight, mean (SD), kg	25.08 (8.35)	22.64 (6.72)	23.84 (7.65)
Target height SDS, mean (SD)	–0.88 (0.95)	–0.68 (1.01)	–0.78 (0.98)

[a] Subjects randomized to receive somatrogon in the main study.
[b] Subjects randomized to receive Genotropin in the main study.
OLE=open-label extension study; SD=standard deviation

Table 2. Efficacy and safety at baseline and Month 12 of the OLE

	Soma/Soma Group[a]				Geno/Soma Group[b]			
Mean (SD)[c]	OLE Baseline	n	OLE Month 12	n	OLE Baseline	n	OLE Month 12	n
Height velocity, cm/y	–	–	7.98 (1.81)	84	–	–	8.23 (1.88)	78
Height SDS	–2.01 (1.07)	103	–1.46 (0.87)	84	–1.94 (1.13)	108	–1.28 (0.78)	78
BMI, kg/m^2	16.95 (2.29)	104	17.84 (2.86)	91	15.53 (1.73)	108	17.58 (2.29)	81
IGF-1 SDS	0.63 (1.35)	102	1.14 (1.22)	82	–0.70 (1.07)	105	1.28 (1.16)	76
IGFBP-3 SDS	–0.05 (0.86)	103	0.27 (0.78)	83	– 0.71 (1.00)	106	0.41 (0.88)	76
Bone age, y	6.39 (2.76)	103	8.29 (3.08)	78	6.37 (2.68)	108	8.34 (2.95)	69
Bone maturation	0.70 (0.17)	103	0.80 (0.16)	78	0.71 (0.17)	108	0.82 (0.15)	69
Change in bone age relative to chronological age (SD)	–	–	1.78 (0.84)	68	–	–	1.64 (0.92)	66
Tanner stage, n (%)								
Tanner I	96 (93.20)	103	62 (77.50)	80	98 (90.74)	108	53 (72.60)	73
Tanner II	5 (4.85)	103	13 (16.25)	80	9 (8.33)	108	12 (16.44)	73
Tanner III	2 (1.94)	103	4 (5.00)	80	1 (0.93)	108	6 (8.22)	73
Tanner IV	–	–	1 (1.25)	80	–	–	2 (2.74)	73

[a] Subjects randomized to receive somatrogon in the main study.
[b] Subjects randomized to receive Genotropin in the main study.
[c] Unless otherwise stated.
Mean (SD) time between between dosing and IGF-1 sampling at OLE Month 12 was 3.54 (1.03) days for the soma/soma group and 3.52 (1.21) days for the Geno/soma group.

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