Effects on Near-Adult Height and Safety of Recombinant Human Growth Hormone in Patients with Growth Hormone Deficiency and Turner Syndrome: Results from the LG Growth Study

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INTRODUCTION

- LG Growth Study (LGS) has been conducted to evaluate the long-term safety and effectiveness of recombinant human growth hormone (rhGH) treatment in Korean children.

OBJECTIVE

- To evaluate effectiveness on near-adult height (NAH) and safety of rhGH (Eutropin® Inj., Eutropin®Plus Inj., and Eutropin®AQ Inj., LG Chem, Ltd.) treatment in children with growth hormone deficiency (GHD) and Turner syndrome (TS) as a subset of LGS.

METHODS

Study design

- A multi-center, long-term, and prospective cohort study

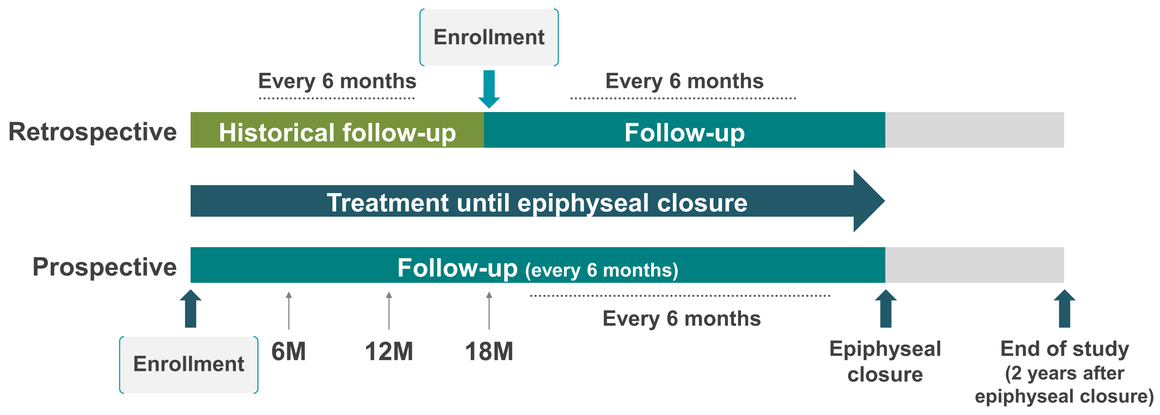


Figure 1. Study design

Study population

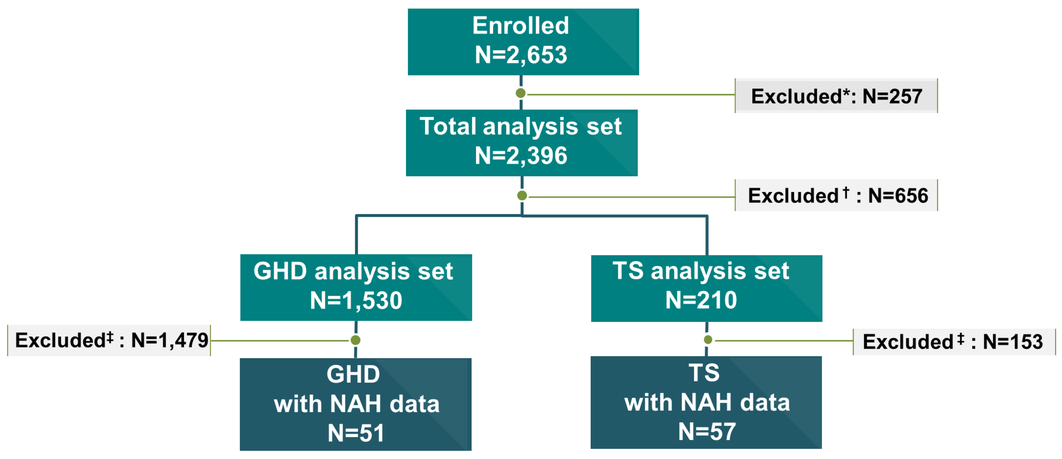
- Children ≥ 2 years of age with GHD and TS
- Written informed consent was obtained from the patients and their parents (or legal guardians)

Statistical analysis

- Interim analysis has been performed using a predefined method in GHD and TS patients who were enrolled from Jan. 2012 to Mar. 2018.
- The data on NAH (height (Ht) at ≥18 years of age, or height velocity (HV) <2 cm/year at ≥16 years for boys or ≥15 years for girls) and safety of rhGH were analyzed.

RESULTS

Patients disposition



*Not treated (N=102), No consent (N=152), others (N=3)
†Idiopathic short stature (N=363), small for gestational age (N=283), chronic renal failure (N=10)
‡Data was not met for the NAH definition.

Figure 2. Patients disposition

Clinical characteristics at baseline and NAH

Table 1. Patients characteristics (*N (%), mean* ± SD or median (min, max))

Treatment group	GHD (N = 51)	TS (N = 57)
Number of patients, Male/Female	29/22	0/57
At baseline		
Age, years	12.24 ± 3.01	10.79 ± 3.23
Bone age, years	10.45 ± 3.14	9.68 ± 2.81
Prepubertal	18 (35.3)	25 (43.9)
Ht Standard Deviation Score (SDS)	-2.80 ± 1.45	-3.51 ± 0.84
Weight SDS	-1.53 ± 1.32	-1.35 ± 1.13
Body Mass Index (BMI) SDS	-0.13 ± 1.21	0.61 ± 1.12
rhGH dose, mg/kg/week	0.24 (0.04, 0.82)	0.30 (0.18, 0.41)
Midparental Ht (MPH) SDS	-1.09 ± 0.88	-0.56 ± 0.83
MPH SDS, prepubertal subset	-0.86 ± 0.68	-0.52 ± 0.75

RESULTS (Cont'd)

Table 1. Patients characteristics (Cont'd) (*N (%), mean* ± SD (95% CI) or median (min, max))

Treatment group	GHD (N = 51)	TS (N = 57)
Difference between Ht SDS and MPH SDS	-1.97 ± 1.32 (-2.44, -1.51)	-2.86 ± 0.95 (-3.17, -2.55)
At NAH		
Age, years	18.43 ± 2.56	17.55 ± 1.63
Bone age, years	15.31 ± 1.15	14.77 ± 1.06
rhGH treatment duration, years	4.90 ± 2.66	5.33 ± 2.47
rhGH dose, mg/kg/week	0.24 (0.02, 0.86)	0.30 (0.18 ,0.41)
Difference between NAH SDS and MPH SDS	-0.22 ± 1.03 (-0.56, 0.11)	-1.72 ± 0.80 (-1.96, -1.49)

Effectiveness on NAH

- Ht SDS at NAH for GHD and TS patients were -1.29 ± 1.62 and -2.36 ± 0.92, respectively. In the subset of patients who initiated the rhGH treatment in the prepubertal stage (prepubertal subset), those were -1.34 ± 1.94 and -2.31 ± 0.91, respectively.
- A difference between NAH SDS and MPH SDS was -0.22 ± 1.03 (95% CI: -0.56 to 0.11) in GHD patients and -1.72 ± 0.80 (95% CI: -1.96 to -1.49) in TS patients. In the prepubertal subset, it was -0.29 ± 1.08 (95% CI: -0.89 to 0.31) and -1.64 ± 0.84 (95% CI: -2.03 to -1.26), respectively.
- The effectiveness on NAH was slightly higher in prepubertal subset patients than in total patients' groups.

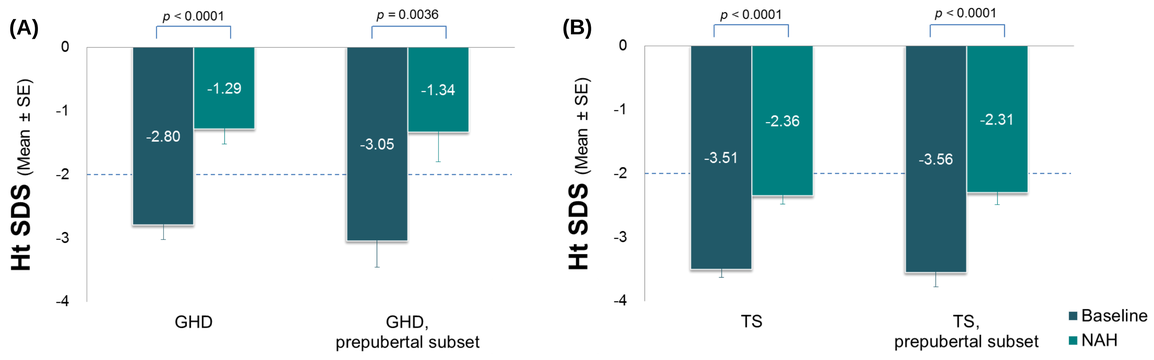


Figure 3. Ht SDS at baseline and NAH (A) GHD patients (B) TS patients

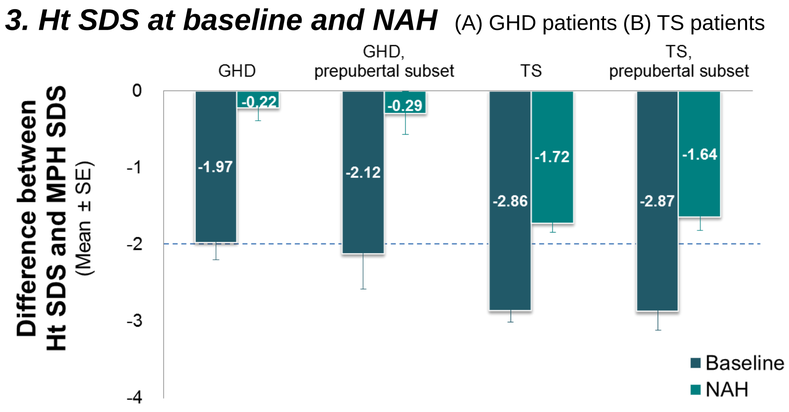


Figure 4. Difference between Ht SDS and MPH SDS at baseline and NAH

Adverse events

- Adverse events (AEs) were reported in 20 GHD patients (39.2%) and 28 TS patients (49.1%) and its intensity was mostly mild. The most common AEs were upper respiratory tract infection (9.3%) and headache (7.4%).
- Among AEs, 5 GHD patients' (9.8%) and two TS patients' (3.5%) AEs were considered to have a relationship with the rhGH treatment. Headache (1.9%) was the major ADR.
- Craniopharyngioma was recurred in two patients with GHD (3.9%) during rhGH treatment, although rhGH treatment started at least one year after surgery and there was no tumor on MRI before rhGH treatment.

Table 2. AEs occurred during GH treatment

Treatment group	GHD (N = 51)	TS (N = 57)
	Incidence rate [N, (%)]	
AE	20 (39.2)	28 (49.1)
ADR	5 (9.8)	2 (3.5)
SAE	6 (11.8)	4 (7.0)
SADR	2 (3.9)	0 (0.0)

AE, Adverse event; ADR, Adverse drug reaction; SAE, Serious AE; SADR, Serious ADR

CONCLUSIONS

- In the 6 years' interim results of LGS, rhGH treatment has increased the Ht SDS and reduced the gap between Ht SDS and MPH SDS at NAH in both patients with GHD and TS.
- There were no other significant AEs caused by rhGH treatment in GHD and TS patients, except for craniopharyngioma. These safety events should be closely monitored further to adjudicate the correlation between the events and medication.

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LGS LG Growth Study