Long-term safety and effectiveness of recombinant human growth hormone in Korean pediatric patients with growth disorders: 7-year interim analysis from LG Growth Study

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INTRODUCTION

- LG Growth Study (LGS) aimed to evaluate the long-term safety and effectiveness of recombinant human growth hormone (rhGH) treatment in Korean pediatric patients.

OBJECTIVE

- To evaluate long-term safety and effectiveness of rhGH (Eutropin® Inj., Eutropin®Pen Inj., Eutropin®Plus Inj., and Eutropin®AQ Inj., LG Chem, Ltd.) in pediatric patients with growth disorders including growth hormone deficiency (GHD), idiopathic short stature (ISS), Turner syndrome (TS), small for gestational age (SGA) and chronic renal failure (CRF).

METHODS

Study design

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

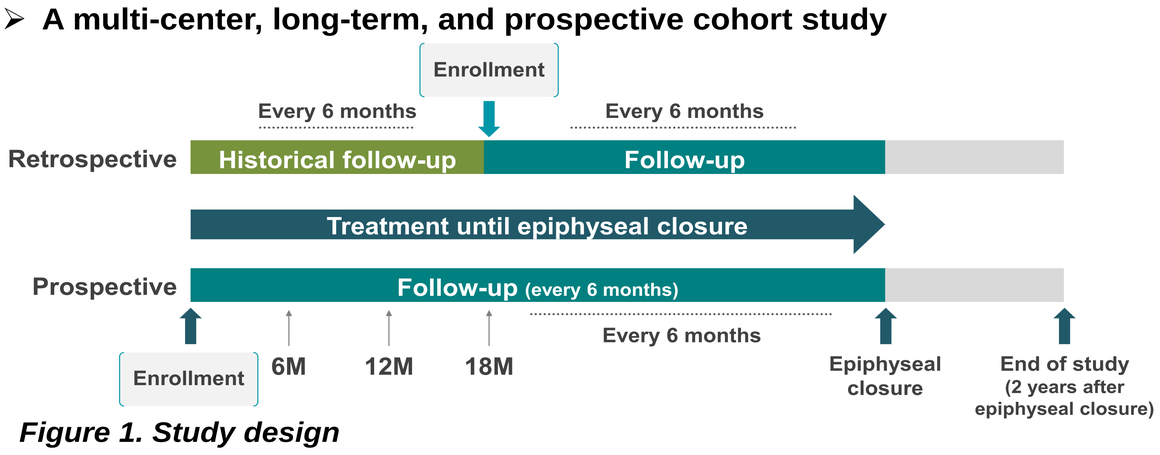


Figure 1. Study design

Study population

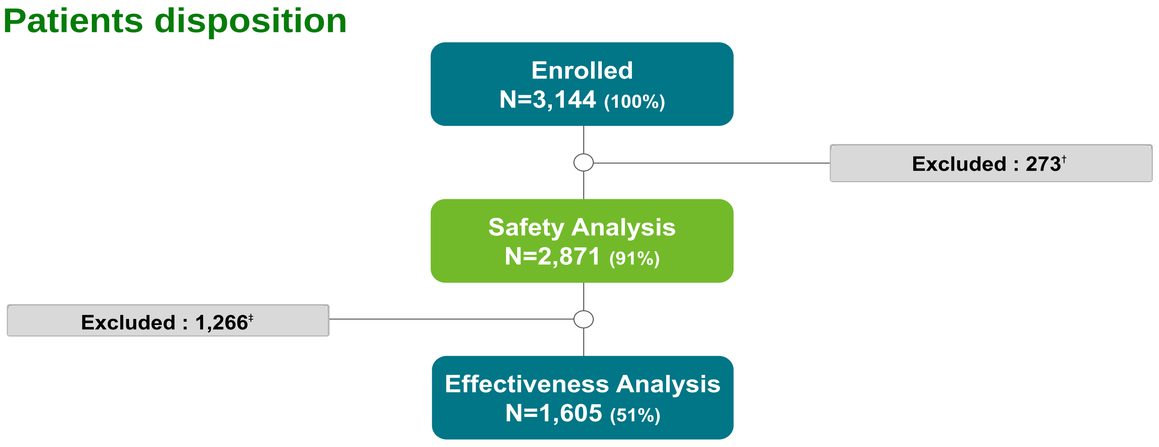
- Pediatric patients ≥ 2 years of age with GHD, ISS, TS, SGA and CRF
- Written informed consent from the patients and their parents (or legal guardians) was obtained.

Statistical analysis

- Interim analysis has been conducted on 7-year accumulated data (from Nov. 2011 to Feb. 2019) of LGS.
- All adverse events (AEs) were reported for safety, and the effectiveness was assessed by height velocity (HV), height standard deviation score (Ht SDS) and insulin like growth factor-1 (IGF-1).

RESULTS

Patients disposition



†Not treated (N=170), No consent(N=98), and other (N=5)
‡Patients with missed data or those who did not meet for the selection criteria

Figure 2. Patients disposition

Clinical characteristics at baseline

Table 1. Patients characteristics by indications (N (%) or mean ± (SD))

Total (N=2,871)		GHD (N=1,853)	ISS (N=426)	TS (N=235)	SGA (N=348)	CRF* (N=9)
Gender	Male (%)	1,084 (58.5)	221 (52.0)	0 (0.0)	181 (52.0)	6 (66.7)
	Female (%)	769 (41.5)	204 (48.0)	235 (100.0)	167 (48.0)	3 (33.3)
Chronological age (year)		7.8 (± 3.1)	8.2 (± 3.1)	8.5 (± 3.5)	6.7 (± 2.5)	8.0 (2.0, 13.0)
Bone age (year)		6.3 (± 3.2)	7.7 (± 3.4)	7.9 (± 3.3)	6.2 (± 2.9)	3.5 (1.5, 13.5)
BA - CA (year)		-1.8 (± 1.2)	-1.0 (± 1.4)	-0.9 (± 1.3)	-0.9 (± 1.1)	-1.4 (-4.9, 0.3)
Height SDS		-2.7 (± 0.8)	-2.5 (± 0.9)	-3.0 (± 0.9)	-2.6 (± 0.7)	-2.5 (-4.0, -0.4)
BMI SDS		-0.4 (± 1.2)	-0.7 (± 1.1)	0.4 (± 1.2)	-0.9 (± 1.2)	-0.5 (-2.0, 2.1)
Tanner Stage I**		615/733 (83.9)	136/200 (68.0)	128/152 (84.2)	102/125 (81.6)	2/2 (100.0)
Treatment Duration (year)		3.8 (± 2.5)	2.4 (± 1.9)	5.2 (± 3.0)	2.7 (± 1.7)	4.1 (0.7, 10.2)

* Data presented as N(%) or median (range) for CRF group
** Tanner stage I: Breast/Genital. Data presented as N/Total and included in the analysis only with the available data.

RESULTS (Cont'd)

Effectiveness on Height

- Height velocity was 8.9 ± 1.9, 8.7±1.6, 7.3±1.8, 9.0±1.6 and 8.3±2.1 cm/year at the first year of treatment in GHD, ISS, TS, SGA and CRF patients, respectively.
- A continuous improvement of height SDS was found in most patients regardless of their disease status, in particular, with a significant increase in height SDS from baseline to 4 years in patients with GHD (from −2.9±0.9 to −1.3±1.1, p<0.0001) and TS (from −3.2±0.8 to −2.2±0.8, p<0.0001).
- Total IGF-1 SDS was significantly increased (from −0.7±1.1 to 0.8±1.7 at 12 months, p<0.0001) and maintained within 0 to 2 SDS throughout the study period.

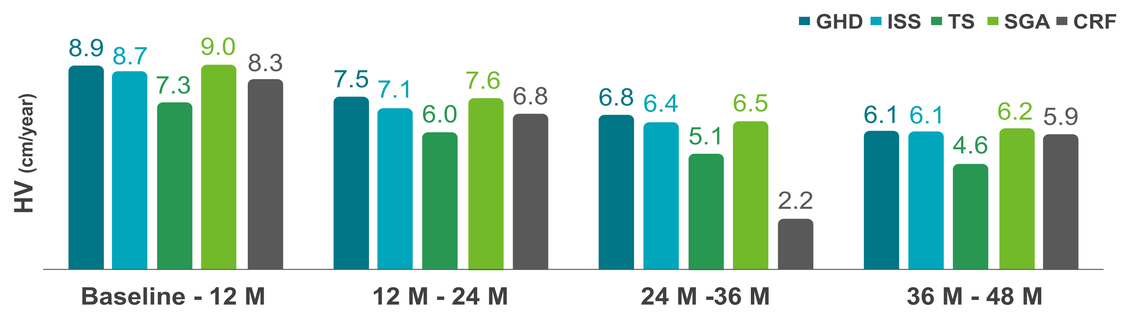
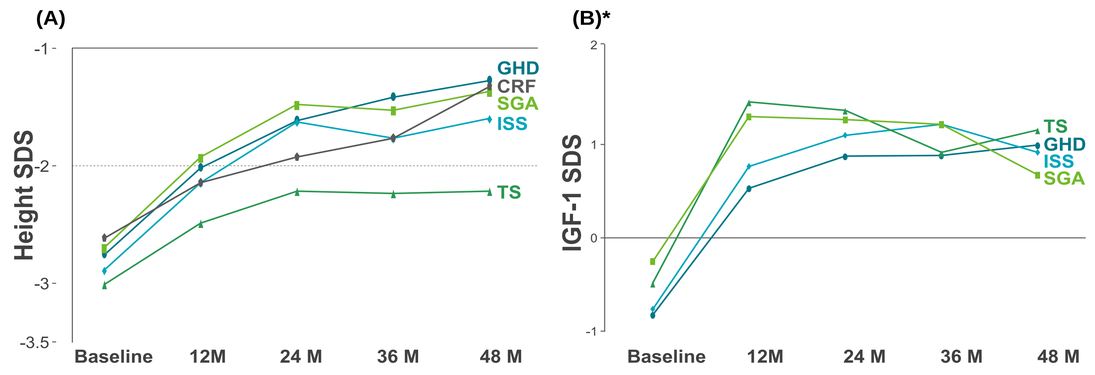


Figure 3. Change of Height velocity during 4 years of rhGH treatment



*Due to small sample size in CRF, the data for this group were not presented on the graph

Figure 4. Change in Height SDS (A) and IGF-1 SDS (B) during 4 years of rhGH treatment

Adverse events

- Adverse events (AEs) were reported in 894 (31.1%) patients, and most AEs were mild.
- Adverse drug reactions (ADRs) were reported in 163 (5.7%) patients, which included headache (0.9%), injection site pain (0.7%), scoliosis (0.6%), and hypothyroidism (0.4%).
- During the follow-up period, 27 neoplasms were reported in 24 (0.8%) patients. Most were benign and/or non-related to rhGH.
- Nine cases of Craniopharyngioma were found in 6 patients with organic GHD, all of them being recurrent cases.

Table 2. AEs occurred during rhGH treatment by indications

Safety set	Total (N=2,871)	GHD (N=1,853)	ISS (N=426)	TS (N=235)	SGA (N=348)	CRF (N=9)
	No. of subjects (%)					
AE	894 (31.1)	587 (31.7)	105 (24.7)	106 (45.1)	90 (25.9)	6 (66.7)
ADR	163 (5.7)	115 (6.2)	21 (4.9)	14 (6.0)	12 (3.5)	1 (11.1)
SAE	107 (3.7)	69 (3.7)	8 (1.9)	20 (8.5)	8 (2.3)	2 (22.2)
SADR	10 (0.4)	9 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)

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

CONCLUSIONS

- In the 7-year interim results of LGS, the incidence of AEs was low, and rhGH therapy was well-tolerated.
- During 4 years of rhGH therapy, significant improvement in height was confirmed in Korean pediatric patients with GHD and TS.

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LGS LG Growth Study

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GH and IGFs

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