COMPARISON OF ACTUAL GH DOSE WITH LABELED DOSE IN CHILDREN WITH SHORT STATURE BASED ON THE LG GROWTH STUDY

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INTRODUCTION

LG Growth Study (LGS)[1,2] is an open-label, multicenter, observational study which has begun in November 2011 to evaluate the long-term safety and effectiveness of recombinant human growth hormone (rhGH) treatment in Korean pediatric patients with growth disorders including growth hormone deficiency (GHD), idiopathic short stature (ISS), small for gestational age (SGA), Turner Syndrome (TS) and chronic renal failure (CRF).

AIM

This study aimed to analyze dosing patterns of recombinant human growth hormone (rhGH) (Eutropin® Inj.., Eutropin® Pen Inj., and Eutropin® AQ Inj. for daily injection, and Eutropin® Plus Inj. for weekly injection, LG Chem, Ltd.) using the collected data of the LG Growth Study (LGS).

METHOD

The LGS data collected until March 2020 was used for this analysis.

Actual GH dose was compared descriptively across indications and to labeled dose per each indication in Korea.

All reported adverse events (AEs) across indications were assessed.

Also the literary comparison of actual GH dose pattern with those from other observational studies in USA and European countries (NordiNet® IOS and ANSWER Program) was done.

RESULTS

During the 8-year study period, a total of 3,813 patients were enrolled, and dosing data from total 3,590 patients were used for this analysis.

Table 1. Baseline Characteristics by indication

Total N = 3,580		GHD (N=2,328)	ISS (N=523)	TS (N=246)	SGA (N=483)
Gender	Male (%)	1,360 (58.4)	272 (52.0)	0 (0.00)	260 (53.8)
	Female (%)	968 (41.6)	251 (48.0)	246 (100.0)	223 (46.2)
Chronological age (year)		7.7 (±3.7)	8.1 (±3.0)	8.5 (±3.5)	6.8 (±2.6)
Bone age (year)		6.3 (±3.1)	7.5 (±3.3)	7.9 (±3.3)	6.2 (±2.8)
BA-CA (year)		-1.8 (±1.1)	-1.1 (±1.4)	-0.9 (±1.3)	-1.0 (±1.1)
Height SDS		-2.6 (±0.8)	-2.4 (±0.9)	-3.0 (±0.9)	-2.5 (±0.6)
BMI SDS		-0.3 (±1.2)	-0.6 (±1.0)	0.3 (±1.2)	-0.8 (±1.1)
Tanner Stage I		934/1,086 (86.0)	193/266 (72.6)	141/166 (84.9)	190/226 (84.1)
Treatment Duration (year)		3.7 (±2.7)	2.5 (±2.0)	5.4 (±3.1)	2.7 (±1.9)

** The data from CRF patients was not presented due to its small number (N=10).*

In patients with GHD, a mean actual GH dose was slightly higher than its labeled dose for both daily and weekly injection products in Korea. However, the mean actual doses in ISS, SGA, and TS were less than those corresponding labeled/recommended doses.

Table 2. Labeled vs. Average GH Weekly dose during the full treatment period by indication

Mean GH dose (mg/kg/week)	GHD (N=1,888)	GHD (N=510)	ISS (N=431)	TS (N=238)	SGA (N=443)
	Daily	Weekly	Daily	Daily	Daily
Labeled dose	*0.17 ~ 0.21*	*0.50*	*0.37*	*0.33*	*0.24 ~ 0.48*
Actually used dose	0.24 (±0.05)	0.59 (±0.15)	0.26 (±0.06)	0.30 (±0.04)	0.28 (±0.06)

** The patients who had the data during the full treatment period were included in this analysis. The data from CRF patients was not presented due to its small number.*

The GH dosing pattern in LGS showed similar pattern as the other observational studies in USA and European countries[3] even though their clinical practice guideline or the recommended doses are different from Korea.

Figure 1. Average GH Daily dose by indication and country

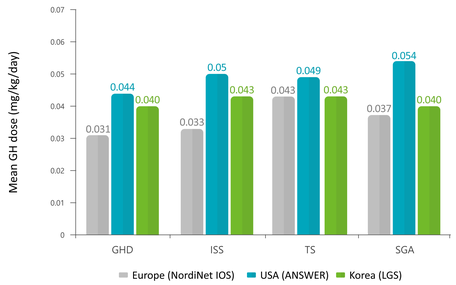

Table 3. Labeled vs. Average GH Daily dose by indication and country

Mean GH dose (mg/kg/day)		Europe (NordiNet IOS)	United States	Korea
GHD	*Labeled*	*0.025 ~ 0.035*	*0.024 ~ 0.034*	*0.028 ~ 0.035*
	Actual	0.031	0.044	0.040
ISS	*Labeled*	*Not approved*	*up to 0.067*	*0.062*
	Actual	0.033	0.050	0.043
TS	*Labeled*	*0.045 ~ 0.067*	*up to 0.067*	*0.047*
	Actual	0.043	0.049	0.043
SGA	*Labeled*	*0.035*	*up to 0.067*	*0.034 ~ 0.069*
	Actual	0.037	0.054	0.040

Among total 1,035 subjects who reported adverse events (AEs), there were 672 (28.9%) patients in GHD, 122 (23.3%) in ISS, 123 (25.5%) in SGA, and 112 (45.5%) in TS. Most of the reported AEs were mild in severity, and 5.3% of them were related with rhGH treatment.

Table 4. Safety Results by indication

	Total	GHD	ISS	TS	SGA
	No. of subject (%)				
Total N	3,580	2,328	528	246	483
AE (Adverse Event)	1,035 (28.8)	672 (28.9)	122 (23.3)	112 (45.5)	123 (25.5)
ADR (Adverse Drug Reaction)	190 (5.3)	127 (5.5)	27 (5.2)	15 (6.1)	20 (4.1)
SAE (Serious Adverse Event)	126 (3.5)	80 (3.4)	12 (2.3)	20 (8.1)	12 (2.5)
SADR (Serious Adverse Drug Reaction)	11 (0.3)	9 (0.4)	1 (0.2)	1 (0.4)	0 (0.0)

** The data from CRF patients was not presented due to its small number (N=10).*

Even though the actual dose per each indication was lower or higher than the labeled dose, there was no correlation between the dosing pattern and the incidences of AEs including ADRs or SAEs.

CONCLUSIONS

In this study, GHD pediatric patients received a slightly higher doses than labeled recommendations while patients with ISS, SGA and TS were treated with lower doses of GH than the labeled dose.

And the incidence rate of AEs was not correlated with the dosing pattern across the indications.

REFERENCES

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