Long-term safety and effectiveness of daily and weekly growth hormone treatment in pediatric GHD patients (4-years' results)

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BACKGROUND

- The weekly sustained-release growth hormone (GH) has been approved for treatment in growth hormone deficiency (GHD) in Korea.
- It provides a practical strategy for improving adherence and convenience to GH treatment.
- LG Growth study (LGS) has been conducted to evaluate the safety and effectiveness of GH treatment among patients in Korea and the 4-year's interim analysis results are presented here.

OBJECTIVE

- To evaluate the long-term safety and effectiveness of two formulations of daily (Eutropin®) and weekly (EutropinPlus®) GH in Korean pediatric GHD patients.

METHODS

Study design

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

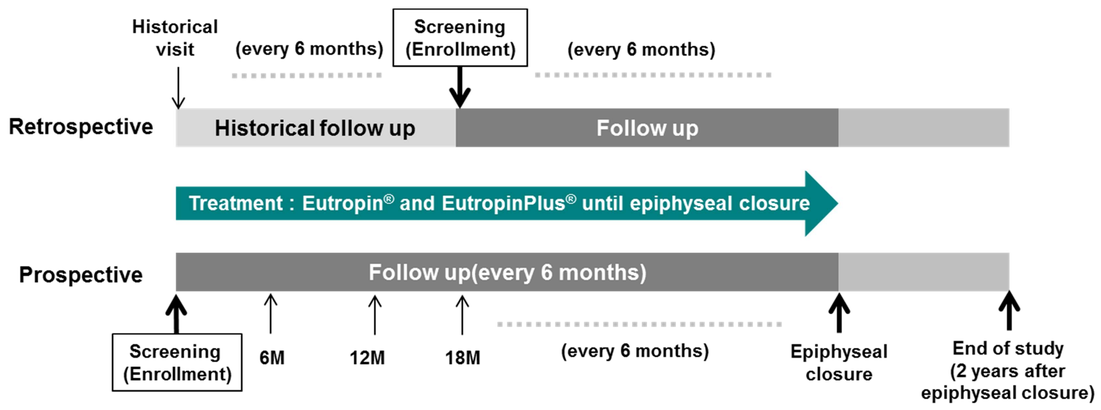


Figure 1. Study design

Study population

- Pediatric patients aged ≥ 2 years with GHD
- Written informed consent from the patients, their parents or legal guardians

Endpoints

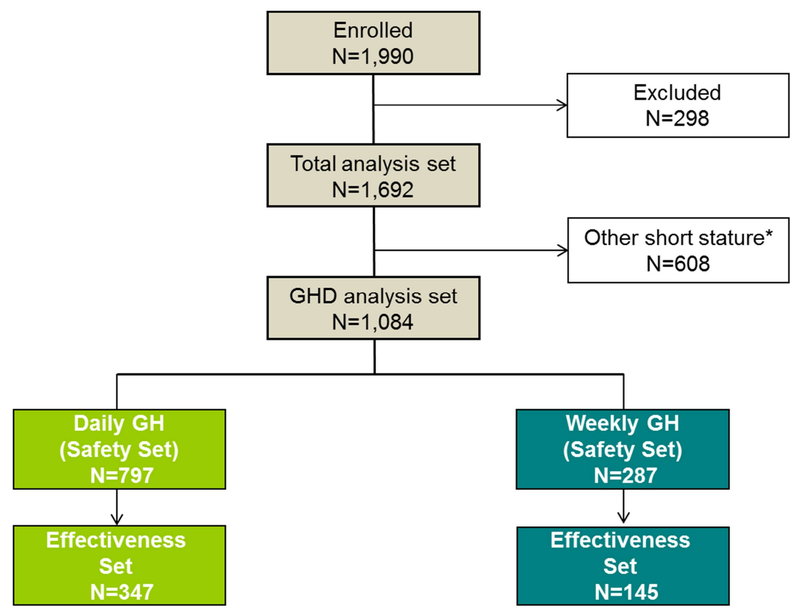
- Effectiveness endpoints: Height Velocity (HV), ΔHeight SDS
- Safety endpoints: IGF-I SDS, Adverse events

Statistical analysis

- Statistical analysis has been conducted annually using a pre-defined method. This 4-year's analysis was for patients who were enrolled from Jan 2012 to Mar 2016.

RESULTS

Subject disposition



* Idiopathic Short Stature(n=276), Turner Syndrome(n=187), Small For Gestational Age(n=138), Chronic Renal Failure(n=7)

Figure 2. Subject disposition

RESULTS(Cont'd)

Baseline characteristics

Table 1. Baseline characteristics

Treatment group (Safety set)	GHD (N=1,084)	Daily (N=797)	Weekly (N=287)
Male	643 (59.3%)	465 (58.3%)	178 (62.0%)
Age(year)	8.13 ± 3.15	7.85 ± 3.08	8.90 ± 3.21*
Bone age(year)	6.62 ± 3.19	6.35 ± 3.14	7.33 ± 3.23*
Height(cm)	116.39 ± 16.24	114.90 ± 16.08	119.92 ± 16.11*
Weight(Kg)	23.88 ± 9.59	23.04 ± 9.63	25.94 ± 9.17*
Height SDS	-2.37 ± 0.76	-2.35 ± 0.77	-2.42 ± 0.72
Weight SDS	-1.66 ± 1.27	-1.65 ± 1.22	-1.64 ± 1.37
BMI SDS	1.14 ± 2.22	1.02 ± 2.06	1.44 ± 2.56*
Height Velocity**(cm/year)	5.12 ± 12.09	4.16 ± 12.84	6.68 ± 10.45

* P<0.05 vs. Daily (Eutropin®), ** Effectiveness Set

Effectiveness

- Height Velocity (HV) and ΔHeight SDS were not significantly different between groups.

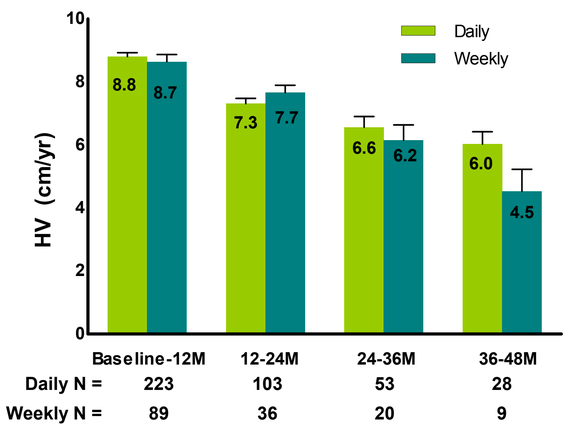


Figure 3. Change of HV

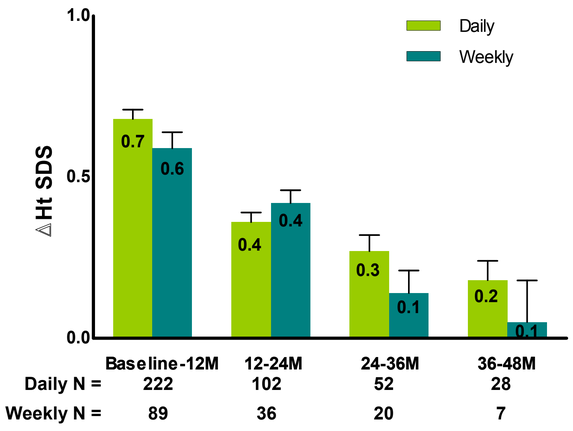


Figure 4. Change(Δ) Height SDS

Safety

- IGF-I SDS ranged from 0 to +2 after 12 months of GH treatment.
- Adverse events (AE) were reported in 17.1% and 15.4% in daily and weekly group, respectively, and most of them were mild.
- Safety results were similar with KIGS study result when it was analyzed by event per person-years.

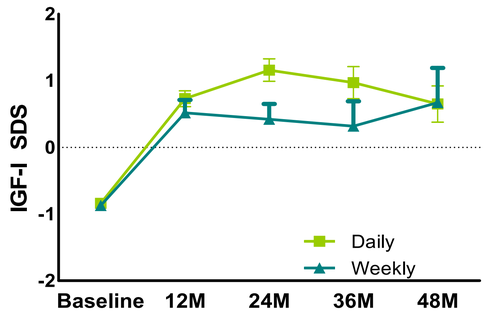


Figure 5. IGF-I SDS

Table 2. Adverse events occurred during GH treatment

Treatment group (Safety set)	No. of subject (%)		
	GHD (N=1,084)	Daily (N=861)*	Weekly (N=376)*
AE	199 (18.4%)	147 (17.1%)	58 (15.4%)
ADR	44 (4.1%)	29 (3.4%)	15 (4.0%)
SAE	27 (2.5%)	15 (1.7%)	12 (3.2%)
SADR	4 (0.4%)	3 (0.4%)†	1 (0.3%)‡

* Subjects who were injected with both daily and weekly formulation were counted in both group
† : Arrhythmia, Craniopharyngioma, Neoplasm recurrence, ‡ : Autoimmune thyroiditis
AE. Adverse events; ADR, Adverse drug reactions; SAE, Serious AE; SADR Serious ADR

Table 3. Adverse events occurred during GH treatment

Safety	AEs / 100,000 Treatment year			
	GHD (N=1,084)	Daily (N=861)	Weekly (N=376)	KIGS* (N=56,123)
AE	10,567	10,745	10,102	10,313

*Ranke MB, Price DA, Reiter EO(eds) : Growth hormone therapy in pediatrics – 20 years of KIGS. Basel, Karger, 2007, pp 432-441

CONCLUSION

- The growth response to weekly GH remained effectively during 4 years and it is comparable to daily GH in GHD. Weekly GH showed a similar profile to daily GH formulation without special safety concerns when used in GHD patients for 4 years.
- Weekly formulation of GH improves compliance with once weekly injection, but also, it has similar effectiveness and safety with daily formulation in GHD children. It can provide a great benefit to patients requiring long-term administration of GH.

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Late Breaking

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