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Growth hormone treatment in most frequent skeletal dysplasias: Short-term results from KIGS

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Introduction

Pfizer International Growth Database (KIGS) contains data from 83 803 patients treated with rhGH of which 748 are diagnosed with a specified or unspecified skeletal dysplasia including hypochondroplasia (Hch, n=238: F=111, M=127), achondroplasia (Ach, n=113: F=51, M=62) and Leri-Weill dyschondrosteosis (LWD, n=88: F=59, M=29). Hch, Ach and LWD are non-approved indications for GH treatment. KIGS primary objective was to assess the safety of rhGH as used to treat pediatric patients in daily clinical practice according to the marketing authorization or as prescribed by the clinical practice of the treating physician/KIGS investigator, with the known limitations of observational surveillance studies.

Objective

To describe the 1st year response in height and body proportions to GH treatment in Hch, Ach and LWD. Only children who remained prepubertal during the first year of treatment were considered. SDS conversion were based on growth references of Prader[1] (height and sitting height) and Fredriks[2] (relative sitting height).

Results

The Table summarizes the findings. Median and 10th to 90th centile distribution is given. The percentage of children with a 1st yr height gain > 0.7 SDS were for Hch, Ach and LWD 27% (n=30), 18% (n=10) and 47% (n=14), respectively. There were no difference in change of relative sitting height, however a tendency to increase in the Ach group was observed (delta of 1.0, p=0.08, n=26).

	Hypochondroplasia		Achondroplasia		Leri-Weill dyschondrosteosis	
	n	median (p10 to p90)	n	median (p10 to p90)	n	median (p10 to p90)
Age at start (yrs)	110	7.8 (3.5 to 10.9)	56	5.3 (1.9 to 10.4)	30	9.1 (4.8 to 11.9)
Height						
at start (SDS)	110	-3.8 (-4.7 to -2.9)	56	-5.5 (-7.2 to -4.1)	30	-2.8 (-3.9 to -2.0)
first year gain (Δ SDS)	110	0.5 (0.2 to 1.1)	56	0.4 (-0.3 to 1.2)	30	0.6 (0.4 to 1.1)
Sitting height & relative sitting height						
first year change in sitting height (Δ SDS)	37	0.6 (-0.1 to 1.1)	26	0.4 (-0.3 to 1.6)	13	0.7 (0.0 to 1.0)
relative sitting height at start (SDS)	43	5.4 (2.0 to 8.4)	26	13.5 (9.1 to 17.5)	15	4.0 (2.6 to 4.2)
first year change in relative sitting height (Δ SDS)	37	0.1 (-1.6 to 1.0)	26	1.0 (-1.7 to 3.5)	13	-0.1 (-1.1 to 0.6)
Mean GH dose first year (µg/kg/day)	110	36 (24 to 52)	56	48 (24 to 66)	30	39 (23 to 52)

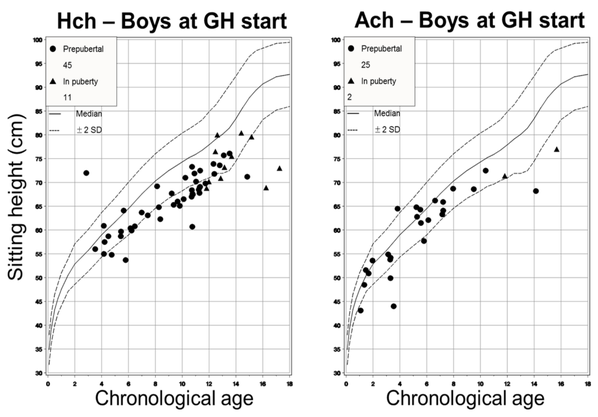

Figure 1: Absolute sitting height in boys with Hch and Ach at start of rhGH treatment. Normal population data showing mean ± 2 SD. Sitting height is generally within the lower, normal range both in Ach and Hch.

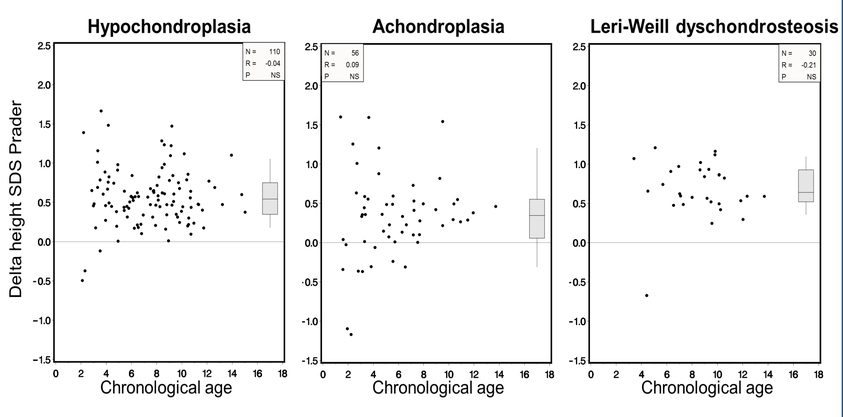

Figure 2: First year GH-treatment response as delta height SDS in children still prepubertal as a function of age. Scatter and box plot (10; 25; 50; 75 and 90 percentiles).

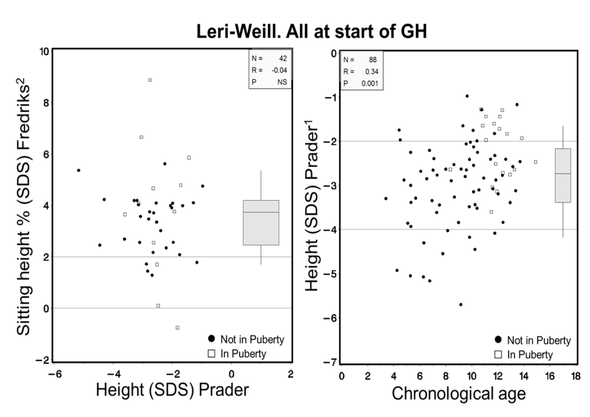

Figure 3: Body proportion and Ht for children with LWD at baseline. Left, "Relative sitting height" SDS in relation to height SDS; Normal limit at 2 SDS shown. Right, height SDS in relation to age (minus 2 and 4 SDS levels shown).

Safety

Reported Serious Adverse Events (SAE) for the 3 patients groups were: Hch: oral discomfort and appendectomy; Ach: gastrointestinal pain, femur fracture, shunt occlusion, headache and hydrocephalus; LWD: scoliosis and limb asymmetry. One SAE reported in Hch was related to therapy (not recovered). All Ach SAEs were not related to therapy as reported by the investigators and 2 patients did not recovered. In LWD the 2 SAEs were related to GH therapy as reported by the investigators and the patients have not recovered at that time.

Conclusions

- Response to GH treatment is at average poor for all three diagnoses but several individuals attained a first year delta height of 1 SDS or more.
- Body disproportion in Hch and LWD was unchanged by rhGH treatment but possibly increased in Ach.

References:
1. Prader A et al. Physical growth of Swiss children from birth to 20 years of age. First Zurich longitudinal study of growth and development. Helv Paediatr Acta Suppl. 1989 Jun;52:1-125.
2. Fredriks AM et al. Nationwide age references for sitting height, leg length, and sitting height/height ratio, and their diagnostic value for disproportionate growth disorders. Arch Dis Child. 2005

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Syndromes : Mechanisms and Management

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