Adult height in children born small for gestational age and treated with GH: Data from the French KIGS database

Michel Polak[a], Paul Czernichow[a] on behalf of the French KIGS (Pfizer International Growth Database) study physicians

[a] *Service d'endocrinologie gynécologie et diabétologie pédiatriques, INSERM U1016 ,affilié IMAGINE, hôpital universitaire Enfants Malades, université Paris Descartes, Paris, France*

Disclosure Statement

INTRODUCTION

Human recombinant growth hormone (GH) is an approved treatment in promoting catch-up growth in children born small for gestational age (SGA) with persistent short stature. Treatment of SGA children with GH increases height velocity (HV) but data on adult height (AH) are still scarce.

Following French authorities' request, the aim of the present study was to report AH in a group of SGA children treated with GH.

PATIENTS AND METHODS

This is a post-marketing longitudinal analysis of SGA children treated with GH after Genotropin® (somatropin, Pfizer, Inc) was indicated in SGA in France.

Patient data were retrieved from the KIGS database. KIGS was established in 1987 as a worldwide pharmaco-epidemiologic registry to monitor outcomes and safety of Genotropin® treatment in children with short stature. KIGS is conducted in accordance with the World Medical Association Declaration of Helsinki.

Selection criterion of study centers were all KIGS centers in France with at least one child having possibly reached AH in 2013.

Selection criteria of children were SGA children included in France, having started Genotropin® after April the 04th, 2005 and having reached AH.

Two populations of analysis were defined:

1. First population: all children having reached AH according to the physicians.
2. Second population: all children with birth height ≤ -2 standard deviation score (SDS), documented data at inclusion and after 1 year of GH treatment and, having reached AH according to a scientific committee (SC) (the 2 authors). AH was defined as: CA > 12 years at the last visit and HV < +0.5 SDS for CA at the last visit or at time of somatropin withdrawal. If HV was missing, CA should be ≥ 18 years at the time of somatropin withdrawal.

All data were checked by a study nurse to confirm with the physician whether the child had effectively reached AH or not. Those data were also independently reviewed by the SC to define children with AH.

Height were converted to SDS adjusted for CA and sex from standard anthropometric data in the French general population, published by Sempé *et al* [Sempé *et al, 1979*]. Children target height was calculated using Tanner's formula [Tanner *et al*, 1970; Karlberg *et al*, 1990].

Median values (25th; 75th percentiles) are shown. Data are displayed by population of analysis and sex.

RESULTS

A total of 74 centers were included in the study corresponding to 432 SGA children including 103 (23.8%) lost-to-follow-up children. Overall, 132 (30.6%) SGA children had reached AH according to the physicians and 8 lost to follow-up children had potentially reached their AH.

Out of the 432 children, 73 (16.9%) children were regarded as having reached AH by the SC including 54 (38.6%) children out of the 140 potentially at AH according to the physicians.

Characteristics of the patients at birth

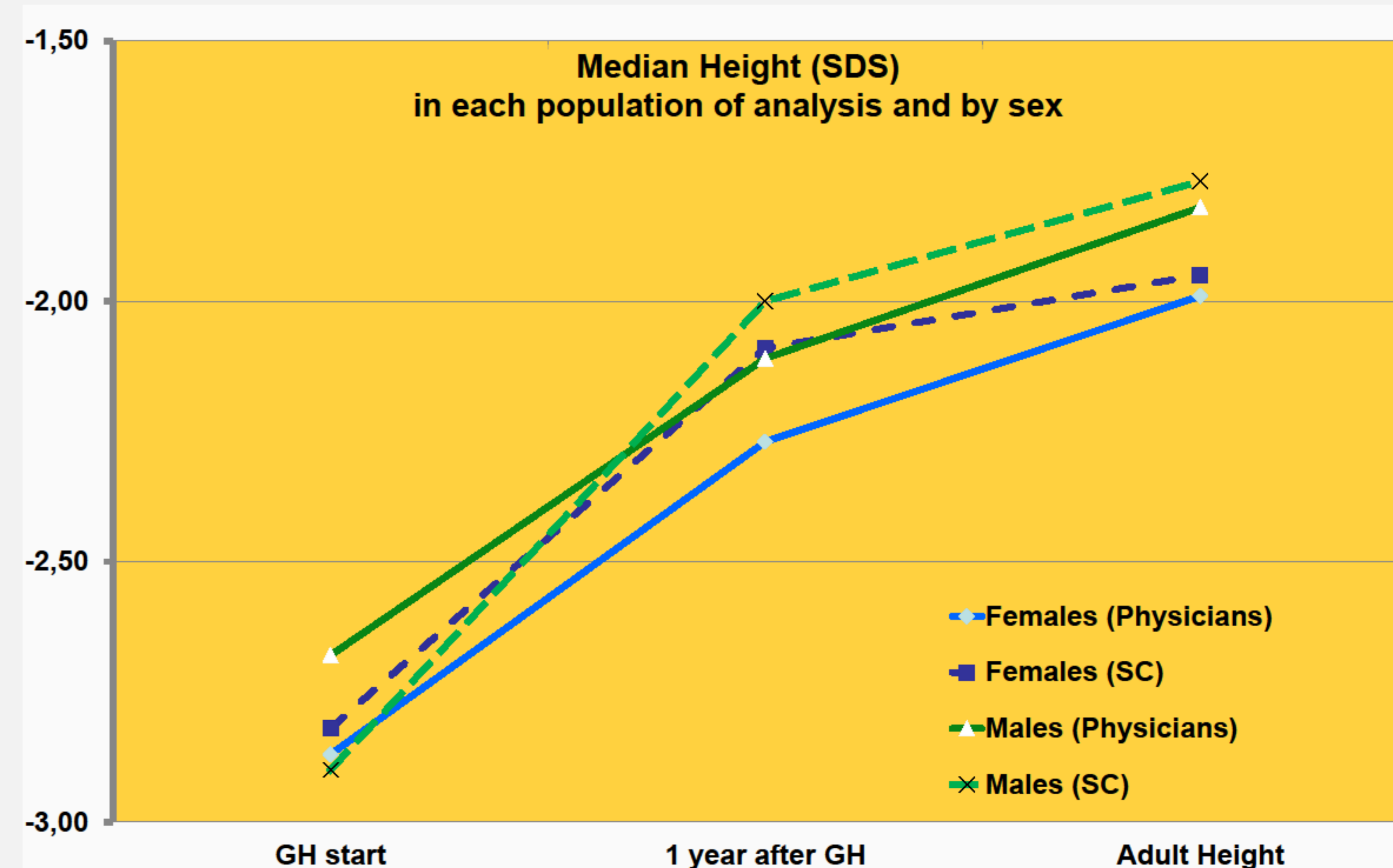|	AH according to the physicians (n=140)		AH according to the SC (n=73)	
	Females	**Males**	**Females**	**Males**
n (% of patients)	72 (51.4%)	68 (48.6%)	39 (53.4%)	34 (46.6%)
Height at birth (cm)	44.0 (42.5; 45.5)	45.0 (41.8; 46.0)	45.0 (42.5; 45.5)	44.5 (41.5; 46.0)
Height at birth (SDS)	-3.12 (-3.68; -2.74)	-3.00 (-3.68; -2.54)	-3.11 (-3.68; -2.81)	-3.00 (-3.95; -2.54)
Birth height < -2 SDS	66 (94.3%)	62 (96.9%)	38 (97.4%)	34 (100.0%)
Weight at birth (kg)	2.29 (1.94; 2.48)	2.34 (1.82; 2.70)	2.35 (2.08; 2.60)	2.37 (1.86; 2.64)
Weight at birth (SDS)	-2.40 (-2.96; -1.80)	-2.05 (-2.81; -1.58)	-2.12 (-2.61; -1.48)	-2.02 (-2.56; -1.55)
Gestational age (weeks)	39 (37; 40)	39 (37; 40)	39 (37; 40)	39 (37; 40)
Father height (cm)	170 (166; 173)	170 (166; 173)	169 (165; 175)	170 (163; 173)
Mother height (cm)	157 (153;160)	158 (154; 161)	157 (153; 162)	159 (155; 163)

AH: Adult Height, CA: Chronological Age; SC: Scientific Committee, SDS: Standard Deviation Score

Start of GH

	AH according to the physicians (n=140)		AH according to the SC (n=73)	
	Females	**Males**	**Females**	**Males**
CA (years)	10 (7; 12)	10 (7; 13)	10 (6; 11)	7 (4; 11)
Puberty (> P2 and/or B2 or G2)	20 (32.3%)	10 (18.9%)	7 (21.2%)	2 (9.1%)
Height (cm)	122.0 (106.5; 34.0)	124.5 (106.0; 136.0)	119.7 (104.5; 131.7)	109.3 (94.0; 120.5)
Height (SDS)	-2.87 (-3.20; -2.31)	-2.68 (-3.06; -2.39)	-2.82 (-3.09; -2.21)	-2.90 (-3.38; -2.33)
HV (cm/year)	4.9 (4.3; 5.7)	5.2 (4.0; 6.9)	5.11 (4.52; 6.04)	5.36 (3.92; 5.98)
HV (SDS)	-0.62 (-2.04; -0.02)	-0.49 (-1.40; +0.74)	-1.03 (-1.98; +0.01)	-0.95 (-1.81; -0.04)
Target Height (cm)	157 (154; 161)	170 (167; 174)	156 (153; 162)	171 (166; 173)
Target Height (SDS)	-1.11 (-1.73; -0.39)	-0.83 (-1.33; - 0.17)	-1.38 (-1.91; -0.30)	-0.67 (-1.42; -0.33)
Δ height at GH start and target height (SDS)	-1.54 (-2.27; -1.00)	-2.01 (-2.72; -1.44)	-1.42 (-2.36; -0.83)	-2.00 (-2.78; -1.44)
First prescribed GH dose (mg/kg.day)	0.054 (0.042; 0.061)	0.054 (0.036; 0.064)	0.054 (0.040; 0.059)	0.060 (0.042; 0.067)

Adult Height

	AH according to the physicians (n=140)		AH according to the SC (n=73)	
	Females	**Males**	**Females**	**Males**
CA in 2013 (years)	19 (18; 20)	19 (18; 21)	19 (17; 20)	19 (18; 20)
Puberty : n (%)	55 (98.2%)	49 (100.0%)	39 (100.0%)	34 (100.0%)
Height (cm)	150.3 (146.0; 153.0)	162.0 (159.3; 165.5)	150.3 (146.0; 152.0)	161.8 (156.7; 165.0)
Height (SDS)	-1.99 (-2.72; -1.60)	-1.82 (-2.33;-1.18)	-1.95 (-2.71; -1.66)	-1.77 (-2.25; -0.96)
Δ between AH and target height (SDS)	-1.02 (-1.88; -0.35)	-0.93 (-1.65; -0.25)	-0.65 (-1.92; -0.28)	-0.68 (-1.73; +0.17)
AH > - 2 SDS: n (%)	36 (50.0%)	37 (54.4%)	22 (56.4%)	20 (58.8%)
Total duration of GH treatment (years)	4.3 (2.5; 7.1)	5.6 (3.9; 9.3)	4.7 (2.9; 7.4)	8.4 (5.6; 10.7)

Median Height (SDS) in each population of analysis and by sex

Legend: Females (Physicians); Females (SC); Males (Physicians); Males (SC). X-axis: GH start, 1 year after GH, Adult Height. Y-axis: -1,50 to -3,00.

Safety

No new safety concern was reported during the follow-up.

CONCLUSION

In a group of children with severe growth retardation at birth, GH treatment enabled an AH slightly lower than the target height. More than 50% of the SGA children reached an AH > - 2 SDS.