



# First-year growth response to growth hormone as a predictor of poor final height outcome in children with idiopathic growth hormone deficiency

S. Straetemans<sup>1,2,3</sup>, M. Thomas<sup>3</sup>, S. Tenoutasse<sup>3,4</sup>, J. De Schepper<sup>3,5,6</sup>, R. Rooman<sup>3</sup>  
and the members of the Belgian Study Group for Pediatric Endocrinology (BSGPE)

1. Department of Pediatric Endocrinology, University Hospital Maastricht, The Netherlands
2. Department of Pediatric Endocrinology, University Hospital Antwerp, Antwerp, Belgium
3. The Belgian Study Group for Pediatric Endocrinology (BSGPE), Belgium
4. Department of Pediatric Endocrinology, University Children's Hospital HUDE, Brussels
5. Department of Pediatric Endocrinology, University Hospital Ghent, Ghent, Belgium
6. Department of Pediatric Endocrinology, University Hospital Brussels, Brussels, Belgium

## 1. Background / Aim

Several definitions of poor growth response to first-year growth hormone (GH) treatment have been proposed based on the observed response in large patient groups. Since a complete compensation of the height deficit is expected in children with idiopathic GH deficiency (iGHD) treated with GH, we have evaluated the different parameters for the first-year growth response as a predictor of the adult height gain in children with iGHD.

## 2. Subjects and methods

Height data at start, after one year of GH treatment, and at near final adult height\* (nFAH) of 142 children (93 boys) with iGHD were retrieved from the National Database of the Belgian Study Group for Pediatric Endocrinology. All included patients had been treated with GH for at least 4 consecutive years with at least one year before pubertal onset. First-year change in height ( $\Delta$ Ht) SDS, first-year height velocity (HV) SDS and total height SDS gain from start of GH treatment to nFAH (total  $\Delta$ Ht SDS) were calculated. A poor final growth outcome was defined as total  $\Delta$ Ht  $<1$ SDS. ROC-curve analysis was used to find the optimal cut off probability of first-year  $\Delta$ Ht SDS and HV SDS with regard to the sensitivity and specificity.

\*nFAH= HV $<2$ cm/year (yr) + chronological age  $>17$ yr in boys and  $>15$ yr in girls or skeletal age  $>16$ yr in boys and  $>14$ yr in girls

## 3. Results

	Characteristics:											
	background, at GH start, after first year, at nFAH											
	total group				combined GHD				isolated GHD			
	n	median	p10	p90	n	median	p10	p90	n	median	p10	p90
<b>background</b>												
birth weight, SDS	136	-0,66	-2,28	0,82	41	-0,56	-2,21	0,44	95	-0,69	-2,45	0,98
birth length, SDS	121	-0,88	-2,41	1,04	36	-0,85	-2,27	0,63	85	-0,95	-2,53	1,05
father height, SDS	138	-1,20	-2,55	0,02	42	-1,05	-2,31	0,55	96	-1,35 <sup>2</sup>	-2,70	-0,20
mother height, SDS	138	-1,11	-2,65	0,24	42	-0,76	-3,28	0,69	96	-1,28	-2,63	0,21
MPH, SDS	138	-1,24	-2,40	-0,09	42	-0,92	-2,45	0,49	96	-1,39 <sup>2</sup>	-2,40	-0,30
maximum GH peak, $\mu$ g/l	142	4,6	1,2	8,6	42	2,9	1,1	6,0	100	5,8 <sup>1</sup>	1,8	8,8
<b>at start GH treatment</b>												
age, years	142	7,1	2,3	11,0	42	5,8	1,8	9,9	100	7,5 <sup>3</sup>	2,7	11,2
height, SDS	142	-3,42	-5,01	-2,50	42	-3,68	-5,71	-2,42	100	-3,37 <sup>3</sup>	-4,55	-2,61
height SDS - MPH SDS	138	-2,34	-3,97	-0,93	42	-2,88	-5,07	-1,23	100	-2,16 <sup>1</sup>	-3,08	-0,76
weight, SDS	136	-2,71	-5,12	-1,38	39	-2,91	-6,28	-1,08	97	-2,63	-4,89	-1,43
BMI, SDS	128	-0,31	-1,97	0,90	35	-0,04	-1,73	1,21	93	-0,37	-1,99	0,78
GH dose, $\mu$ g/kg.day	136	27,3	22,1	36,4	39	27,6	22,0	39,2	97	27,3	22,2	36,4
<b>after 1 year GH treatment</b>												
height, SDS	142	-2,57	-3,63	-1,64	42	-2,36	-4,12	-1,03	100	-2,62	-3,60	-1,66
height SDS - MPH SDS	138	-1,26	-2,64	-0,13	42	-1,60	-3,39	-0,18	96	-1,16 <sup>3</sup>	-2,38	-0,04
<b>at nFAH</b>												
age, years	142	17,4	14,9	19,3	42	17,9	15,9	19,3	100	17,1 <sup>3</sup>	14,8	19,3
duration GH therapy, years	142	9,6	5,2	13,7	42	10,7	7,1	15,0	100	8,8 <sup>2</sup>	5,0	13,6
duration GH therapy before puberty, years	140	5,2	1,8	9,2	42	6,7	2,7	10,6	98	4,4 <sup>2</sup>	1,5	8,6
nFAH, SDS	142	-1,69	-3,26	-0,17	42	-1,36	-2,88	0,20	100	-1,79 <sup>3</sup>	-3,30	-0,26
BMI, SDS	132	-0,02	-1,83	1,32	42	0,11	-1,63	1,32	90	-0,07	-1,93	1,30

MPH = midparental height; GH= growth hormone; BMI= body mass index; nFAH= near-final adult height  
p-values for comparison of combined and isolated GHD: <sup>1</sup>p<0,001; <sup>2</sup>p<0,01; <sup>3</sup>p<0,05

	First-year responses to GH treatment											
	total group											
	total group				combined GHD				isolated GHD			
	n	median	p10	p90	n	median	p10	p90	n	median	p10	p90
$\Delta$ height SDS <sup>a</sup>	142	0,76	0,34	1,74	42	1,21	0,48	2,81	100	0,67 <sup>1</sup>	0,28	1,56
HV, cm/year	142	9,4	7,0	13,6	42	11,8	7,9	15,6	100	8,9 <sup>1</sup>	6,9	12,4
HV, SDS	119	2,57	0,83	6,39	34	4,06	1,51	7,95	85	2,36 <sup>1</sup>	0,71	5,02
HV for 1 <sup>st</sup> year GH treatment <sup>b</sup> , SDS	135	0,25	-0,77	1,54	41	0,65	-0,62	1,90	94	0,00 <sup>1</sup>	-0,86	1,26
$\Delta$ BMI SDS <sup>c</sup>	135	-0,18	-1,23	0,42	39	-0,55	-1,27	0,11	96	0,10 <sup>1</sup>	-1,09	0,52

HV= height velocity; GH= growth hormone; BMI= body mass index  
<sup>a</sup>gain in height SDS after first-year GH treatment, <sup>b</sup>KIGS growth targets for first-year GH response; <sup>c</sup>gain in BMI SDS after first-year GH treatment  
p-values for comparison of combined and isolated GHD: <sup>1</sup>p<0,001; <sup>2</sup>p<0,01; <sup>3</sup>p<0,05

	Final outcome after GH treatment											
	total group											
	total group				combined GHD				isolated GHD			
	n	median	p10	p90	n	median	p10	p90	n	median	p10	p90
<b>nFAH (all), SDS</b>	142	<b>-1,69</b>	-3,26	-0,17	42	-1,36	-2,88	0,20	100	-1,79 <sup>3</sup>	-3,30	-0,26
nFAH (males), cm	93	169,2	159,0	178,4	31	172,3	161,7	182,4	62	168,5	158,0	175,4
nFAH (males), SDS	93	-1,65	-3,30	-0,35	31	-1,30	-2,89	0,20	62	-1,84	-3,45	-0,85
nFAH (females), cm	49	156,0	149,3	167,0	11	155,7	144,8	172,6	38	156,5	149,1	166,8
nFAH (females), SDS	49	-1,79	-2,92	0,07	11	-1,84	-3,67	1,01	38	-1,70	-2,95	0,04
<b>nFAH SDS - MPH SDS</b>	138	<b>-0,37</b>	-1,58	0,73	42	-0,42	-1,77	0,91	96	-0,33	-1,51	0,73
<b>total <math>\Delta</math> height SDS<sup>a</sup></b>	142	<b>1,73</b>	0,66	3,27	42	2,27	1,06	4,58	100	1,56 <sup>1</sup>	0,39	2,92

GH= growth hormone; nFAH= near-final adult height; MPH = midparental height  
<sup>a</sup>gain in height SDS from start of GH treatment until nFAH  
p-values for comparison of combined and isolated GHD: <sup>1</sup>p<0,001; <sup>2</sup>p<0,01; <sup>3</sup>p<0,05

## ROC-curve analysis:

First-year HV SD  $<0.70$ , and first-year  $\Delta$ Ht SDS  $<0.3$  have a high specificity (97%) to predict a total gain in height SDS  $<1$ . Corresponding sensitivities: 20%, and 27% resp. Area's under the curve (AUC): 77.1%, and 79% resp. Accuracies of the tests: 80.7%, and 83.8% resp.

Regression models for nFAH  $<-2$ SD and nFAH-MPH  $<-1.3$  SD in relation to first-year growth responses are weak (AUC 54-62%), implicating a low discriminatory power.

ROC curve analysis: cut off values for first-year $\Delta$ Ht SDS, with its sensitivity and specificity to predict total $\Delta$ Ht SDS $<1$			ROC curve analysis: cut off values for first-year HV SDS, with its sensitivity and specificity to predict total $\Delta$ Ht SDS $<1$		
first-year $\Delta$ Ht SDS	sensitivity (%)	specificity (%)	first-year HV SDS	sensitivity (%)	specificity (%)
0,08	4	100	0,06	12	100
0,30	27	97	0,42	16	99
0,38	46	94	0,70	20	97
0,48	50	87	0,88	32	96
0,49	54	85	1,18	44	93
0,54	58	84	1,32	48	89
0,58	62	82	1,76	56	76
0,60	65	79	1,89	64	72
0,62	73	77	2,40	68	64
0,68	77	68	2,49	80	63
0,76	85	58	2,56	84	59
0,99	89	46	2,87	88	54
1,12	96	37	3,37	92	44
1,92	100	7	4,76	100	23

## 4. Conclusion

Our results show that a first-year change in height SDS  $<0.3$  and first-year HV SDS  $<0.7$  will detect almost all subjects with poor final height outcome (total  $\Delta$ Ht SDS  $<1$ ), but due to the low sensitivity of these limits relatively "good" first-year responders ( $\Delta$ Ht SDS  $>0.3$  and HV SD  $>0.7$ ) can also have a poor final height outcome. Depending on the chosen sensitivity or specificity, different cut offs for poor first-year response can be determined by ROC analysis.

Members of the BSGPE: Beauvoys Véronique, Beckers Dominique, Boros Erika, Brachet Cécile, Bourguignon Jean-Pierre, Casteels Kristina, Chivu Olympia, Cools Martine, Craen Margarita, De Beaufort Carine, Depoorter Sylvia, De Schepper Jean, De Waele Kathleen, de Zegher Francis, den Brinker Marieke, Dotremont Hilde, France Annick, Francois Inge, Gies Inge, Heinrichs Claudine, Lebrethon Marie-Christine, Logghe Karl, Lysy Philippe, Maes Marc, Massa Guy, Mouraux Thierry, Parent Anne-Simone, Reynaers Nele, Rooman Raoul, Tenoutasse Sylvie, Van Aken Sara, Van Helvoirt Maria, Vanbesien Jesse, Vanderstraeten Saskia, Witsch Michael, Zeevaert Renate

NO CONFLICT OF INTEREST