Clinical trial results:
Neuromuscular Changes In Small For Gestational Age (SGA) Children During Somatropin Therapy - A Prospective Randomized, Controlled, Open-Label Multicenter Trial (SGA-Power Study)

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2006-004304-39
Trial protocol	DE
Global end of trial date	14 March 2011

Results information

Result version number	v2 (current)
This version publication date	27 April 2016
First version publication date	01 July 2015
Version creation reason	• Correction of full data set error resolution

Trial information

Trial identification

Sponsor protocol code	A6281283

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00625872
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 1 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 1 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 March 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objective was to determine whether growth hormone therapy improved the motor- performance and coordinative skills in pre-pubertal individuals with SGA as defined by efficiency of muscular function.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator:

Treated versus untreated group during 6 month study period.

Actual start date of recruitment	01 July 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	23
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 23 subjects were enrolled in 5 centres of Germany. Study started from 01 Jul 2008 and completed on 14 Mar 2011.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Somatropin

Arm description:

Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.035 milligram/kilogram/day (mg/kg/day) was administered subcutaneously (s.c) according to exact body weight specific calculation for 12 months. Dose adjustments were made at 6 month intervals.

Arm title	Control

Arm description:

No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.

Arm type	Control
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

No treatment for initial 6 months in control group. After 6 months, somatropin 0.067 mg/kg/day was administered s.c. according to exact body weight specific calculation, for the next 12 months.

Number of subjects in period 1	Somatropin	Control
Started	12	11
Treated	12	10
Completed	8	5
Not completed	4	6
Consent withdrawn by subject	1	-
Did not meet entrance criteria	1	-
Randomized but not treated	-	1
Study terminated by sponsor	2	5

Baseline characteristics

Reporting groups	
Reporting group title	Somatropin
Reporting group description:	
Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.	
Reporting group title	Control
Reporting group description:	
No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.	

Reporting group values	Somatropin	Control	Total
Number of subjects	12	11	23
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	6.6	7.6	
standard deviation	± 1	± 1.4	-
Gender categorical			
Units: Subjects			
Female	3	8	11
Male	9	3	12

End points

End points reporting groups

Reporting group title	Somatropin
Reporting group description:	
Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.	
Reporting group title	Control
Reporting group description:	
No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.	

Primary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

End point title	Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6
End point description:	
Peak jump power (PJP) was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during two-leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population. Analysis was done on the full analysis set (FAS) population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.	
End point type	Primary
End point timeframe:	
Baseline, Month 6	

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[1]	8[2]		
Units: Watt/kilogram (W/kg)				
least squares mean (standard error)	-0.15 (± 1.01)	0.28 (± 0.51)		

Notes:

[1] - Number of subjects analyzed (N) signifies the number of subjects evaluable for this outcome measure.
[2] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Statistical Analysis at Month 6
Statistical analysis description:	
Analysis of covariance (ANCOVA) method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.	
Comparison groups	Somatropin v Control

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7232 [3]
Method	ANCOVA
Parameter estimate	Least squares (LS) mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.93
upper limit	3.08
Variability estimate	Standard error of the mean
Dispersion value	1.1

Notes:

[3] - The statistical test was 2-sided and performed at the 5 percent significance level.

Primary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6

End point title	Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6

End point description:

PJP was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during two-leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population. Analysis was done on the per protocol (PP) population- subjects who received the study medication for at least 22 weeks.

End point type	Primary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[4]	6[5]		
Units: W/kg				
least squares mean (standard error)	-1.02 (± 0.43)	0.59 (± 0.27)		

Notes:

[4] - N signifies the number of subjects evaluable for this outcome measure.

[5] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Statistical Analysis at Month 6

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control

Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1941 [6]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.04
upper limit	4.82
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[6] - The statistical test was 2-sided and performed at the 5 percent significance level.

Primary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

End point title	Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6[7]

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during two-leg jump. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[8]	8[9]		
Units: Newtons				
least squares mean (standard error)	-0.7 (± 0.62)	-0.55 (± 0.29)		

Notes:

[8] - N signifies the number of subjects evaluable for this outcome measure.

[9] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6

End point title	Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6[10]

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during two-leg jump. The SDS indicates how similar the subject was to the reference population. Analysis was done on the PP population- subjects who received the study medication for at least 22 weeks.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses.

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[11]	6[12]		
Units: Newtons				
least squares mean (standard error)	-0.83 (± 1.27)	-0.85 (± 0.73)		

Notes:

[11] - N signifies the number of subjects evaluable for this outcome measure.

[12] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

End point title	Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6[13]

End point description:

Vmax was measured by Leonardo Jumping Platform during two-leg jump. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses.

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[14]	11		
Units: Meter/second (m/s)				
least squares mean (standard error)	0.01 (± 0.08)	0.12 (± 0.09)		

Notes:

[14] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Per Protocol (PP) Population at Month 6

End point title	Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Per Protocol (PP) Population at Month 6[15]

End point description:

Vmax was measured by Leonardo Jumping Platform during two-leg jump. Analysis was done on the PP population- subjects who received the study medication for at least 22 weeks.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[16]	9		
Units: m/s				
least squares mean (standard error)	0.01 (± 0.05)	0.25 (± 0.06)		

Notes:

[16] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Month 6

End point title	Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Month 6

End point description:

K-ABC was assessed in children between 2.5-12.5 years. Comprised of 16 subtests; 10 mental processing (intelligence) and 6 achievement subtests. Achievement subtests: expressive vocabulary, faces&places, arithmetic, riddles, reading/decoding, reading/comprehension. Sixteen subtests were weighted accordingly to form 5 global scales: sequential processing, simultaneous processing, achievement, non-verbal and mental processing composite. Scores were rated as upper extreme [greater than (>) 131], above average (116-130), average (85-115), below average (70-84), lower extreme [less than (<) 69]. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (Sequential Processing)	25.7 (± 8.35)	28.5 (± 8.33)		
Change at Month 6 (Sequential Processing)	2.6 (± 5.82)	-1.9 (± 4.15)		
Baseline (Simultaneous Processing)	45.7 (± 7.2)	49.8 (± 12.74)		
Change at Month 6 (Simultaneous Processing)	-0.1 (± 4.53)	1.5 (± 4.3)		
Baseline (Achievement)	300.7 (± 66.83)	341.8 (± 76.88)		
Change at Month 6 (Achievement)	32.1 (± 48.79)	16.7 (± 27.52)		
Baseline (Nonverbal)	46.2 (± 8.65)	49.8 (± 13.21)		
Change at Month 6 (Nonverbal)	-1.4 (± 3.78)	0 (± 5.35)		
Baseline (Mental Processing Composite)	70 (± 12.38)	78.1 (± 19.95)		
Change at Month 6 (Mental Processing Composite)	1.4 (± 6.39)	-0.9 (± 7.28)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Sequential Processing

Statistical analysis description:

For K-ABC Test (Sequential Processing): Kruskal-Wallis Analysis of Variance (ANOVA) model was used to calculate p-value.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0532 [17]
Method	Kruskal-wallis

Notes:

[17] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Simultaneous Processing

Statistical analysis description:

For K-ABC Test (Simultaneous Processing): Kruskal-Wallis ANOVA model was used to calculate p-value.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3383 [18]
Method	Kruskal-wallis

Notes:

[18] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Achievement

Statistical analysis description:

For K-ABC Test (Achievement): Kruskal-Wallis ANOVA model was used to calculate p-value.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.683 [19]
Method	Kruskal-wallis

Notes:

[19] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Non-Verbal

Statistical analysis description:

For K-ABC Test (Non-Verbal): Kruskal-Wallis ANOVA model was used to calculate p-value.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4935 [20]
Method	Kruskal-wallis

Notes:

[20] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Mental Processing

Statistical analysis description:

For K-ABC Test (Mental Processing Composite): Kruskal-Wallis ANOVA model was used to calculate p-value.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3458 [21]
Method	Kruskal-wallis

Notes:

[21] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Months 12 and 18

End point title	Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Months 12 and 18

End point description:

K-ABC was assessed in children between 2.5-12.5 years. Comprised of 16 subtests; 10 mental processing (intelligence) and 6 achievement subtests. Achievement subtests: expressive vocabulary, faces&places, arithmetic, riddles, reading/decoding, reading/comprehension. Sixteen subtests were weighted accordingly to form 5 global scales: sequential processing, simultaneous processing, achievement, non-verbal and mental processing composite. Scores were rated as upper extreme [greater than (>) 131], above average (116-130), average (85-115), below average (70-84), lower extreme [less than (<) 69].

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[22] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[23] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Month 6

End point title	Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Month 6

End point description:

The KITAP is a computer aided standardized neuro-cognitive development test which allows examination of a wide range of attention and executive functions such as shift of attention (Distractibility); simple reaction time (Alertness); "Sustained Attention", change of reaction (Flexibility); "Divided Attention", controlled reaction disposition (Go/No go) and "Vigilance". It has been designed appropriately for children between the age of 6 to 10 years to allow optimal motivation during testing and to increase validity of results. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. Here, 'n' signifies subjects who received the study drug and evaluated at the time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[24]	11		
Units: Seconds				
arithmetic mean (standard deviation)				
Baseline (Distractibility)	554.3 (± 201.08)	514.5 (± 127.41)		
Change at 6 Month (Distractibility) (n= 7, 10)	5.6 (± 230.95)	-11.4 (± 139.52)		
Baseline (Alertness)	433.9 (± 140.74)	384.6 (± 124.94)		
Change at 6 Month (Alertness) (n= 8, 10)	-16.1 (± 80.85)	4 (± 107.42)		
Baseline (Flexibility)	1350 (± 470)	1313 (± 477.19)		

Change at 6 Month (Flexibility) (n= 8, 10)	-192 (± 492.73)	-211 (± 589.41)		
Baseline (Go/No Go)	539.8 (± 106.73)	514.9 (± 91.95)		
Change at 6 Month (Go/No Go) (n= 8, 9)	35.6 (± 113.38)	-50.2 (± 69.9)		
Baseline (Vigilance)	822.2 (± 200.65)	693.4 (± 118.01)		
Change at 6 Month (Vigilance) (n= 7, 10)	-146 (± 278.6)	-31.2 (± 107.62)		

Notes:

[24] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Statistical Analysis for Distractibility
Statistical analysis description: For KITAP Test (Distractibility): Kruskal-Wallis ANOVA model was used to calculate p-value.	
Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6256
Method	Kruskal-wallis

Statistical analysis title	Statistical Analysis for Alertness
Statistical analysis description: For KITAP Test (Alertness): Kruskal-Wallis ANOVA model was used to calculate p-value.	
Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.859
Method	Kruskal-wallis

Statistical analysis title	Statistical Analysis for Flexibility
Statistical analysis description: For KITAP Test (Flexibility): Kruskal-Wallis ANOVA model was used to calculate p-value.	
Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Kruskal-wallis

Statistical analysis title	Statistical Analysis for Go/No Go
Statistical analysis description: For KITAP Test (Go/No Go): Kruskal-Wallis ANOVA model was used to calculate p-value.	
Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1234
Method	Kruskal-wallis

Statistical analysis title	Statistical Analysis for Vigilance
Statistical analysis description: For KITAP Test (Vigilance): Kruskal-Wallis ANOVA model was used to calculate p-value.	
Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3291
Method	Kruskal-wallis

Secondary: Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Months 12 and 18

End point title	Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Months 12 and 18

End point description:

The KITAP is a computer aided standardized neuro-cognitive development test which allows examination of a wide range of attention and executive functions such as shift of attention (Distractibility); simple reaction time (Alertness); "Sustained Attention", change of reaction (Flexibility); "Divided Attention", controlled reaction disposition (Go/No go) and "Vigilance". It has been designed appropriately for children between the age of 6 to 10 years to allow optimal motivation during testing and to increase validity of results.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	0[26]		
Units: Seconds				
arithmetic mean (standard deviation)	()	()		

Notes:

[25] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[26] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Month 6

End point title	Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Month 6

End point description:

NVLT was assessed for visual memorization that was difficult to verbalize. Test recorded instability index, T-scores (sum of differences of correct {C} - incorrect {IC} "Yes" answers [1]; sum of C "Yes" answers [2]; sum of IC "Yes" answers [3]; sum of differences of C-IC "Yes" answers with high associative items {87%-95%} [4]; sum of differences of C-IC "Yes" answers with low associative items {54%-64%} [5]; difference between difference values for high and low associative items [6]). Scores were rated as below average (<40), average (40-60), above average (>60) and working time ranging between 9-12 minutes. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[27]	11		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (Instability Index)	0.3 (± 0.15)	0.2 (± 0.21)		
Change at Month 6 (Instability Index)	-0.1 (± 0.11)	-0.1 (± 0.2)		
Baseline (Working Time)	227 (± 44.27)	218.3 (± 76.89)		
Change at Month 6 (Working Time)	10.6 (± 92.95)	-11.1 (± 34.86)		
Baseline [T-scores (1)]	39.9 (± 13.6)	43.9 (± 16.53)		
Change at Month 6 [T-scores (1)]	4.4 (± 11.64)	6.7 (± 12.12)		
Baseline [T-scores (2)]	41.6 (± 12.97)	46.8 (± 14.4)		
Change at Month 6 [T-scores (2)]	5 (± 10.72)	-0.6 (± 5.5)		
Baseline [T-scores (3)]	45.9 (± 14.89)	48.1 (± 18.2)		
Change at Month 6 [T-scores (3)]	1.5 (± 5.15)	8.3 (± 12.24)		
Baseline [T-scores (4)]	39.3 (± 16.97)	46.4 (± 16.03)		
Change at Month 6 [T-scores (4)]	5.6 (± 15.53)	1.4 (± 11.75)		
Baseline [T-scores (5)]	43.3 (± 11.12)	43.6 (± 15.13)		
Change at Month 6 [T-scores (5)]	2.6 (± 9.83)	7.7 (± 12.59)		
Baseline [T-scores (6)]	44.9 (± 15.83)	52.9 (± 19.96)		
Change at Month 6 [T-scores (6)]	0.9 (± 16.55)	-7.4 (± 14.88)		
Baseline [Age-corrected T-scores (1)]	33.4 (± 12.18)	38.6 (± 13.43)		

Change at Month 6 [Age-corrected T-scores (1)]	6 (± 10.21)	5.2 (± 11.26)		
Baseline [Age-corrected T-scores (2)]	51.3 (± 7.55)	54.5 (± 8.1)		
Change at Month 6 [Age-corrected T-scores (2)]	3.1 (± 5.59)	-0.1 (± 3.38)		
Baseline [Age-corrected T-scores (3)]	40 (± 13.86)	41.1 (± 16.38)		
Change at Month 6 [Age-corrected T-scores (3)]	0.6 (± 4.47)	7.8 (± 12.13)		
Baseline [Age-corrected T-scores (4)]	37.4 (± 17.01)	45 (± 15.21)		
Change at Month 6 [Age-corrected T-scores (4)]	6.3 (± 14.57)	4.1 (± 10.63)		
Baseline [Age-corrected T-scores (5)]	35 (± 11.88)	37.3 (± 13.48)		
Change at Month 6 [Age-corrected T-scores (5)]	3.3 (± 10.73)	6.9 (± 12.57)		
Baseline [Age-corrected T-scores (6)]	50 (± 16.49)	55.5 (± 16.64)		
Change at Month 6 [Age-corrected T-scores (6)]	1.5 (± 19.06)	-4.1 (± 13.77)		

Notes:

[27] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Months 12 and 18

End point title	Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Months 12 and 18

End point description:

NVLT was assessed for visual memorization that was difficult to verbalize. Test recorded instability index, T-scores (sum of differences of correct {C} - incorrect {IC} "Yes" answers [1]; sum of C "Yes" answers [2]; sum of IC "Yes" answers [3]; sum of differences of C-IC "Yes" answers with high associative items {87%-95%} [4]; sum of differences of C-IC "Yes" answers with low associative items {54%-64%} [5]; difference between difference values for high and low associative items [6]). Scores were rated as below average (<40), average (40-60), above average (>60) and working time ranging between 9-12 minutes.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[28] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[29] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Child Behavior Checklist 4-18 Years (CBCL 4-18) at Months 6, 12 and 18

End point title	Change From Baseline in Intellectual Performance of Children Using Child Behavior Checklist 4-18 Years (CBCL 4-18) at Months 6, 12 and 18

End point description:

CBCL was standardized for children ages 4 to 18 years and measured child internalizing and externalizing behaviors and total problems. The 4-18 years' checklist contains 140 questions and responses were recorded on a Likert scale: 0 = Not True, 1 = Somewhat or Sometimes True, 2 = Very True or Often True. The range of possible values was 0-280 (0=good to 280=worst).

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[30] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[31] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; One-leg-jump) at Months 6, 12 and 18

End point title	Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; One-leg-jump) at Months 6, 12 and 18

End point description:

PJP was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during one leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: W/kg				
arithmetic mean (standard deviation)	()	()		

Notes:

[32] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[33] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; One-leg-jump) at Months 6, 12 and 18

End point title	Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; One-leg-jump) at Months 6, 12 and 18

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during one leg jump. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	0[35]		
Units: Newtons				
arithmetic mean (standard deviation)	()	()		

Notes:

[34] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[35] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximum Jump Velocity (Vmax; One-leg-jump) at Months 6, 12 and 18

End point title	Change From Baseline in Maximum Jump Velocity (Vmax; One-leg-jump) at Months 6, 12 and 18

End point description:

Vmax was measured by Leonardo Jumping Platform during one leg jump.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	0[37]		
Units: m/s				
arithmetic mean (standard deviation)	()	()		

Notes:

[36] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[37] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test- Peak Jump Power (PJP) at Month 6

End point title	Change From Baseline in Five-chair Rising Test- Peak Jump Power (PJP) at Month 6

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJP is defined as the peak of the calculated power (force multiplied by velocity). Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[38]	9[39]		
Units: kilowatt (kW)				
arithmetic mean (standard deviation)				
Baseline	0.1 (± 0.07)	0.1 (± 0.05)		
Change at Month 6	0 (± 0.07)	0 (± 0.05)		

Notes:

[38] - N signifies the number of subjects evaluable for this outcome measure.

[39] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Power (PJP) at Months 12 and 18

End point title	Change From Baseline in Five-chair Rising Test-Peak Jump Power (PJP) at Months 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJP is defined as the peak of the calculated power (force multiplied by velocity).

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	0[41]		
Units: kW				
arithmetic mean (standard deviation)	()	()		

Notes:

[40] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[41] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Month 6

End point title	Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Month 6

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest. Analysis was done on the FAS population included- who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[42]	9[43]		
Units: kilonewton (kN)				
arithmetic mean (standard deviation)				
Baseline	0.4 (± 0.11)	0.4 (± 0.19)		

Change at Month 6	0 (± 0.23)	0 (± 0.2)		

Notes:

[42] - N signifies the number of subjects evaluable for this outcome measure.

[43] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Months 12 and 18

End point title	Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Months 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[44]	0[45]		
Units: kN				
arithmetic mean (standard deviation)	()	()		

Notes:

[44] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[45] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Month 6

End point title	Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Month 6

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). Vmax is defined as the maximum jump velocity. Analysis was done on the FAS population-subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[46]	9[47]		
Units: m/s				
arithmetic mean (standard deviation)				
Baseline	0.7 (± 0.22)	0.6 (± 0.16)		
Change at Month 6	0.2 (± 0.29)	0 (± 0.18)		

Notes:

[46] - N signifies the number of subjects evaluable for this outcome measure.

[47] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Months 12 and 18

End point title	Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Months 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). Vmax is defined as the maximum jump velocity.

End point type	Secondary

End point timeframe:

Baseline, Month 12 and Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[48]	0[49]		
Units: m/s				
arithmetic mean (standard deviation)	()	()		

Notes:

[48] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[49] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Month 6

End point title	Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Month 6

End point description:

Chair rising test is performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: 5 repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over chest (time to perform tasks, maximal PJP, maximal velocity and maximal PJF). Time to perform task includes: Average (avg) rise time which is avg time to perform 1 rise, average time per test is the average time to perform 1 test (rise and sitting down) and total time to perform 5 tests. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[50]	9[51]		
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (Average rise time)	1.2 (± 0.9)	0.7 (± 0.31)		
Change at Month 6 (Average rise time)	-0.5 (± 1.15)	0.1 (± 0.27)		
Baseline (Average time per test)	2 (± 0.7)	2.3 (± 0.6)		
Change at Month 6 (Average time per test)	-0.2 (± 0.54)	-0.1 (± 0.87)		
Baseline (Total time to perform 5 tests)	9.6 (± 3.91)	10.8 (± 2.24)		
Change at Month 6 (Total time to perform 5 tests)	0.1 (± 3.04)	2 (± 8.48)		

Notes:

[50] - N signifies subjects evaluable for the measure.

[51] - N signifies subjects evaluable for the measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Months 12 and 18

End point title	Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Months 12 and 18

End point description:

Chair rising test is performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: 5 repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over chest (time to perform tasks, maximal PJP, maximal velocity and maximal PJF). Time to perform task includes: Average (avg) rise time which is avg time to perform 1 rise, avg time per test is the avg time to perform 1 test (rise and sitting down) and total time to perform 5 tests.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[52]	0[53]		
Units: seconds				
arithmetic mean (standard deviation)	()	()		

Notes:

[52] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[53] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test-Peak Jump Power (PJP) at Months 6, 12 and 18

End point title	Change From Baseline in One-chair Rising Test-Peak Jump Power (PJP) at Months 6, 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising). PJP is defined as the peak of the calculated power (force multiplied by velocity).

End point type	Secondary

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[54]	0[55]		
Units: kW				
arithmetic mean (standard deviation)	()	()		

Notes:

[54] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[55] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test-Peak Jump Force (PJF) at Months 6, 12 and 18

End point title	Change From Baseline in One-chair Rising Test-Peak Jump Force (PJF) at Months 6, 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest.

End point type	Secondary

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[56]	0[57]		
Units: kN				
arithmetic mean (standard deviation)	()	()		

Notes:

[56] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[57] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test (Time to Perform the Tasks) at Months 6, 12 and 18

End point title	Change From Baseline in One-chair Rising Test (Time to Perform the Tasks) at Months 6, 12 and 18

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising).

End point type	Secondary

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[58]	0[59]		
Units: seconds				
arithmetic mean (standard deviation)	()	()		

Notes:

[58] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[59] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Month 6

End point title	Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Month 6

End point description:

MIGF was assessed using standard adjustable Jamar dynamometer. MIGF (in Newtons) was calculated by multiplying the dynamometer reading (in kilograms) by a factor of 9.81. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[60]	11		
Units: kg				
least squares mean (standard error)	1.28 (± 1.69)	1.13 (± 1.64)		

Notes:

[60] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Statistical Analysis at Month 6

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.956 [61]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	0.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.71
upper limit	6
Variability estimate	Standard error of the mean
Dispersion value	2.54

Notes:

[61] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Months 12 and 18

End point title	Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Months 12 and 18

End point description:

MIGF was assessed using standard adjustable Jamar dynamometer. MIGF (in Newtons) was calculated by multiplying the dynamometer reading (in kilograms) by a factor of 9.81. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[62]	0[63]		
Units: kg				
least squares mean (standard error)	()	()		

Notes:

[62] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[63] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Upper Arm Circumference

End point title	Mean Upper Arm Circumference

End point description:

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[64]	0[65]		
Units: centimeter (cm)]				
arithmetic mean (standard deviation)	()	()		

Notes:

[64] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[65] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Thigh Circumference

End point title	Mean Thigh Circumference

End point description:

Thigh measurements were taken as a mean of 3 consecutive measurements at upper thigh about an inch down from the crotch line.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[66]	0[67]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[66] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[67] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Calf Circumference

End point title	Mean Calf Circumference

End point description:

Calf measurements were taken as a mean of 3 consecutive measurements at largest part of calf muscle, usually about 4 inches down from below the knee.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12 and Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[68]	0[69]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[68] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[69] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height at Month 6

End point title	Mean Height at Month 6

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: cm				
arithmetic mean (standard deviation)	112.8 (± 5.13)	115 (± 7.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height at Months 12 and 18

End point title	Mean Height at Months 12 and 18

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer.

End point type	Secondary

End point timeframe:

Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[70]	0[71]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[70] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[71] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity at Month 6

End point title	Mean Growth Velocity at Month 6

End point description:

Growth velocity measures the annual rate of increase in height. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: cm/year				
arithmetic mean (standard deviation)	8.2 (± 1.93)	4.6 (± 1.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity at Months 12 and 18

End point title	Mean Growth Velocity at Months 12 and 18

End point description:

Growth velocity measures the annual rate of increase in height.

End point type	Secondary

End point timeframe:

Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[72]	0[73]		
Units: cm/year				
arithmetic mean (standard deviation)	()	()		

Notes:

[72] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[73] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height-Standard Deviation Score (SDS) at Month 6

End point title	Mean Height-Standard Deviation Score (SDS) at Month 6

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: cm				
arithmetic mean (standard deviation)	-3.1 (± 0.86)	-3.7 (± 0.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height-Standard Deviation Score (SDS) at Months 12 and 18

End point title	Mean Height-Standard Deviation Score (SDS) at Months 12 and 18

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Month 12 and Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[74]	0[75]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[74] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[75] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity-Standard Deviation Score (SDS) at Month 6

End point title	Mean Growth Velocity-Standard Deviation Score (SDS) at Month 6

End point description:

Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: cm/year				
arithmetic mean (standard deviation)	3.4 (± 2.62)	-1.1 (± 1.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

End point title	Mean Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

End point description:

End point type	Secondary

End point timeframe:

Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[76]	0[77]		
Units: cm/year				
arithmetic mean (standard deviation)	()	()		

Notes:

[76] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[77] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height-Standard Deviation Score (SDS) at Month 6

End point title	Change From Baseline in Height-Standard Deviation Score (SDS) at Month 6

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population included subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: cm				
least squares mean (standard error)	0.33 (± 0.21)	-0.22 (± 0.25)		

Statistical analyses

Statistical analysis title	Statistical Analysis at Month 6

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1107 [78]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	1.25
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[78] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Height-Standard Deviation Score (SDS) at Months 12 and 18

End point title	Change From Baseline in Height-Standard Deviation Score (SDS) at Months 12 and 18

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[79]	0[80]		
Units: cm				
least squares mean (standard error)	()	()		

Notes:

[79] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[80] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Month 6

End point title	Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Month 6

End point description:

Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[81]	9[82]		
Units: cm/year				
least squares mean (standard error)	3.89 (± 1.02)	-0.77 (± 1.4)		

Notes:

[81] - N signifies subjects evaluable for the measure.

[82] - N signifies subjects evaluable for the measure.

Statistical analyses

Statistical analysis title	Statistical Analysis at Month 6

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0161 [83]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	4.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	8.21
Variability estimate	Standard error of the mean
Dispersion value	1.54

Notes:

[83] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

End point title	Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

End point description:

Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[84]	0[85]		
Units: cm/year				
least squares mean (standard error)	()	()		

Notes:

[84] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[85] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Sitting Height-Standard Deviation Score (SDS)

End point title	Sitting Height-Standard Deviation Score (SDS)

End point description:

Sitting height was measured using a stadiometer with a specialized chair. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[86]	0[87]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[86] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[87] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Body Mass Index-Standard Deviation Score (BMI-SDS)

End point title	Body Mass Index-Standard Deviation Score (BMI-SDS)

End point description:

The BMI was used to measure body fat based on height and weight. It was calculated by body weight (kg) divided by the height (m) squared. The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[88]	0[89]		
Units: Kilogram per square meter (kg/m^2)				
arithmetic mean (standard deviation)	()	()		

Notes:

[88] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[89] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference at Months 6, 12 and 18

End point title	Change From Baseline in Head Circumference at Months 6, 12 and 18

End point description:

The maximum head circumference (usually horizontal just above the eyebrow ridges), was measured from just above the glabella area to the area near the top of the occipital bone (opisthocranion).

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[90]	0[91]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[90] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[91] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference-Standard Deviation Score (SDS) at Months 6, 12 and 18

End point title	Change From Baseline in Head Circumference-Standard Deviation Score (SDS) at Months 6, 12 and 18

End point description:

The maximum head circumference (usually horizontal just above the eyebrow ridges), was measured from just above the glabella area to the area near the top of the occipital bone (opisthocranion). The SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[92]	0[93]		
Units: cm				
arithmetic mean (standard deviation)	()	()		

Notes:

[92] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[93] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Month 6

End point title	Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Month 6

End point description:

Triceps, supra-iliac and subscapular skinfolds were measured on the right side of the body to the nearest 0.1 mm with a Holtain skinfold caliper. The measurement was performed at the left side of the subject. Triceps skinfold thickness was measured halfway down the left upper arm, while the arm was hanging relaxed at the subject's side. Suprascapular skinfold was measured laterally just below the angle of the left scapula. Suprailiac skinfold was measured just above the iliac crest in the middle-axillary line. SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Millimeter (mm)				
least squares mean (standard error)				
Change at Month 6 (Triceps SDS)	-0.41 (± 0.16)	-0.06 (± 0.18)		
Change at Month 6 (Subscapular SDS)	-0.3 (± 0.1)	-0.16 (± 0.13)		
Change at Month 6 (Suprailiac SDS)	-0.6 (± 0.07)	-0.33 (± 0.12)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Triceps SDS

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.187 [94]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.25

Notes:

[94] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Subscapular SDS

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3494 [95]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[95] - The statistical test was 2-sided and performed at the 5 percent significance level.

Statistical analysis title	Statistical Analysis for Suprailiac SDS

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

Comparison groups	Somatropin v Control
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0458 [96]
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[96] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Months 12 and 18

End point title	Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Months 12 and 18

End point description:

Triceps, supra-iliac and subscapular skinfolds were measured on the right side of the body to the nearest 0.1 mm with a Holtain skinfold caliper. The measurement was performed at the left side of the subject. Triceps skinfold thickness was measured halfway down the left upper arm, while the arm was hanging relaxed at the subject's side. Suprascapular skinfold was measured laterally just below the angle of the left scapula. Suprailiac skinfold was measured just above the iliac crest in the middle-axillary line. SDS indicates how similar the subject was to the reference population.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[97]	0[98]		
Units: mm				
least squares mean (standard error)	()	()		

Notes:

[97] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[98] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Density Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point title	Change From Baseline in Bone Density Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point description:

Bone Mineral Density (BMD) was measured by pqCT. The Z-score measures the distance of the measured BMD value from the appropriate normal age matched population mean value in units of standard deviation of this population. More negative scores indicate less BMD compared to age matched population and more positive scores indicate higher BMD compared to age matched population.

End point type	Other pre-specified

End point timeframe:

Baseline, Month 6, Month 12 and Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[99]	0[100]		
Units: z-score				
least squares mean (standard error)	()	()		

Notes:

[99] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[100] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Structure Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point title	Change From Baseline in Bone Structure Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point description:

Bone structure was measured by pqCT. Parameters included: total area, cortical area, marrow area, cortical thickness, cortical density of the radius, bone strength, cross-sectional muscle and fat area, total bone density, bone mineral count, trabecular BMD, bone cross-sectional area. Baseline and post-baseline SDS values transformed to age and sex specific z-score([Ln(test result/M)]/S); Ln=natural logarithm; M=age-/height- and sex-specific mean value; S=age-/height- and sex-specific coefficient of variation). Positive values are above the average for subject’s age and sex; negative values are below.

End point type	Other pre-specified

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[101]	0[102]		
Units: z-score				
least squares mean (standard error)	()	()		

Notes:

[101] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[102] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Stability Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point title	Change From Baseline in Bone Stability Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

End point description:

Bone stability was measured by pqCT. Baseline and post-baseline SDS values transformed to age and sex specific z-score (Ln(test result/M)]/S); Ln=natural logarithm; M=age- (or height-) and sex-specific mean value; S=age-(or height-) and sex-specific coefficient of variation) then change from baseline is calculated. Positive values are above the average for subject's age and sex; negative values are below the average.

End point type	Other pre-specified

End point timeframe:

Baseline, Month 6, Month 12, Month 18

End point values	Somatropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[103]	0[104]		
Units: z-score				
least squares mean (standard error)	()	()		

Notes:

[103] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.
[104] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment emergent adverse events were reported from time of first dose of study treatment up to 28 days after last dose of study treatment.	
Adverse event reporting additional description:	
EU BR specific adverse event tables were generated separately as per EU format using latest coding.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Control
Reporting group description:	
No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.	
Reporting group title	Somatropin
Reporting group description:	
Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.	

Serious adverse events	Control	Somatropin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Control	Somatropin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	10 / 12 (83.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Concussion			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 11 (18.18%)	2 / 12 (16.67%)	
occurrences (all)	2	3	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Eczema			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Enuresis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lordosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lice infestation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Otitis media			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Scarlet fever			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	6	
Urinary tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2008	Changes were requested by the Ethics Committee and the Competent Authorities. Determination of positive effects of growth hormone on bone density, bone structure and enhancement of bone stability were eliminated from the secondary objectives; performance of bone densitometry using pqCT was eliminated from all the visits; measurement of insulin, glucose and glycosylated haemoglobin were changed from optional to obligatory.
04 December 2009	The primary endpoint was changed from ''changes in PJP, PJF and maximal jump velocity after six months'' to ''efficiency of muscular function after six months''; efficiency of muscular function (Emf) after 12 months, changes in PJP, PJF and maximal jump velocity were added to the secondary endpoints; changes in evaluating attention performance were made due to practicability issues (vigilanz was changed to an optional subtest); measurement of Emf was added to Neuropsychological evaluation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was prematurely discontinued, therefore not all data was powered.

Notes: