Clinical trial results:
Treatment With Recombinant Human Growth Hormone Genotonorm (Registered) in Children With Short Stature Secondary to a Long Term Corticoid Therapy. A Study of Efficacy and Safety.

Summary

EudraCT number	2014-004104-30
Trial protocol	Outside EU/EEA
Global end of trial date	23 September 2011

Results information

Result version number	v1
This version publication date	29 March 2016
First version publication date	09 July 2015

Trial information

Trial identification

Sponsor protocol code	307-MET-9002-0009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00174187
WHO universal trial number (UTN)	-
Other trial identifiers	Alias protocol number: A6281016

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., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 800-718-1021, 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	22 March 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 September 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of a long-term treatment by Genotonorm on linear growth in children with short stature receiving steroid therapy.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2000
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	France: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	17
Adolescents (12-17 years)	13
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:

This study was conducted in France. The study start date was 21 September 2000 and study end date w as 23 September 2011.

Period 1

Period 1 title	Period 1 (up to 3 years)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)

Arm description:

Subjects with juvenile idiopathic arthritis (JIA) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	Genotonorm, Genotropin
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received somatropin 1.4 International Units per kilogram per week (IU/kg/week), equivalent to 0.46 milligram/kg/week (mg/kg/week), divided in 7 daily doses for up to 3 years.

Arm title	Somatropin- Up To Year 3 (Nephrotic Syndrome)

Arm description:

Subjects with nephrotic syndrome (NeS) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	Genotonorm, Genotropin
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received somatropin 1.4 IU/kg/week, equivalent to 0.46 mg/kg/week, divided in 7 daily doses for up to 3 years.

Number of subjects in period 1	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin- Up To Year 3 (Nephrotic Syndrome)
Started	15	15
Completed	15	11
Not completed	0	4
Consent withdrawn by subject	-	1
Non compliance	-	1
Unspecified	-	1
Serious adverse event	-	1

Period 2	
Period 2 title	Between Period 1 and Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Somatropin- After Year 3

Arm description:

Included subjects with JIA or NeS who received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years in this study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Somatropin- After Year 3
Started	26
Consented	24
Completed	21
Not completed	5
Did not consent to continue treatment	2
Consented, not assigned to treatment	3

Period 3

Period 3 title	Period 2 (after 3 years)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Somatropin- After Year 3

Arm description:

Subjects with JIA/NeS, who consented to receive treatment beyond 3 years, received somatropin (Genotropin, Genotonorm) 1.4 IU/kg/week subcutaneously until the additional study drug dose evaluation visit and thereafter received somatropin (Genotropin, Genotonorm) up to 50 microgram per kilogram per day (mcg/kg/day) subcutaneously until the final height (FH) was reached or up to Year 11. Final height was confirmed to have been achieved if the growth velocity was less than or equal to (<=) 1.5 centimeter (cm) per year during the preceding 12 months and bone age was greater than or equal to (>=) 17 years for boys and 15 years for girls.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	Genotonorm, Genotropin
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received somatropin 1.4 IU/kg/week equivalent to 0.46 mg/kg/week divided in 7 daily doses until the additional study drug dose evaluation visit and thereafter received somatropin up to 50 mcg/kg/day until the FH was reached or up to Year 11.

Number of subjects in period 3	Somatropin- After Year 3
Started	21
Completed	13
Not completed	8
Consent withdrawn by subject	1
Unspecified	5
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)
Reporting group description:	
Subjects with juvenile idiopathic arthritis (JIA) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.	
Reporting group title	Somatropin- Up To Year 3 (Nephrotic Syndrome)
Reporting group description:	
Subjects with nephrotic syndrome (NeS) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.	

Reporting group values	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin- Up To Year 3 (Nephrotic Syndrome)	Total
Number of subjects	15	15	30
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	11.14	11.96	
standard deviation	± 3.32	± 3.8	-
Gender, Male/Female			
Units: participants			
Female	9	2	11
Male	6	13	19

End points

End points reporting groups

Reporting group title	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)

Reporting group description:

Subjects with juvenile idiopathic arthritis (JIA) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Reporting group title	Somatropin- Up To Year 3 (Nephrotic Syndrome)

Reporting group description:

Subjects with nephrotic syndrome (NeS) received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Reporting group title	Somatropin- After Year 3

Reporting group description:

Included subjects with JIA or NeS who received somatropin (Genotropin, Genotonorm) subcutaneously for up to 3 years in this study.

Reporting group title	Somatropin- After Year 3

Reporting group description:

Subjects with JIA/NeS, who consented to receive treatment beyond 3 years, received somatropin (Genotropin, Genotonorm) 1.4 IU/kg/week subcutaneously until the additional study drug dose evaluation visit and thereafter received somatropin (Genotropin, Genotonorm) up to 50 microgram per kilogram per day (mcg/kg/day) subcutaneously until the final height (FH) was reached or up to Year 11. Final height was confirmed to have been achieved if the growth velocity was less than or equal to (<=) 1.5 centimeter (cm) per year during the preceding 12 months and bone age was greater than or equal to (>=) 17 years for boys and 15 years for girls.

Primary: Change from Baseline in Height Standard Deviation Score According to Chronological Age (SDS/CA) at Year 3

End point title	Change from Baseline in Height Standard Deviation Score According to Chronological Age (SDS/CA) at Year 3[1]

End point description:

Height was measured using a wall mounted device (example, Harpenden stadiometer). Height SDS/CA was obtained by measuring the height, subtracting chronological age- and gender-appropriate mean height and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. Full Analysis Set (FAS) up to Year 3: included all subjects who had at least 1 post-baseline height measurement and were treated with the study drug for at least 1 year.

End point type	Primary

End point timeframe:

Baseline, Year 3

Notes:

[1] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin- Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: Standard Deviation Score (SDS)				

median (inter-quartile range (Q1-Q3))				
Baseline	-3.6 (-5.1 to -2.3)	-2.5 (-2.8 to -2.2)		
Change at Year 3	0.2 (-1.5 to 1.8)	1.1 (0.8 to 1.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Height Standard Deviation Score According to Chronological Age (SDS/CA) at Final Height

End point title	Change from Baseline in Height Standard Deviation Score According to Chronological Age (SDS/CA) at Final Height[2]

End point description:

Height was measured using a wall mounted device (example, Harpenden stadiometer). Height SDS/CA was obtained by measuring the height, subtracting chronological age- and gender-appropriate mean height and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. FAS- after Year 3: included all subjects who received at least 1 dose of the study treatment and who had at least 1 post-baseline height measurement. Here, 'n' signifies those subjects who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

Baseline, when final height was reached (assessed up to Year 11)

Notes:

[2] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Somatropin-After Year 3			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: SDS				
median (full range (min-max))				
Baseline (n = 21)	-2.86 (-5.61 to -1)			
Change at Final Height (n = 4)	0.71 (0.27 to 3.08)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Weight Standard Deviation Score (SDS) at Final Height

End point title	Change from Baseline in Weight Standard Deviation Score (SDS) at Final Height[3]

End point description:

Body weight was measured using a balance scale. Weight SDS was obtained by measuring the weight,

subtracting age- and gender-appropriate mean weight and dividing the result by standard deviation of that mean (as obtained from age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. FAS- after Year 3: included all subjects who received at least one dose of the study treatment and who had at least one post-baseline height measurement. Here, 'n' signifies those subjects who were evaluable for this measure at given time point.

End point type	Primary

End point timeframe:

Baseline, when final height was reached (assessed up to Year 11)

Notes:

[3] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Somatropin-After Year 3			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: SDS				
median (full range (min-max))				
Baseline (n = 21)	-1.53 (-4.77 to 2.64)			
Change at Final Height (n = 4)	-0.43 (-1.37 to 1.09)			

Statistical analyses

No statistical analyses for this end point

Primary: Puberty Stage at Final Height

End point title	Puberty Stage at Final Height[4]

End point description:

Pubertal stage (graded from I to V for breast development and pubic hair development) according to the Tanner's method was collected. A low stage (Stage I) corresponds to a pre-pubertal stage and a high stage (Stage V) to an adult stage. FAS- after Year 3: included all subjects who received at least one dose of study treatment and who had at least one post-baseline height measurement. Here, 'n' signifies subjects who were evaluable for given components of puberty assessment.

End point type	Primary

End point timeframe:

When final height was reached (assessed up to Year 11)

Notes:

[4] - 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: Only descriptive data was planned to be reported for this endpoint.

End point values	Somatropin-After Year 3			
Subject group type	Reporting group			
Number of subjects analysed	4[5]			
Units: subjects				
Pubic hair: Stage I (n=4)	0			
Pubic hair: Stage II (n=4)	0			
Pubic hair: Stage III (n=4)	0			

Pubic hair: Stage IV (n=4)	0			
Pubic hair: Stage V (n=4)	4			
Breast development: Stage I (n=1)	0			
Breast development: Stage II (n=1)	0			
Breast development: Stage III (n=1)	0			
Breast development: Stage IV (n=1)	0			
Breast development: Stage V (n=1)	1			

Notes:

[5] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Age

End point title	Bone Age

End point description:

Bone age was determined by the Greulich and Pyle method using left wrist and hand X-ray. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at given time points for each group, respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: years				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 14, 15)	8.9 (7 to 10)	10.5 (7 to 13)		
Year 1 (n = 14, 15)	9.5 (7.8 to 11.5)	11.5 (7 to 14)		
Year 2 (n = 15, 13)	10 (8 to 13)	14 (10 to 14.5)		
Year 3 (n = 15, 14)	11.3 (8.8 to 14.5)	14 (11.5 to 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lean Body Mass

End point title	Lean Body Mass

End point description:

Lean body mass, a measurement of body composition, was assessed by Dual Energy X-ray Absorptiometry (DEXA) scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: kilogram (kg)				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	17.69 (14.96 to 19.96)	23.56 (16.77 to 32.43)		
Year 1 (n = 15, 13)	19.77 (16.62 to 24.58)	31.16 (20.77 to 39.1)		
Year 2 (n = 14, 12)	21.2 (18.79 to 25.13)	34.14 (25.3 to 46.3)		
Year 3 (n = 14, 11)	23.21 (20.88 to 25.55)	36.38 (26.49 to 42.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Percent Change in Lean Body Mass at Year 1, 2 and 3

End point title	Annual Percent Change in Lean Body Mass at Year 1, 2 and 3

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan. Annual percent change: (Lean body mass at current year minus lean body mass at previous year) divided by lean body mass at previous year, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Annual Change at Year 1 (n = 15, 13)	18.95 (10.04 to 21.83)	22.97 (17.54 to 28.8)		
Annual Change at Year 2 (n = 14, 11)	7.75 (1.31 to 12.16)	7.33 (4.76 to 18.91)		
Annual Change at Year 3 (n = 13, 9)	9.83 (2.67 to 13.33)	7.9 (1.88 to 15.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Lean Body Mass at Year 3

End point title	Percent Change From Baseline in Lean Body Mass at Year 3

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan. Percent change: (Lean body mass at Year 3 minus lean body mass at baseline) divided by lean body mass at baseline, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year.

End point type	Secondary

End point timeframe:

Baseline, Year 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[6]	11[7]		
Units: percent change				
median (inter-quartile range (Q1-Q3))	36.82 (22.45 to 52.39)	54.44 (43.06 to 62.3)		

Notes:

[6] - Subjects who were evaluable for this measure.

[7] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Lean Body Mass as Percentage of Total Weight

End point title	Lean Body Mass as Percentage of Total Weight

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage of total weight				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	70.56 (58.25 to 80.1)	60.69 (55.29 to 69.14)		
Year 1 (n = 15, 13)	76.57 (64.16 to 83.89)	65.97 (59.58 to 76.19)		
Year 2 (n = 14, 12)	73.32 (63.85 to 80.96)	69.95 (59.55 to 80.07)		
Year 3 (n = 14, 11)	72.94 (66.79 to 78.21)	67.24 (59.83 to 74.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lean Body Mass Standard Deviation Score According to Chronological Age (SDS/CA)

End point title	Lean Body Mass Standard Deviation Score According to Chronological Age (SDS/CA)

End point description:

Lean body mass was assessed by DEXA scan. Lean body mass SDS/CA was obtained by measuring lean body mass, subtracting the chronological age- and gender-appropriate mean lean body mass and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject’s value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	-1.5 (-1.81 to -0.94)	-0.9 (-1.4 to -0.54)		
Year 1 (n = 15, 13)	-1.13 (-1.64 to -0.67)	-0.52 (-0.97 to 0.2)		
Year 2 (n = 14, 12)	-1.26 (-1.94 to -0.78)	-0.87 (-1.4 to -0.32)		
Year 3 (n = 13, 11)	-1.75 (-1.96 to -0.94)	-1.29 (-2.36 to -0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fat Mass

End point title	Fat Mass

End point description:

Fat mass, a measurement of body composition, was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: kg				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	5.47 (4.04 to 11.34)	13.62 (9.51 to 18.05)		
Year 1 (n = 15, 13)	4.81 (2.64 to 10.21)	10.99 (7.22 to 18.97)		
Year 2 (n = 14, 12)	6.97 (3.12 to 11.48)	16.7 (5.99 to 20.59)		
Year 3 (n = 14, 11)	6.9 (4.94 to 11.33)	15.19 (10.28 to 22.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Percent Change in Fat Mass at Year 1, 2 and 3

End point title	Annual Percent Change in Fat Mass at Year 1, 2 and 3

End point description:

Fat mass, a measurement of body composition, was assessed by DEXA scan. Annual percent change: (Fat mass at current year minus fat mass at previous year) divided by fat mass at previous year, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Annual Change at Year 1 (n = 15, 13)	-11.21 (-24.18 to 27.46)	-3.71 (-19.44 to 15.73)		
Annual Change at Year 2 (n = 14, 11)	29.52 (4.97 to 34.56)	-1.05 (-20.82 to 79.15)		
Annual Change at Year 3 (n = 13, 9)	26.61 (-4.54 to 52.9)	19.37 (10.6 to 40.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from baseline in Fat Mass at Year 3

End point title	Percent Change from baseline in Fat Mass at Year 3

End point description:

Fat mass, a measurement of body composition, was assessed by DEXA scan. Percent change: (Fat mass at Year 3 minus fat mass at baseline) divided by fat mass at baseline, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year.

End point type	Secondary

End point timeframe:

Baseline, Year 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[8]	11[9]		
Units: percent change				
median (inter-quartile range (Q1-Q3))	19.46 (3.83 to 73.79)	37.56 (8.18 to 44.15)		

Notes:

[8] - Subjects who were evaluable for this measure.

[9] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Fat Mass as Percentage of Total Weight

End point title	Fat Mass as Percentage of Total Weight

End point description:

Fat mass, a measurement of body composition, was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage of total weight				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	25 (13.7 to 35.8)	33.8 (29.5 to 37.2)		
Year 1 (n = 15, 13)	17.4 (12.3 to 31.4)	30 (21.9 to 34.7)		
Year 2 (n = 14, 12)	21.1 (14.2 to 32.4)	27.1 (15 to 36.2)		
Year 3 (n = 14, 11)	21.3 (17.1 to 28.6)	26.4 (19.1 to 37.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fat Mass Standard Deviation Score According to Chronological Age (SDS/CA)

End point title	Fat Mass Standard Deviation Score According to Chronological Age (SDS/CA)

End point description:

Fat mass was assessed by DEXA scan. Fat mass SDS/CA was obtained by measuring fat mass, subtracting chronological age- and gender-appropriate mean fat mass and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	1.51 (0.5 to 2.22)	2.2 (1.95 to 2.39)		
Year 1 (n = 15, 13)	0.8 (-0.33 to 1.64)	1.98 (0.88 to 2.23)		
Year 2 (n = 14, 12)	0.86 (-0.15 to 1.66)	1.79 (0.55 to 2.33)		
Year 3 (n = 13, 11)	1.27 (0.25 to 1.55)	1.74 (0.9 to 2.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Bone Mineral Density of Lumbar Spine (BMAD [LS])

End point title	Apparent Bone Mineral Density of Lumbar Spine (BMAD [LS])

End point description:

BMAD (LS) was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: gram per cubic centimeter (g/cm^3)				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 14)	0.184 (0.168 to 0.242)	0.223 (0.211 to 0.241)		
Year 1 (n = 14, 13)	0.209 (0.163 to 0.243)	0.237 (0.201 to 0.244)		
Year 2 (n = 15, 14)	0.215 (0.181 to 0.248)	0.249 (0.217 to 0.266)		
Year 3 (n = 13, 12)	0.239 (0.205 to 0.254)	0.242 (0.223 to 0.266)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Bone Mineral Density Standard Deviation Score of Lumbar Spine According to Chronological Age (BMAD [LS] [SDS/CA])

End point title	Apparent Bone Mineral Density Standard Deviation Score of Lumbar Spine According to Chronological Age (BMAD [LS] [SDS/CA])

End point description:

BMAD (LS) was assessed by DEXA scan. BMAD (LS) (SDS/CA) was obtained by measuring the BMAD (LS), subtracting chronological age- and gender-appropriate mean BMAD (LS) and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject’s value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 14)	-3.21 (-4.02 to -1.26)	-1.53 (-1.94 to -1.35)		
Year 1 (n = 14, 13)	-2.66 (-3.7 to -1.07)	-1.51 (-2.32 to -0.95)		
Year 2 (n = 15, 14)	-2.55 (-3.74 to -0.95)	-1.42 (-1.86 to -0.72)		
Year 3 (n 12, 12)	-1.77 (-2.43 to -1.21)	-1.63 (-2.43 to -0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Bone Mineral Density Standard Deviation Score of Lumber Spine According to Tanner Puberty Stage (BMAD [LS] [SDS/Tanner Puberty Stage])

End point title	Apparent Bone Mineral Density Standard Deviation Score of Lumber Spine According to Tanner Puberty Stage (BMAD [LS] [SDS/Tanner Puberty Stage])

End point description:

BMAD (LS) was assessed by DEXA scan. BMAD (LS) (SDS/Tanner Puberty Stage) was obtained by measuring BMAD (LS), subtracting Tanner puberty stage- and gender-appropriate mean BMAD (LS) and dividing the result by standard deviation of that mean (as obtained from Tanner puberty stage- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 8, 8)	-4.27 (-5.47 to -2.38)	-3.09 (-3.36 to -2.31)		
Year 1 (n = 10, 7)	-3.7 (-4.8 to -2.48)	-3.23 (-4.64 to -1.74)		

Year 2 (n = 10, 9)	-4.11 (-4.36 to -1.72)	-2.6 (-3.04 to -2.17)		
Year 3 (n = 10, 8)	-3.04 (-4.06 to -2.27)	-2.96 (-3.37 to -2.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Mineral Density of Total Body (BMD [TB])

End point title	Bone Mineral Density of Total Body (BMD [TB])

End point description:

BMD (TB) was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: gram per square centimeter (g/cm^2)				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	0.78 (0.76 to 0.86)	0.9 (0.81 to 1)		
Year 1 (n = 15, 14)	0.8 (0.76 to 0.87)	0.92 (0.85 to 1.02)		
Year 2 (n = 14, 11)	0.81 (0.77 to 0.89)	0.96 (0.86 to 1.09)		
Year 3 (n = 13, 11)	0.84 (0.8 to 0.91)	0.99 (0.89 to 1.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Mineral Density of Lumbar Spine (BMD [LS])

End point title	Bone Mineral Density of Lumbar Spine (BMD [LS])

End point description:

BMD (LS) was assessed by DEXA scan. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group

respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: g/cm^2				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	0.55 (0.47 to 0.64)	0.72 (0.67 to 0.85)		
Year 1 (n = 14, 14)	0.61 (0.48 to 0.74)	0.76 (0.66 to 0.91)		
Year 2 (n = 15, 14)	0.64 (0.56 to 0.84)	0.85 (0.77 to 1.04)		
Year 3 (n = 13, 12)	0.74 (0.6 to 0.85)	0.93 (0.79 to 1.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Mineral Content of Total Body (BMC [TB])

End point title	Bone Mineral Content of Total Body (BMC [TB])

End point description:

DEXA scan of BMC was used to evaluate potential bone effects of treatment. BMC is an estimate of the amount of mineral (such as calcium) in the bone. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: gram				

median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	636.36 (498.47 to 939.71)	1233.58 (772.41 to 1650.08)		
Year 1 (n = 15, 14)	775.46 (578.97 to 1119.6)	1576.15 (939.71 to 1739.38)		
Year 2 (n = 14, 11)	855.7 (690.07 to 1059.67)	2003.49 (1070.42 to 2243.61)		
Year 3 (n = 13, 11)	1112.78 (807.3 to 1176.7)	1997.74 (1296 to 2195.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Percent Change in Bone Mineral Content of Total Body (BMC [TB]) at Year 1, 2 and 3

End point title	Annual Percent Change in Bone Mineral Content of Total Body (BMC [TB]) at Year 1, 2 and 3

End point description:

BMC is an estimate of the amount of mineral (such as calcium) in the bone. Annual percent change: (BMC [TB] at current year minus BMC [TB] at previous year) divided by BMC [TB] at previous year, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Year 1 (n = 15, 14)	12.51 (7.66 to 21.86)	20.16 (11.74 to 23.05)		
Year 2 (n = 14, 11)	17.47 (12.2 to 19.93)	13.91 (10.63 to 18.93)		
Year 3 (n = 12, 9)	12.03 (4.5 to 14.54)	7.39 (7.29 to 13.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Bone Mineral Content of Total Body (BMC [TB]) at Year 3

End point title	Percent Change from Baseline in Bone Mineral Content of Total Body (BMC [TB]) at Year 3

End point description:

BMC is an estimate of the amount of mineral (such as calcium) in the bone. Percent change: (BMC [TB] at Year 3 minus BMC [TB] at baseline) divided by BMC [TB] at baseline, multiplied by 100. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year.

End point type	Secondary

End point timeframe:

Baseline, Year 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[10]	11[11]		
Units: percent change				
median (inter-quartile range (Q1-Q3))	46.63 (24.94 to 73.91)	60.56 (36.49 to 67.79)		

Notes:

[10] - Subjects who were evaluable for this measure.

[11] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Mineral Content Standard Deviation Score of Total Body According to Chronological Age (BMC [TB] [SDS/CA])

End point title	Bone Mineral Content Standard Deviation Score of Total Body According to Chronological Age (BMC [TB] [SDS/CA])

End point description:

BMC (TB) was measured by DEXA scan. BMC (TB) (SDS/CA) was obtained by measuring BMC (TB), subtracting the chronological age- and gender-appropriate mean BMC (TB) and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject’s value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 15, 15)	-1.95 (-2.6 to -1.03)	-0.42 (-1.23 to 0.19)		
Year 1 (n = 15, 14)	-1.85 (-2.43 to -0.73)	-0.19 (-1.13 to 0.37)		
Year 2 (n = 14, 11)	-1.66 (-2.27 to -1.14)	-0.37 (-1.24 to 0.43)		
Year 3 (n = 12, 11)	-1.65 (-2.22 to -0.35)	-0.09 (-0.72 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Mineral Content Standard Deviation Score of Total Body According to Tanner Puberty Stage (BMC [TB] [SDS/Tanner Puberty Stage])

End point title	Bone Mineral Content Standard Deviation Score of Total Body According to Tanner Puberty Stage (BMC [TB] [SDS/Tanner Puberty Stage])

End point description:

BMC (TB) was measured by DEXA scan. BMC (TB) (SDS/Tanner Puberty Stage) was obtained by measuring BMC (TB), subtracting the Tanner puberty stage- and gender-appropriate mean BMC (TB) and dividing the result by standard deviation of that mean (as obtained from Tanner puberty stage- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject's value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Secondary

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 8, 8)	-2.19 (-2.47 to -0.96)	1.41 (-0.39 to 2.46)		
Year 1 (n = 10, 8)	-1.56 (-2.24 to -0.92)	-0.52 (-1.53 to 1.65)		

Year 2 (n = 9, 7)	-2.38 (-2.72 to -1.14)	-0.47 (-1.53 to 0.37)		
Year 3 (n = 9, 7)	-2.38 (-2.56 to -1.28)	-0.17 (-1.22 to 0.83)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Growth Velocity (GV)

End point title	Growth Velocity (GV)

End point description:

Growth velocity measures the annual rate of increase in height. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: cm/year				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 11, 14)	2.9 (1.1 to 4.8)	3.8 (2.7 to 4.4)		
Year 1 (n = 14, 15)	6.5 (3.5 to 8.6)	8.3 (5.4 to 8.7)		
Year 2 (n = 14, 15)	5.3 (1.8 to 6.9)	7 (4.1 to 9.2)		
Year 3 (n = 14, 14)	4.5 (1.9 to 6.8)	5.9 (2.3 to 7.2)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Growth Velocity Standard Deviation Score According to Chronological Age (GV [SDS/CA])

End point title	Growth Velocity Standard Deviation Score According to Chronological Age (GV [SDS/CA])

End point description:

GV measures the annual rate of increase in height. GV (SDS/CA) was obtained by measuring GV, subtracting the chronological age- and gender-appropriate mean GV and dividing the result by standard deviation of that mean (as obtained from chronological age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject’s value was relative to the mean of the reference population. FAS up to Year 3:

included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 10, 14)	-1.7 (-2.8 to -1.3)	-2.2 (-2.9 to -1.3)		
Year 1 (n = 14, 15)	1 (-1.5 to 3.9)	1.3 (-0.7 to 1.9)		
Year 2 (n = 14, 15)	0.1 (-1.9 to 3.7)	2.9 (1.4 to 4.2)		
Year 3 (n = 14, 14)	0.4 (-0.5 to 2.1)	2.9 (-0.1 to 5.7)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Growth Velocity Standard Deviation Score According to Bone Age (GV [SDS/BA])

End point title	Growth Velocity Standard Deviation Score According to Bone Age (GV [SDS/BA])

End point description:

GV measures the annual rate of increase in height. GV (SDS/BA) was obtained by measuring GV, subtracting the bone age- and gender-appropriate mean GV and dividing the result by standard deviation of that mean (as obtained from bone age- and gender-specific population reference data). SDS indicated how many standard deviations higher (in case of positive SDS) or lower (in case of negative SDS) subject’s value was relative to the mean of the reference population. FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline, Year 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: SDS				
median (inter-quartile range (Q1-Q3))				
Baseline (n = 9, 14)	-2.8 (-3.9 to -1.7)	-2.1 (-2.4 to -1.1)		
Year 1 (n = 13, 15)	0.8 (-0.9 to 2.9)	0.6 (-0.6 to 2.4)		
Year 2 (n = 14, 13)	-0.3 (-3.9 to 1.1)	1.4 (-0.6 to 2)		
Year 3 (n = 14, 14)	-0.9 (-2.2 to 0.9)	0.1 (-1.7 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Insulin-like Growth Factor-1 (IGF-1) Concentration up to Year 3

End point title	Insulin-like Growth Factor-1 (IGF-1) Concentration up to Year 3

End point description:

FAS up to Year 3: included all subjects who had at least one post-baseline height measurement and were treated with the study drug for at least 1 year. Here, 'n' signifies those subjects who were evaluable for this measure at the given time point for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline, Year 1, 2, 3

End point values	Somatropin-Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin-Up To Year 3 (Nephrotic Syndrome)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: nanogram per milliliter (ng/mL)				
median (full range (min-max))				
Baseline (n = 15, 12)	157 (61 to 345)	344.5 (191 to 719)		
Year 1 (n = 15, 15)	400 (154 to 1370)	952 (424 to 1658)		
Year 2 (n = 15, 14)	388 (188 to 1338)	880 (311 to 1718)		
Year 3 (n = 15, 14)	405 (239 to 1160)	657 (323 to 1298)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Insulin-like Growth Factor-1 (IGF-1) Concentration After Year 3

End point title	Insulin-like Growth Factor-1 (IGF-1) Concentration After Year 3

End point description:

FAS after year 3: included all subjects who received at least 1 dose of the study treatment and who had at least 1 post-baseline height measurement. Here, 'n' signifies those subjects who were evaluable for this measure at given time point.

End point type	Other pre-specified

End point timeframe:

Year 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10; 0.5 and 1 year after somatropin discontinuation, Final Height (assessed up to Year 11)

End point values	Somatropin-After Year 3			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: milligram per deciliter (mg/dL)				
median (full range (min-max))				
Year 3.5 (n = 8)	0.05 (0.04 to 0.09)			
Year 4 (n = 19)	0.06 (0.03 to 0.1)			
Year 4.5 (n = 16)	0.06 (0.02 to 0.14)			
Year 5 (n = 17)	0.05 (0.02 to 0.09)			
Year 5.5 (n = 11)	0.06 (0.02 to 0.09)			
Year 6 (n = 14)	0.05 (0.02 to 0.08)			
Year 6.5 (n = 8)	0.07 (0.02 to 0.09)			
Year 7 (n = 8)	0.06 (0.02 to 0.07)			
Year 7.5 (n = 4)	0.05 (0.03 to 0.07)			
Year 8 (n = 6)	0.06 (0.03 to 0.07)			
Year 8.5 (n = 2)	0.08 (0.07 to 0.08)			
Year 9 (n = 2)	0.06 (0.06 to 0.07)			
Year 9.5 (n = 1)	0.07 (0.07 to 0.07)			

Year 10 (n = 1)	0.05 (0.05 to 0.05)			
0.5 years after somatropin discontinuation (n = 2)	0.03 (0.03 to 0.04)			
1 year after somatropin discontinuation (n = 2)	0.03 (0.02 to 0.05)			
Final height (n = 3)	0.06 (0.05 to 0.07)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 7 days after last dose of study drug

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)

Reporting group description:

Subjects with JIA received somatropin (Genotropin, Genotonorm) 1.4 IU/kg/week, equivalent to 0.46 mg/kg/week, divided in 7 daily doses subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Reporting group title	Somatropin- Up To Year 3 (Nephrotic Syndrome)

Reporting group description:

Subjects with NeS received somatropin (Genotropin, Genotonorm) 1.4 IU/kg/week, equivalent to 0.46 mg/kg/week, divided in 7 daily doses subcutaneously for up to 3 years. After treatment for 3 years, subjects in this group were assigned to Somatropin- After Year 3 group.

Reporting group title	Somatropin- After Year 3

Reporting group description:

Subjects with JIA/NeS, who consented to receive treatment beyond 3 years, received somatropin (Genotropin, Genotonorm) 1.4 IU/kg/week, equivalent to 0.46 mg/kg/week divided in 7 daily doses subcutaneously until the additional study drug dose evaluation visit and thereafter received somatropin (Genotropin, Genotonorm) up to 50 mcg/kg/day subcutaneously until the FH was reached or up to Year 11. Final height was confirmed to have been achieved if the growth velocity was <=1.5 cm per year during the preceding 12 months and bone age was >=17 years for boys and 15 years for girls.

Serious adverse events	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin- Up To Year 3 (Nephrotic Syndrome)	Somatropin- After Year 3
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 15 (66.67%)	10 / 15 (66.67%)	19 / 21 (90.48%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid neoplasm			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 21 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Biopsy kidney			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratopathy			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	4 / 21 (19.05%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			

subjects affected / exposed	0 / 15 (0.00%)	6 / 15 (40.00%)	4 / 21 (19.05%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Juvenile idiopathic arthritis			
subjects affected / exposed	3 / 15 (20.00%)	0 / 15 (0.00%)	5 / 21 (23.81%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	1 / 1	2 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Somatropin- Up To Year 3 (Juvenile Idiopathic Arthritis)	Somatropin- Up To Year 3 (Nephrotic Syndrome)	Somatropin- After Year 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)	14 / 15 (93.33%)	21 / 21 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Hyperthermia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Oedema			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	3 / 21 (14.29%)
occurrences (all)	0	2	3
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Injection site haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	2
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	2
Investigations			
Blood cholesterol			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Blood triglycerides			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Insulin-like growth factor increased			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	3 / 21 (14.29%)
occurrences (all)	0	3	3

Red blood cell sedimentation rate increased			
subjects affected / exposed	5 / 15 (33.33%)	0 / 15 (0.00%)	4 / 21 (19.05%)
occurrences (all)	10	0	7
Blood follicle stimulating hormone increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Blood HIV RNA increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
Radius fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Hand fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Left ventricular hypertrophy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			

subjects affected / exposed	2 / 15 (13.33%)	3 / 15 (20.00%)	3 / 21 (14.29%)
occurrences (all)	3	4	4
Hypotonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Hypercoagulation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 21 (14.29%)
occurrences (all)	1	0	5
Ocular hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	4 / 21 (19.05%)
occurrences (all)	2	2	5
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	2 / 21 (9.52%)
occurrences (all)	2	1	2
Vomiting			

subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	2 / 21 (9.52%)
occurrences (all)	1	2	2
Cheilitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acanthosis nigricans			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	1 / 21 (4.76%)
occurrences (all)	0	2	1
Acne			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
Eczema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Nail dystrophy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Hypercalciuria			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Nephrotic syndrome			
subjects affected / exposed	0 / 15 (0.00%)	11 / 15 (73.33%)	7 / 21 (33.33%)
occurrences (all)	0	35	32
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)	6 / 15 (40.00%)	3 / 21 (14.29%)
occurrences (all)	0	11	6
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	4 / 21 (19.05%)
occurrences (all)	3	1	6
Joint effusion			
subjects affected / exposed	4 / 15 (26.67%)	0 / 15 (0.00%)	4 / 21 (19.05%)
occurrences (all)	5	0	5
Juvenile idiopathic arthritis			
subjects affected / exposed	3 / 15 (20.00%)	0 / 15 (0.00%)	6 / 21 (28.57%)
occurrences (all)	4	0	9
Osteopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Synovitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Amyotrophy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Knee deformity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Muscle atrophy			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Limb asymmetry			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	1	1	1
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	2 / 21 (9.52%)
occurrences (all)	0	4	3
Gastroenteritis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	4 / 21 (19.05%)
occurrences (all)	1	2	4
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	3 / 21 (14.29%)
occurrences (all)	0	4	5
Perichondritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	2 / 21 (9.52%)
occurrences (all)	0	3	2
Tracheobronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2

Viral tracheitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Fluid retention			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Hyperinsulinism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	1 / 21 (4.76%)
occurrences (all)	0	2	1
Malnutrition			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Sodium retention			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Glucose tolerance impaired			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
Insulin resistance			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 21 (19.05%)
occurrences (all)	0	0	4
Mineral deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2001	The study duration was increased from 48 months to 69 months.
20 October 2003	For the children who did not wish to continue the treatment beyond 36 months, it was proposed that they had to undergo an evaluation of body composition by a DEXA scan and glucose tolerance by an oral glucose tolerance test, 1 year after the discontinuation of treatment.
29 November 2007	Treatment with somatropin was adapted according to IGF-1 level. If the level of IGF-1 was greater than (>)+2 standard deviation (SD) for the chronological age and sex, the dose of the growth hormone was to be decreased by 20 percent (%).

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.

Results for secondary and other pre-specified endpoints (except IGF-1) are reported for only up to 3 years because data beyond Year 3 was not summarized as the study was terminated due to Good Clinical Practice (GCP) non-compliance issues.

Notes: