Clinical trial results:
A two-year multi-centre, randomized two arm study of Genotropin treatment in very young children born small for gestational age: Early Growth and Neurodevelopment (EGN)

Summary

EudraCT number	2007-003949-32
Trial protocol	SE CZ BE ES AT GB FR IT DE NL
Global end of trial date	30 December 2013

Results information

Result version number	v1 (current)
This version publication date	13 June 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	A6281287

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00627523
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., 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	23 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of 24 months of treatment with growth hormone (GH) therapy at a dose of 0.035 milligram per kilogram per day (mg/kg/d) on height in short small for gestational age (SGA) children starting treatment at 24-30 months of age, compared to untreated controls, in randomized subjects.

Protection of trial subjects:

The study was in compliance with with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (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	26 February 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	Netherlands: 1
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Switzerland: 6
Worldwide total number of subjects	43
EEA total number of subjects	37

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	18

months)	
Children (2-11 years)	25
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:

This randomized controlled trial enrolled small for gestational age (SGA) children at 16 centers in 8 countries. In total, 52 subjects were screened for the study, of these, 9 subjects were considered screen failures. The remaining 43 subjects were randomized to receive either study drug (Genotropin) or were not treated (Control).

Pre-assignment

Screening details:

Subjects aged between 19 to 29 months at Screening visit, born SGA (birth length and/or weight less than (<) 2 standard deviations (SD) for gestational age, using country specific standards), height below -2.5 SD at Screening (19-29 months of age),and had at least one measurement of length between 12 and 18 months of age were enrolled in this study

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Genotropin

Arm description:

Subjects received Genotropin at a dose of 0.035 mg/kg/d for 24 months. The dose was calculated based on the actual body weight, and the closest dosing step of the 5 mg pen used. The starting dose for the first 2 weeks was 1/3 of the calculated dose. After 2 weeks the dose was increased to 2/3 of the calculated dose. After 4 weeks the daily dose was the dose calculated on body weight at randomization.

Arm type	Experimental
Investigational medicinal product name	Genotropin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Genotropin at a dose of 0.035 mg/kg/d for 24 months.

Arm title	Control

Arm description:

This group was the untreated control group and was not administered placebo.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Genotropin	Control
Started	21	22
Completed	19	20
Not completed	2	2
'Not specified '	1	-
Withdrawal by Subject	-	2

Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Genotropin
Reporting group description:	
Subjects received Genotropin at a dose of 0.035 mg/kg/d for 24 months. The dose was calculated based on the actual body weight, and the closest dosing step of the 5 mg pen used. The starting dose for the first 2 weeks was 1/3 of the calculated dose. After 2 weeks the dose was increased to 2/3 of the calculated dose. After 4 weeks the daily dose was the dose calculated on body weight at randomization.	
Reporting group title	Control
Reporting group description:	
This group was the untreated control group and was not administered placebo.	

Reporting group values	Genotropin	Control	Total
Number of subjects	21	22	43
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	24.91	24.44	
standard deviation	± 3.262	± 3.324	-
Gender categorical			
Units: Subjects			
Female	13	11	24
Male	8	11	19

End points

End points reporting groups

Reporting group title	Genotropin

Reporting group description:

Subjects received Genotropin at a dose of 0.035 mg/kg/d for 24 months. The dose was calculated based on the actual body weight, and the closest dosing step of the 5 mg pen used. The starting dose for the first 2 weeks was 1/3 of the calculated dose. After 2 weeks the dose was increased to 2/3 of the calculated dose. After 4 weeks the daily dose was the dose calculated on body weight at randomization.

Reporting group title	Control

Reporting group description:

This group was the untreated control group and was not administered placebo.

Primary: Change From Baseline in Height Standard Deviation Score (SDS) at Month 24

End point title	Change From Baseline in Height Standard Deviation Score (SDS) at Month 24

End point description:

Height SDS was calculated at the relevant visit by means of the following formula:Height SDS=(subject height)-(normal height)/normal height standard deviation. Where subject height refers to the subject's height at the relevant visit, and normal height and the normal height standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. The change from Baseline value for height SDS was calculated as the difference between the parameter values at a specific visit, and the Baseline parameter values. The scores were centred around 0. Negative score indicated a subject was smaller for their age/gender.Full Analysis Set (FAS) included subjects who were randomized to treatment and completed at least 1 post-baseline efficacy measure. Missing values were imputed using LOCF method. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control for safety analysis.

End point type	Primary

End point timeframe:

Baseline and Month 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
least squares mean (standard error)	1.63 (± 0.13)	0.43 (± 0.13)		

Statistical analyses

Statistical analysis title	Genotropin, Control

Statistical analysis description:

The null hypothesis was that there was no difference in the mean change from Baseline after 24 months in height SDS between the Genotropin® and the untreated control groups. The alternative hypothesis was that there was a difference between the treatment groups.

Comparison groups	Genotropin v Control

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.59
Variability estimate	Standard error of the mean
Dispersion value	0.19

Notes:

[1] - Analysis of covariance (ANCOVA) model, fitting treatment as a factor, and the baseline parameter value as covariate was used. All hypotheses were tested at a 5% level of significance.No adjustments were made for multiple comparisons.

Secondary: Change From Baseline in Growth Velocity SDS at Month 24

End point title	Change From Baseline in Growth Velocity SDS at Month 24

End point description:

The growth velocity SDS was calculated at the relevant visit by means of the following formula: Growth velocity SDS = (subject growth velocity) - (normal growth velocity)/normal growth velocity standard deviation. Where, subject growth velocity refers to the subject's growth velocity at the relevant visit, and normal growth velocity and the normal growth velocity standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. The change from baseline value for growth velocity SDS was calculated as the difference between the parameter values at a specific visit, and the Baseline parameter values. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. Missing values were imputed using LOCF method.1 subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control for safety analysis.

End point type	Secondary

End point timeframe:

Baseline and Month 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
least squares mean (standard error)	0.74 (± 0.57)	-0.03 (± 0.57)		

Statistical analyses

Statistical analysis title	Genotropin®, Control

Statistical analysis description:

The null hypothesis was that there was no difference between the Genotropin® and the untreated control group in terms of the relevant secondary endpoints. The alternative hypothesis was that a difference existed.

Comparison groups	Genotropin v Control

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.348
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	2.42
Variability estimate	Standard error of the mean
Dispersion value	0.81

Notes:

[2] - ANCOVA model, fitting treatment as a factor, and the baseline parameter value as covariate was used. All hypotheses were tested at a 5% level of significance. No adjustments were made for multiple comparisons.

Secondary: Change From Baseline in Height SDS at Month 12

End point title	Change From Baseline in Height SDS at Month 12

End point description:

Height SDS was calculated at the relevant visit by means of the following formula: Height SDS = (subject height) - (normal height)/normal height standard deviation. Where subject height refers to the subject's height at the relevant visit, and normal height and the normal height standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. The change from baseline value for height SDS was calculated as the difference between the parameter values at a specific visit, and the baseline parameter values. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. Missing values were imputed using LOCF method. 1 subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control for safety analysis.

End point type	Secondary

End point timeframe:

Baseline and month 12

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
least squares mean (standard error)	1.03 (± 0.12)	0.14 (± 0.12)		

Statistical analyses

Statistical analysis title	Genotropin, Control

Statistical analysis description:

The null hypothesis was that there was no difference between the Genotropin and the untreated control group in terms of the relevant secondary endpoints. The alternative hypothesis was that a difference existed.

Comparison groups	Genotropin v Control

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.23
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[3] - ANCOVA model, fitting treatment as a factor, and the baseline parameter value as covariate was used. All hypotheses were tested at a 5% level of significance. No adjustments were made for multiple comparisons.

Secondary: Change From Baseline in Growth Velocity SDS at Month 12

End point title	Change From Baseline in Growth Velocity SDS at Month 12

End point description:

The growth velocity SDS was calculated at the relevant visit by means of the following formula: Growth velocity SDS = (subject growth velocity) - (normal growth velocity)/normal growth velocity standard deviation. Where, subject growth velocity refers to the subject's growth velocity at the relevant visit, and normal growth velocity and the normal growth velocity standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. The change from Baseline value for growth velocity SDS was calculated as the difference between the parameter values at a specific visit, and the Baseline parameter values. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. Missing values were imputed using LOCF method. 1 subject was randomized to Genotropin® but did not receive any treatment. This subject was excluded from FAS but included in Control for safety analysis.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
least squares mean (standard error)	1.65 (± 0.56)	-1.59 (± 0.56)		

Statistical analyses

Statistical analysis title	Genotropin®, Control

Statistical analysis description:

The null hypothesis was that there was no difference between the Genotropin® and the untreated control group in terms of the relevant secondary endpoints. The alternative hypothesis was that a difference existed.

Comparison groups	Genotropin v Control

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	4.85
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[4] - ANCOVA model, fitting treatment as a factor, and the baseline parameter value as covariate was used. All hypotheses were tested at a 5% level of significance. No adjustments were made for multiple comparisons.

Secondary: Change From Baseline in Mental Development Using the Mental Development Index (MDI) of Bayley Scale at Month 12

End point title	Change From Baseline in Mental Development Using the Mental Development Index (MDI) of Bayley Scale at Month 12

End point description:

The Bayley Scale of Infant Development (BSID-II) measured the mental and motor development and test behavior of subjects from 1 to 42 months of age. The scale was used to describe the current developmental functioning of infants and to assist in diagnosis and treatment planning for infants with developmental delays or disabilities. The BSID-II provided the mental raw score which was used to calculate the MDI score. Possible MDI scores ranged from 50-150. The MDI score of 69 and below indicated significantly delayed performance, 70 to 84 indicated mildly delayed performance, 85 to 114 indicated normal limit, and 115 and above indicated accelerated performance. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in control group for safety analysis.

End point type	Secondary

End point timeframe:

Baseline and month 12

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: Units on a scale				
least squares mean (standard error)	10.97 (± 5.34)	8.55 (± 4.74)		

Statistical analyses

Statistical analysis title	Genotropin®, Control

Statistical analysis description:

The null hypothesis was that there was no difference between the Genotropin® and the untreated control group in terms of the relevant secondary endpoints. The alternative hypothesis was that a

difference existed.ANCOVA model, fitting treatment as a factor, and the baseline parameter value, age, and gender as covariates were used. All hypotheses were tested at a 5% level of significance.No adjustments were made for multiple comparisons.

Comparison groups	Genotropin v Control
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.738
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.27
upper limit	17.12
Variability estimate	Standard error of the mean
Dispersion value	7.19

Secondary: Change From Baseline in Psychomotor Development Using the Psychomotor Development Index (PDI) of Bayley Scale at Month 12

End point title	Change From Baseline in Psychomotor Development Using the Psychomotor Development Index (PDI) of Bayley Scale at Month 12

End point description:

BSID-II measured the mental and motor development and test behavior of subjects from 1 to 42 months of age. The scale was used to describe the current developmental functioning of infants and to assist in diagnosis and treatment planning for infants with developmental delays or disabilities. The BSID-II provided the psychomotor raw score which was used to calculate the PDI score. The PDI score of 69 and below indicated significantly delayed performance, 70 to 84 indicated mildly delayed performance, 85 to 114 indicated normal limit, and 115 and above indicated accelerated performance. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control group for safety analysis.

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: Units on a scale				
least squares mean (standard error)	4.04 (± 3.04)	8.55 (± 2.84)		

Statistical analyses

Statistical analysis title	Genotropin, Control

Statistical analysis description:

The null hypothesis was that there was no difference between the Genotropin and the untreated control group in terms of the relevant secondary endpoints. The alternative hypothesis was that a difference existed.

Comparison groups	Control v Genotropin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.301
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.27
upper limit	4.26
Variability estimate	Standard error of the mean
Dispersion value	4.27

Notes:

[5] - ANCOVA model, fitting treatment as a factor, and the baseline parameter value, age, and gender as covariates were used. All hypotheses were tested at a 5% level of significance. No adjustments were made for multiple comparisons.

Secondary: Head Circumference SDS at Months 3, 6, 12, 18 and 24

End point title	Head Circumference SDS at Months 3, 6, 12, 18 and 24

End point description:

Head circumference SDS was calculated by means of the following formula = (Subject head circumference) - (Normal head circumference) / Normal head circumference standard deviation. Where subject head circumference refers to the subject's head circumference at the relevant visit, and normal head circumference and the normal head circumference standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control group for safety analysis.

End point type	Secondary

End point timeframe:

Months 3, 6, 12, 18 and 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
arithmetic mean (standard deviation)				
Month 3 (n = 21, 19)	-0.93 (± 1.217)	-1.37 (± 1.122)		
Month 6 (n = 21, 19)	-1.2 (± 1.31)	-1.72 (± 1.077)		
Month 12 (n = 20, 18)	-0.87 (± 1.33)	-1.84 (± 1.158)		
Month 18 (n = 20, 19)	-0.56 (± 1.89)	-1.76 (± 1.153)		

Month 24 (n = 20, 20)	-0.75 (± 1.384)	-1.65 (± 1.227)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference SDS at Months 3, 6, 12, 18 and 24

End point title	Change From Baseline in Head Circumference SDS at Months 3, 6, 12, 18 and 24

End point description:

Head circumference SDS was calculated by means of the following formula = (Subject head circumference)-(Normal head circumference)/Normal head circumference standard deviation. Where subject head circumference refers to the subject's head circumference at the relevant visit, and normal head circumference and the normal head circumference standard deviation equals the population mean and standard deviation values for subjects of a similar age and gender. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. One subject was randomized to Genotropin® but did not receive any treatment. This subject was excluded from FAS but included in Control group for safety analysis.

End point type	Secondary

End point timeframe:

Baseline, Months 3, 6, 12, 18 and 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: SDS				
arithmetic mean (standard deviation)				
Month 3 (n = 21, 19)	0.27 (± 0.977)	0.36 (± 0.693)		
Month 6 (n = 21, 19)	0 (± 0.423)	0.07 (± 0.495)		
Month 12 (n = 20, 18)	0.26 (± 0.516)	0.02 (± 0.587)		
Month 18 (n = 20, 19)	0.57 (± 1.094)	0.04 (± 0.506)		
Month 24 (n = 20, 20)	0.39 (± 0.638)	0.08 (± 0.602)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight at Months 3, 6, 12, 18, and 24

End point title	Change From Baseline in Body Weight at Months 3, 6, 12, 18, and 24

End point description:

Body weight was measured at all the relevant visits. The change from Baseline in body weight was calculated as the difference between the parameter values at each visit, and the Baseline parameter values. FAS included subjects who were randomized to treatment and completed at least one post-

baseline efficacy measure. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in control group for safety analysis.

End point type	Secondary

End point timeframe:

Baseline, Months 3, 6, 12, 18, and 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: kilogram(s)				
arithmetic mean (standard deviation)				
Month 3 (n = 21, 19)	0.57 (± 0.154)	0.53 (± 0.406)		
Month 6 (n = 21, 20)	1.08 (± 0.269)	1.01 (± 0.659)		
Month 12 (n = 20, 19)	2.34 (± 0.389)	1.66 (± 0.397)		
Month 18 (n = 20, 19)	3.48 (± 0.669)	2.41 (± 0.709)		
Month 24 (n = 20, 20)	4.79 (± 0.814)	3.19 (± 0.601)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) at Months 3, 6, 12, 18, and 24

End point title	Change From Baseline in Body Mass Index (BMI) at Months 3, 6, 12, 18, and 24

End point description:

BMI was calculated for all visits by means of the following formula: BMI Kilogram per meters square (kg/m^2) = Weight Kilogram per height meters square (kg) / (Height[m])^2. The change from baseline BMI was calculated as the difference between the parameter values at each visit, and the baseline parameter values. FAS included subjects who were randomized to treatment and completed at least one post-baseline efficacy measure. One subject was randomized to Genotropin but did not receive any treatment. This subject was excluded from FAS but included in Control group for safety analysis.

End point type	Secondary

End point timeframe:

Baseline, Months 3, 6, 12, 18, and 24

End point values	Genotropin	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: Kilogram/meters^2				
arithmetic mean (standard deviation)				
Month 3 (n = 21, 19)	-0.28 (± 0.419)	-0.05 (± 0.811)		
Month 6 (n = 21, 20)	-0.57 (± 0.537)	0.08 (± 1.013)		

Month 12 (n = 20, 19)	-0.62 (± 0.65)	-0.29 (± 0.683)		
Month 18 (n = 20, 19)	-0.78 (± 0.93)	-0.25 (± 0.806)		
Month 24 (n = 20, 20)	-0.58 (± 0.823)	-0.55 (± 0.776)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from screening (Visit 1) until the follow-up visit for subjects in both treatment groups.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v16.1

Reporting groups

Reporting group title	Genotropin

Reporting group description:

Subjects received Genotropin at a dose of 0.035 mg/kg/d for 24 months. The dose was calculated based on the actual body weight, and the closest dosing step of the 5 mg pen used. The starting dose for the first 2 weeks was 1/3 of the calculated dose. After 2 weeks the dose was increased to 2/3 of the calculated dose. After 4 weeks the daily dose was the dose calculated on body weight at randomization.

Reporting group title	Control

Reporting group description:

This group was the untreated control group and was not administered placebo.

Serious adverse events	Genotropin	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 21 (28.57%)	2 / 22 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Conductive deafness			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hordeolum			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Genotropin	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	18 / 22 (81.82%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Irritability			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	9 / 21 (42.86%)	4 / 22 (18.18%)	
occurrences (all)	13	7	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Milk allergy			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Asthma			

subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	1	2	
Bronchial dysplasia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	3 / 21 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	5	1	
Increased bronchial secretion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Respiratory disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	2	0	

Syncope			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Tympanic membrane disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 21 (14.29%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	4 / 21 (19.05%)	0 / 22 (0.00%)	
occurrences (all)	8	0	
Dysphagia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Regurgitation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	4 / 21 (19.05%)	4 / 22 (18.18%)	
occurrences (all)	6	5	
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Lipoatrophy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Growing pains			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 21 (28.57%)	6 / 22 (27.27%)	
occurrences (all)	12	11	
Bronchopneumonia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	3 / 21 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Exanthema subitum			

subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
Gastroenteritis viral			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	4 / 21 (19.05%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
Molluscum contagiosum			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	9 / 21 (42.86%)	6 / 22 (27.27%)	
occurrences (all)	23	9	
Otitis media			
subjects affected / exposed	3 / 21 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	5	1	
Otitis media acute			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Pharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Pharyngotonsillitis			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	4	4	
Scarlet fever			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	7	1	
Upper respiratory tract infection			
subjects affected / exposed	8 / 21 (38.10%)	1 / 22 (4.55%)	
occurrences (all)	23	5	
Varicella			
subjects affected / exposed	4 / 21 (19.05%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Viral infection			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2007	Amended to include updated Pfizer standard wording for SAE reporting.
22 February 2012	Revision of safety and Hy's law sections.
22 February 2012	Revision of AE reporting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported