Clinical trial results:
Long-Term Study of PNU-180307 For Short Children Born Small for Gestational Age (SGA) Without Epiphyseal Closure (Extension of The Study 307-MET-0021-002)

Summary

EudraCT number	2015-004552-21
Trial protocol	Outside EU/EEA
Global end of trial date	20 August 2015

Results information

Result version number	v1 (current)
This version publication date	12 August 2016
First version publication date	12 August 2016

Trial information

Trial identification

Sponsor protocol code	GENASG-0021-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	ClinicalTrials.gov_Inquiries@pfizer.com, Pfizer Inc., 1 8007181021, ClinicalTrials.govCallCenter@pfizer.com
Scientific contact	ClinicalTrials.gov_Inquiries@pfizer.com, Pfizer Inc., 1 8007181021, ClinicalTrials.govCallCenter@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	20 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2015
Global end of trial reached?	Yes
Global end of trial date	20 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate safety of long-term administration of PNU-180307 (Genotropin) until a final height is reached in short children born small for gestational age (SGA) without epiphyseal closure

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	14 October 2002
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	Japan: 61
Worldwide total number of subjects	61
EEA total number of subjects	0

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)	61
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Before enrolled this study, participants with short stature due to SGA had completed the 1-year(12-month) treatment in previous study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose-Increasing Group

Arm description:

Participants who were treated with somatropin 0.033 mg/kg/day in previous study for 12 months received a dose of 0.067 mg/kg/day

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

Dosage and administration details:

0.067 mg/kg/day

Arm title	Dose-Remaining Group

Arm description:

Participants who were treated with somatropin 0.067 mg/kg/day in previous study for 12 months were maintained on the same dose

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

Dosage and administration details:

0.067 mg/kg/day

Number of subjects in period 1	Dose-Increasing Group	Dose-Remaining Group
Started	29	32
Completed	15	15
Not completed	14	17
Physician decision	2	4
Consent withdrawn by subject	11	10
Adverse event, non-fatal	-	1
Family Matters	-	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Dose-Increasing Group
Reporting group description:	
Participants who were treated with somatropin 0.033 mg/kg/day in previous study for 12 months received a dose of 0.067 mg/kg/day	
Reporting group title	Dose-Remaining Group
Reporting group description:	
Participants who were treated with somatropin 0.067 mg/kg/day in previous study for 12 months were maintained on the same dose	

Reporting group values	Dose-Increasing Group	Dose-Remaining Group	Total
Number of subjects	29	32	61
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	29	32	61
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous | Units: years			
arithmetic mean	5.2	5.4	
standard deviation	± 1.64	± 1.27	-
Gender, Male/Female Units: Participants			
Female	14	14	28
Male	15	18	33

End points

End points reporting groups

Reporting group title	Dose-Increasing Group
Reporting group description:	
Participants who were treated with somatropin 0.033 mg/kg/day in previous study for 12 months received a dose of 0.067 mg/kg/day	
Reporting group title	Dose-Remaining Group
Reporting group description:	
Participants who were treated with somatropin 0.067 mg/kg/day in previous study for 12 months were maintained on the same dose	

Primary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)
End point description:	
End point type	Primary
End point timeframe:	
Month 12 (at the end of previous study) to 156	

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: participant				
AE	27	31		
SAE	10	5		

Statistical analyses

Statistical analysis title	The number of participants with adverse event
Statistical analysis description:	
The number of participants with adverse event by treatment group was tabulated by system organ class and by preferred term.	
Comparison groups	Dose-Increasing Group v Dose-Remaining Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Number of participants with AE
Point estimate	0

Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	0
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0

Secondary: Height Velocity Standard Deviation Score (SDS) for Chronological Age

End point title	Height Velocity Standard Deviation Score (SDS) for Chronological Age

End point description:

Height velocity is the yearly height gain. Height velocity SDS is calculated as following formula; Height velocity SDS = (height velocity - mean) / standard deviation, where mean and standard deviation were based on standard Japanese values of the participants age and gender. The scores were centred around zero. Negative score indicated a participant was smaller for their age/gender.

End point type	Secondary

End point timeframe:

Month 12 (at the end of previous study) to 156

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: SDS				
arithmetic mean (standard deviation)				
Month 12-24 (Increasing:n=28, Remaining:n=32)	2.782 (± 1.978)	2.595 (± 1.731)		
Month 24-36 (Increasing:n=26, Remaining:n=28)	1.812 (± 1.526)	1.696 (± 2.111)		
Month 36-48 (Increasing:n=24, Remaining:n=23)	1.48 (± 1.543)	0.824 (± 1.527)		
Month 48-60 (Increasing:n=21, Remaining:n=20)	-0.041 (± 2.081)	0.48 (± 1.651)		
Month 60-72 (Increasing:n=20, Remaining:n=16)	-0.293 (± 1.585)	-0.046 (± 2.434)		
Month 72-84 (Increasing:n=15, Remaining:n=16)	-0.488 (± 3.117)	-1.511 (± 2.692)		
Month 84-96 (Increasing: n=11, Remaining: n=14)	0.263 (± 1.802)	-0.114 (± 1.964)		
Month 96-108 (Increasing:n=9, Remaining:n=8)	0.521 (± 2.058)	-0.466 (± 2.055)		
Month 108-120 (Increasing:n=6, Remaining:n=6)	-0.668 (± 2.126)	-0.59 (± 2.693)		
Month 120-132 (Increasing:n=5, Remaining:n=4)	-1.08 (± 1.953)	1.173 (± 3.042)		
Month 132-144 (Increasing:n=4, Remaining:n=2)	2.655 (± 4.329)	0.73 (± 2.022)		
Month 144-156 (Increasing:n=3, Remaining:n=0)	3.373 (± 1.995)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Height Velocity

End point title	Height Velocity
End point description:	
Height velocity is the yearly height gain	
End point type	Secondary
End point timeframe:	
Month 12 (at the end of previous study) to 156	

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: cm/year				
arithmetic mean (standard deviation)				
Month 12-24(Increasing:n=28, Remaining:n=32)	7.83 (± 1.33)	7.7 (± 1.19)		
Month 24-36 (Increasing:n=26, Remaining:n=28)	6.88 (± 0.94)	6.75 (± 1.52)		
Month 36-48 (Increasing:n=24, Remaining:n=23)	6.68 (± 0.98)	6.08 (± 1.14)		
Month 48-60 (Increasing:n=21, Remaining:n=20)	6.06 (± 1.49)	6.3 (± 1.24)		
Month 60-72 (Increasing:n=20, Remaining: n=16)	6.08 (± 1.45)	6.49 (± 1.37)		
Month 72-84 (Increasing:n=15, Remaining:n=16)	4.89 (± 2.18)	4.88 (± 1.86)		
Month 84-96 (Increasing:n=11, Remaining:n=14)	5.16 (± 1.2)	4.82 (± 2.12)		
Month 96-108 (Increasing:n=9, Remaining:n=8)	5.18 (± 2.16)	5.55 (± 2.42)		
Month 108-120 (Increasing:n=6, Remaining:n=6)	5.72 (± 2.24)	5.03 (± 1.86)		
Month 120-132 (Increasing:n=5, Remaining:n=4)	4.84 (± 1.3)	4.3 (± 1.84)		
Month 132-144 (Increasing:n=4, Remaining:n=2)	4.38 (± 1.1)	2.6 (± 0.14)		
Month144-156(Increasing:n=3, Remaining:n=0)	3.1 (± 1.92)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Height SDS for Chronological Age

End point title	Height SDS for Chronological Age

End point description:

Height SDS is calculated as following formula; Height SDS = (height - mean) / standard deviation, where mean and standard deviation were based on standard Japanese values on the participant age and gender. The scores were centred around zero. Negative score indicated a participant was smaller for their age/gender.

End point type	Secondary

End point timeframe:

Month 12 (at the end of previous study) to 156

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: SDS				
arithmetic mean (standard deviation)				
Month 12 (Increasing:n=29, Remaining:n=32)	-2.53 (± 0.92)	-2.17 (± 0.96)		
Month 24 (Increasing:n=28, Remaining:n=32)	-2.02 (± 0.97)	-1.7 (± 1.03)		
Month 36 (Increasing:n=26, Remaining:n=28)	-1.8 (± 0.99)	-1.53 (± 1.1)		
Month 48 (Increasing:n=24, Remaining:n=23)	-1.48 (± 1.05)	-1.49 (± 1.15)		
Month 60 (Increasing:n=21, Remaining:n=20)	-1.53 (± 1.06)	-1.44 (± 1.1)		
Month 72 (Increasing:n=20, Remaining:n=16)	-1.56 (± 1.11)	-1.43 (± 1.06)		
Month 84 (Increasing:n=15, Remaining:n=16)	-1.73 (± 1.13)	-1.58 (± 1.17)		
Month 96 (Increasing:n=11, Remaining:n=14)	-1.52 (± 0.89)	-1.87 (± 1.36)		
Month 108 (Increasing:n=9, Remaining:n=8)	-1.52 (± 1.01)	-1.63 (± 1.48)		
Month 120 (Increasing:n=6, Remaining:n=6)	-1.52 (± 1.2)	-1.25 (± 0.59)		
Month 132 (Increasing:n=5, Remaining:n=4)	-1.96 (± 1.11)	-0.98 (± 0.51)		
Month 144 (Increasing:n=4, Remaining:n=2)	-1.73 (± 0.87)	-0.7 (± 0.42)		
Month 156 (Increasing:n=3, Remaining:n=0)	-1.77 (± 0.76)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Height Velocity SDS for Bone Age

End point title	Height Velocity SDS for Bone Age

End point description:

To measure bone age, X-ray images of the left hand were centrally assessed by an independent specialist using the Tanner-Whitehouse 2 (RUS) method standardized for Japanese children. Height velocity is the yearly height gain. Height velocity SDS for bone age is calculated as following formula; Height velocity SDS = (height velocity - mean) / standard deviation, where mean and standard deviation were based on standard Japanese values corresponding to bone age and gender. The scores were centred around zero. Negative score indicated a participant was smaller for their age/gender.

End point type	Secondary

End point timeframe:

Month 12 (at the end of previous study) to 156

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: SDS				
arithmetic mean (standard deviation)				
Month 12-24 (Increasing: n=26, Remaining: n=31)	2.586 (± 2.268)	2.461 (± 1.99)		
Month 24-36 (Increasing: n=24, Remaining: n=27)	1.503 (± 1.83)	1.091 (± 1.852)		
Month 36-48 (Increasing: n=22, Remaining: n=22)	1.196 (± 1.409)	0.51 (± 1.809)		
Month 48-60 (Increasing: n=20, Remaining: n=19)	-0.062 (± 1.775)	0.913 (± 2.146)		
Month 60-72 (Increasing: n=16, Remaining: n=14)	0.281 (± 2.814)	0.949 (± 2.729)		
Month 72-84 (Increasing: n=13, Remaining: n=13)	-1.249 (± 2.558)	0.932 (± 2.545)		
Month 84-96 (Increasing: n=10, Remaining: n=13)	0.804 (± 3.44)	0.286 (± 2.351)		
Month 96-108 (Increasing: n=8, Remaining: n=7)	-0.634 (± 2.419)	-0.223 (± 1.352)		
Month 108-120 (Increasing: n=5, Remaining: n=5)	0.07 (± 4.12)	0.532 (± 1.809)		
Month 120-132 (Increasing: n=4, Remaining: n=4)	1.553 (± 3.019)	2.718 (± 0.864)		
Month 132-144 (Increasing: n=3, Remaining: n=2)	2.31 (± 1.711)	2.185 (± 0.304)		
Month 144-156 (Increasing: n=2, Remaining: n=0)	2.71 (± 2.942)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Height SDS for Bone Age

End point title	Height SDS for Bone Age

End point description:

To measure bone age, X-ray images of the left hand were centrally assessed by an independent specialist using the Tanner-Whitehouse 2 (RUS) method standardized for Japanese children. Height SDS for bone age is calculated as following formula; Height SDS = (height - mean) / standard deviation, where mean and standard deviation were based on standard Japanese values corresponding to bone age and gender. The scores were centred around zero. Negative score indicated a participant was smaller for their age/gender.

End point type	Secondary

End point timeframe:

Month 12 (at the end of previous study) to 156

End point values	Dose-Increasing Group	Dose-Remaining Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: SDS				
arithmetic mean (standard deviation)				
Month 12 (Increasing: n=27, Remaining: n=31)	-1.19 (± 1.2)	-0.68 (± 1.54)		
Month 24 (Increasing:n=26, Remaining:n=31)	-1.15 (± 1.15)	-0.88 (± 1.79)		
Month 36 (Increasing:n=24, Remaining:n=27)	-1.2 (± 1.35)	-1.17 (± 1.62)		
Month 48 (Increasing:n=22, Remaining:n=22)	-0.74 (± 1.32)	-1.46 (± 1.01)		
Month 60 (Increasing:n=20, Remaining:n=19)	-1.16 (± 1.21)	-1.8 (± 0.97)		
Month 72 (Increasing:n=16, Remaining:n=14)	-1.78 (± 1.02)	-1.7 (± 0.77)		
Month 84 (Increasing:n=13, Remaining:n=13)	-1.85 (± 1.17)	-2.15 (± 0.92)		
Month 96 (Increasing:n=10, Remaining:n=13)	-1.77 (± 1.12)	-2.27 (± 1.06)		
Month 108 (Increasing:n=8, Remaining:n=7)	-1.41 (± 0.97)	-1.94 (± 1.37)		
Month 120 (Increasing:n=5, Remaining:n=5)	-1.58 (± 1.5)	-1.38 (± 0.98)		
Month 132 (Increasing:n=4, Remaining:n=4)	-2.1 (± 1.21)	-0.98 (± 0.74)		
Month 144 (Increasing:n=3, Remaining:n=2)	-1.4 (± 0.17)	-0.65 (± 0.64)		
Month 156 (Increasing:n=2, Remaining:n=0)	-1.55 (± 0.92)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Month 12 (at the end of previous study) to 156	
Assessment type	Systematic

Dictionary used	
Dictionary name	WHO-ART, 2001(014)
Dictionary version	2001 (014)

Reporting groups	
Reporting group title	Dose-Remainig Group
Reporting group description:	
Participants in the 0.067 mg/kg/day group in previous study were maintained on the dose in this expention study	
Reporting group title	Dose-Increasing Group
Reporting group description:	
Participants who were treated with somatropin 0.033 mg/kg/day in previous study for 12 months received a dose of 0.067 mg/kg/day	

Serious adverse events	Dose-Remainig Group	Dose-Increasing Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 32 (15.63%)	10 / 29 (34.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
HYPOSPADIAS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CRYPTORCHISM			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
INFLICTED INJURY			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	1 / 32 (3.13%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
GASTROENTERITIS			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
HERNIA INGUINAL			
subjects affected / exposed	1 / 32 (3.13%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVARIAN DISORDER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
PHARYNGITIS			
subjects affected / exposed	2 / 32 (6.25%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			

subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESP TRACT INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASTHMA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
ADENOID HYPERTROPHY			
subjects affected / exposed	2 / 32 (6.25%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
INFECTION VIRAL			
subjects affected / exposed	1 / 32 (3.13%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OTITIS MEDIA			
subjects affected / exposed	1 / 32 (3.13%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEALING IMPAIRED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 29 (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: 5 %

Non-serious adverse events	Dose-Remainig Group	Dose-Increasing Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	27 / 29 (93.10%)	
General disorders and administration site conditions			
PURPURA			
subjects affected / exposed	5 / 32 (15.63%)	6 / 29 (20.69%)	
occurrences (all)	8	6	
HAEMATOMA			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
ALLERGIC REACTION			
subjects affected / exposed	3 / 32 (9.38%)	0 / 29 (0.00%)	
occurrences (all)	9	0	
FEVER			
subjects affected / exposed	1 / 32 (3.13%)	11 / 29 (37.93%)	
occurrences (all)	3	18	
PAIN			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
INFLUENZA-LIKE SYMPTOMS			
subjects affected / exposed	15 / 32 (46.88%)	16 / 29 (55.17%)	
occurrences (all)	28	24	
VARICELLA			
subjects affected / exposed	2 / 32 (6.25%)	3 / 29 (10.34%)	
occurrences (all)	2	3	
INFLICTED INJURY			
subjects affected / exposed	4 / 32 (12.50%)	2 / 29 (6.90%)	
occurrences (all)	5	2	
MOLLUSCUM CONTAGIOSUM			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	4	0	
SCOLIOSIS			

subjects affected / exposed	2 / 32 (6.25%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
LACERATION			
subjects affected / exposed	3 / 32 (9.38%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
Reproductive system and breast disorders			
OVARIAN DISORDER			
subjects affected / exposed	0 / 32 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	4	
Respiratory, thoracic and mediastinal disorders			
COUGHING			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
PHARYNGITIS			
subjects affected / exposed	9 / 32 (28.13%)	7 / 29 (24.14%)	
occurrences (all)	16	9	
PNEUMONIA			
subjects affected / exposed	2 / 32 (6.25%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
RHINITIS			
subjects affected / exposed	12 / 32 (37.50%)	8 / 29 (27.59%)	
occurrences (all)	29	14	
SINUSITIS			
subjects affected / exposed	4 / 32 (12.50%)	5 / 29 (17.24%)	
occurrences (all)	6	6	
UPPER RESP TRACT INFECTION			
subjects affected / exposed	28 / 32 (87.50%)	25 / 29 (86.21%)	
occurrences (all)	157	214	
BRONCHITIS			
subjects affected / exposed	10 / 32 (31.25%)	9 / 29 (31.03%)	
occurrences (all)	25	31	
ASTHMA			
subjects affected / exposed	6 / 32 (18.75%)	6 / 29 (20.69%)	
occurrences (all)	34	20	
Injury, poisoning and procedural complications			

INJECTION SITE BLEEDING			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
STING			
subjects affected / exposed	4 / 32 (12.50%)	1 / 29 (3.45%)	
occurrences (all)	4	1	
Congenital, familial and genetic disorders			
SKELETAL MALFORMATION			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
TOOTH MALFORMATION			
subjects affected / exposed	1 / 32 (3.13%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Cardiac disorders			
HYPOTENSION POSTURAL			
subjects affected / exposed	1 / 32 (3.13%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 32 (9.38%)	4 / 29 (13.79%)	
occurrences (all)	4	5	
Blood and lymphatic system disorders			
EOSINOPHILIA			
subjects affected / exposed	3 / 32 (9.38%)	2 / 29 (6.90%)	
occurrences (all)	4	7	
LEUKOCYTOSIS			
subjects affected / exposed	4 / 32 (12.50%)	2 / 29 (6.90%)	
occurrences (all)	5	3	
LYMPHADENOPATHY			
subjects affected / exposed	3 / 32 (9.38%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
LYMPHOCYTES ATYPICA			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Eye disorders			

CONJUNCTIVITIS			
subjects affected / exposed	12 / 32 (37.50%)	8 / 29 (27.59%)	
occurrences (all)	16	17	
EYE ABNORMALITY			
subjects affected / exposed	5 / 32 (15.63%)	4 / 29 (13.79%)	
occurrences (all)	8	5	
MYOPIA			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	4 / 32 (12.50%)	3 / 29 (10.34%)	
occurrences (all)	6	5	
DIARRHOEA			
subjects affected / exposed	2 / 32 (6.25%)	5 / 29 (17.24%)	
occurrences (all)	2	5	
VOMITING			
subjects affected / exposed	3 / 32 (9.38%)	5 / 29 (17.24%)	
occurrences (all)	3	7	
ABDOMINAL PAIN			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
GASTROENTERITIS			
subjects affected / exposed	10 / 32 (31.25%)	17 / 29 (58.62%)	
occurrences (all)	22	34	
NAUSEA			
subjects affected / exposed	2 / 32 (6.25%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
STOMATITIS			
subjects affected / exposed	1 / 32 (3.13%)	2 / 29 (6.90%)	
occurrences (all)	3	6	
TOOTH CARIES			
subjects affected / exposed	2 / 32 (6.25%)	4 / 29 (13.79%)	
occurrences (all)	2	6	
TOOTH DISORDER			

subjects affected / exposed	3 / 32 (9.38%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
ENTEROCOLITIS			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
SGOT INCREASED			
subjects affected / exposed	1 / 32 (3.13%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
SGPT INCREASED			
subjects affected / exposed	1 / 32 (3.13%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	3 / 32 (9.38%)	2 / 29 (6.90%)	
occurrences (all)	3	2	
DERMATITIS			
subjects affected / exposed	2 / 32 (6.25%)	3 / 29 (10.34%)	
occurrences (all)	3	12	
ECZEMA			
subjects affected / exposed	5 / 32 (15.63%)	6 / 29 (20.69%)	
occurrences (all)	10	20	
PRURITUS			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
RASH			
subjects affected / exposed	1 / 32 (3.13%)	3 / 29 (10.34%)	
occurrences (all)	1	4	
RASH ERYTHEMATOUS			
subjects affected / exposed	1 / 32 (3.13%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
RASH PUSTULAR			
subjects affected / exposed	2 / 32 (6.25%)	4 / 29 (13.79%)	
occurrences (all)	2	4	
SKIN DISORDER			

subjects affected / exposed	1 / 32 (3.13%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
URTICARIA			
subjects affected / exposed	2 / 32 (6.25%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
DERMATITIS CONTACT			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
OTITIS EXTERNA			
subjects affected / exposed	2 / 32 (6.25%)	3 / 29 (10.34%)	
occurrences (all)	2	3	
BULLOUS ERUPTION			
subjects affected / exposed	2 / 32 (6.25%)	2 / 29 (6.90%)	
occurrences (all)	2	3	
VERRUCA			
subjects affected / exposed	4 / 32 (12.50%)	1 / 29 (3.45%)	
occurrences (all)	5	1	
Renal and urinary disorders			
URINARY INCONTINENCE			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
HAEMATURIA			
subjects affected / exposed	3 / 32 (9.38%)	0 / 29 (0.00%)	
occurrences (all)	6	0	
Endocrine disorders			
SIALOADENITIS			
subjects affected / exposed	2 / 32 (6.25%)	3 / 29 (10.34%)	
occurrences (all)	2	3	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	5 / 32 (15.63%)	4 / 29 (13.79%)	
occurrences (all)	7	4	
Infections and infestations			
INFECTION BACTERIAL			
subjects affected / exposed	6 / 32 (18.75%)	4 / 29 (13.79%)	
occurrences (all)	9	8	

INFECTION VIRAL			
subjects affected / exposed	0 / 32 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
OTITIS MEDIA			
subjects affected / exposed	14 / 32 (43.75%)	13 / 29 (44.83%)	
occurrences (all)	31	32	
HERPES ZOSTER			
subjects affected / exposed	1 / 32 (3.13%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
ABSCESS			
subjects affected / exposed	2 / 32 (6.25%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
GLUCOSE TOLERANCE ABNORMAL			
subjects affected / exposed	3 / 32 (9.38%)	1 / 29 (3.45%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported