Clinical trial results:
A Clinical Study of Immune Globulin Subcutaneous (Human) (IGSC), 20% for the Evaluation of Efficacy, Safety, and Pharmacokinetics in Subjects with Primary Immunodeficiency Diseases

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-019459-23
Trial protocol	DE AT GB HU SE NL BE
Global end of trial date	13 May 2014

Results information

Result version number	v1 (current)
This version publication date	13 February 2016
First version publication date	13 February 2016

Trial information

Trial identification

Sponsor protocol code	170903

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Baxalta Innovations GmbH
Sponsor organisation address	Industriestrasse 67, Vienna, Austria, 1221
Public contact	Clinical Trials Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com
Scientific contact	Clinical Trials Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2014
Global end of trial reached?	Yes
Global end of trial date	13 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of Immune Globulin Subcutaneous (Human) (IGSC), 20% in subjects with PID.

Protection of trial subjects:

This study was conducted in accordance with the standards of Good Clinical Practice (GCP) in effect at the time of the study.
The study was conducted in accordance with the principles and guidelines described in the study protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Hungary: 22
Worldwide total number of subjects	49
EEA total number of subjects	49

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)	13
Adolescents (12-17 years)	12
Adults (18-64 years)	21
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was conducted in Europe at 16 sites.

Pre-assignment

Screening details:

A total of 55 subjects provided informed consent and were screened for study participation, of which there were 6 screen failures. 49 subjects started in Epoch 1.

Pre-assignment period milestones

Number of subjects started	55[1]
Number of subjects completed	49

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen Failure: 6

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 55 subjects provided informed consent and were screened for study participation, of which there were 6 screen failures. 49 subjects started in Epoch 1.

Period 1

Period 1 title	Epoch 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	IGIV

Arm description:

Subjects treated with IGIV 10%.

Arm type	Experimental
Investigational medicinal product name	KIOVIG (IGIV, 10%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

once every 3 or 4 weeks, dose as during pre-study period (300 mg/kg – 1.0 g/kg body weight [BW]/4 weeks)

Arm title	IGSC

Arm description:

Subjects treated with SUBCUVIA.

Arm type	Experimental
Investigational medicinal product name	SUBCUVIA (IGSC, 16%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

once every week or once every two weeks, dose as during pre-study period (300 mg/kg – 1.0 g/kg BW/4 weeks)

Number of subjects in period 1	IGIV	IGSC
Started	33	16
Completed	32	16
Not completed	1	0
Pregnancy	1	-

Period 2

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

Arms

Arm title	IGSC 20%
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Immune Globulin Subcutaneous (Human) (IGSC), 20%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

every week, at the same dose as used during Study Epoch 1, to be calculated on the basis of weekly equivalents (300 mg/kg – 1.0 g/kg BW/4 weeks)

Number of subjects in period 2	IGSC 20%
Started	48
Completed	45
Not completed	3
Consent withdrawn by subject	3

Baseline characteristics

Reporting groups	
Reporting group title	Epoch 1
Reporting group description:	
Epoch 1	

Reporting group values	Epoch 1	Total	
Number of subjects	49	49	
Age categorical Units: Subjects			
From 65-84 years	3	3	
Adults (18-64 years)	21	21	
Adolescents (12-17 years)	12	12	
Children (2-11 years)	13	13	
Gender categorical Units:			
Female	19	19	
Male	30	30	

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Point estimate for rate of VASBIs/year				
number (not applicable)	0	0.022	0.27	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough levels of IgG at the end of the treatment interval

End point title	Trough levels of IgG at the end of the treatment interval

End point description:

The analysis of IgG Total was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	SC 1 Week	SC 2 Weeks	IV 4 Weeks	SC 20% 1 Week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	2	11	40
Units: g/L				
median (full range (min-max))	9.53 (5.41 to 12.28)	8.98 (8.77 to 9.19)	7.52 (5.25 to 12.75)	8.26 (4.27 to 15.87)

Statistical analyses

No statistical analyses for this end point

Secondary: Trough level of Anti-Tetanus Antibody

End point title	Trough level of Anti-Tetanus Antibody

End point description:

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: IU/mL				
median (full range (min-max))				
IV 3 Weeks - Epoch 1 Infusion 4 (n=4)	1.88 (1.1 to 2.71)			
IV 3 Weeks - Epoch 1 Infusion 5 (n=5)	1.52 (1.11 to 2.75)			
IV 4 Weeks - Epoch 1 Infusion 3 (n=27)	1.6 (0.73 to 5.85)			
IV 4 Weeks - Epoch 1 Infusion 4 (n=27)	1.62 (0.91 to 6.57)			
SC 1 Week - Epoch 1 Infusion 12 (n=13)	2.38 (1.31 to 3.81)			
SC 1 Week - Epoch 2 Infusion 1 (n=11)	2.66 (1.44 to 8.3)			
SC 2 Weeks - Epoch 1 Infusion 6 (n=2)	2.72 (2.49 to 2.94)			
SC 2 Weeks - Epoch 2 Infusion 1 (n=1)	4.31 (4.31 to 4.31)			
SC 20% 1 Week - Epoch 2 Infusion 21 (n=43)	2.91 (1.16 to 8.3)			
SC 20% 1 Week - Epoch 2 Infusion 27 (n=42)	2.78 (0.22 to 7.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough level of Hepatitis B Antibody

End point title	Trough level of Hepatitis B Antibody

End point description:

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: mIU/mL				
median (full range (min-max))				
IV 3 Weeks - Epoch 1 Infusion 4 (n=5)	339 (222 to 906)			
IV 3 Weeks - Epoch 1 Infusion 5 (n=4)	511.5 (299 to 1000)			
IV 4 Weeks - Epoch 1 Infusion 3 (n=27)	335 (170 to 740)			

IV 4 Weeks - Epoch 1 Infusion 4 (n=27)	327 (161 to 657)			
SC 1 Week - Epoch 1 Infusion 12 (n=13)	264 (112 to 478)			
SC 1 Week - Epoch 2 Infusion 1 (n=12)	230 (115 to 483)			
SC 2 Weeks - Epoch 1 Infusion 6 (n=2)	337.5 (331 to 344)			
SC 2 Weeks - Epoch 2 Infusion 1 (n=1)	315 (315 to 315)			
SC 20% 1 Week - Epoch 2 Infusion 21 (n=43)	244 (120 to 446)			
SC 20% 1 Week - Epoch 2 Infusion 27 (n=42)	230 (120 to 438)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough level of Haemophilus Influenzae Antibody

End point title	Trough level of Haemophilus Influenzae Antibody

End point description:

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: mg/L				
median (full range (min-max))				
IV 3 Weeks - Epoch 1 Infusion 4 (n=5)	2.56 (1.19 to 2.89)			
IV 3 Weeks - Epoch 1 Infusion 5 (n=5)	2.73 (1.11 to 2.8)			
IV 4 Weeks - Epoch 1 Infusion 3 (n=27)	1.93 (1.09 to 4.2)			
IV 4 Weeks - Epoch 1 Infusion 4 (n=27)	1.76 (1.23 to 3.94)			
SC 1 Week - Epoch 1 Infusion 12 (n=13)	2.94 (1.62 to 10.84)			
SC 1 Week - Epoch 2 Infusion 1 (n=11)	3.02 (1.64 to 10.35)			
SC 2 Weeks - Epoch 1 Infusion 6 (n=2)	3.41 (2.74 to 4.07)			
SC 2 Weeks - Epoch 2 Infusion 1 (n=1)	4.01 (4.01 to 4.01)			
SC 20 % 1 Week - Epoch 2 Infusion 21 (n=43)	2.08 (1.27 to 6.85)			

SC 20 % 1 Week - Epoch 2 Infusion 27 (n=41)	2.04 (0.97 to 7.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve (AUC) for IgG total by treatment

End point title	Area under the curve (AUC) for IgG total by treatment

End point description:

Assessments were performed in subjects 12 years and older. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

Epoch 1: between infusion 3 and infusion 4 for subjects under IGIV, 10% and between infusion 12 of epoch 1 and infusion 1 of IGSC, 20% for subjects under IGSC, 16%. Epoch 2: between infusion 21 and infusion 22 of IGSC, 20%.

End point values	SC 1 Week	SC 2 Weeks	IV 3 Weeks	IV 4 Weeks
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	3	22
Units: g*days/L				
median (full range (min-max))	68.4 (27.66 to 86.99)	132.68 (113.52 to 151.85)	252.1 (177.47 to 335.46)	278.94 (168.63 to 393.35)

End point values	SC 20% 1 Week			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: g*days/L				
median (full range (min-max))	62.52 (37.51 to 137.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (for intravenous) and apparant clearance (for subcutaneous) for IgG total by treatment

End point title	Clearance (for intravenous) and apparant clearance (for subcutaneous) for IgG total by treatment

End point description:

Assessments were performed in subjects 12 years and older. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

Epoch 1: between infusion 3 and infusion 4 for subjects under IGIV, 10% and between infusion 12 of epoch 1 and infusion 1 of IGSC, 20% for subjects under IGSC, 16%. Epoch 2: between infusion 21 and infusion 22 of IGSC, 20%.

End point values	SC 1 Week	SC 2 Weeks	IV 3 Weeks	IV 4 Weeks
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	2	3	16
Units: mL/kg/days				
median (full range (min-max))	1.62 (1.37 to 3.47)	1.62 (1.54 to 1.7)	1.05 (0.97 to 1.97)	1.42 (1.04 to 2.39)

End point values	SC 20% 1 Week			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: mL/kg/days				
median (full range (min-max))	1.7 (1.12 to 3.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) and minimum concentration (Cmin) for IgG total by treatment

End point title	Maximum concentration (Cmax) and minimum concentration (Cmin) for IgG total by treatment

End point description:

Assessments were performed in subjects 12 years and older. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

Epoch 1: between infusion 3 and infusion 4 for subjects under IGIV, 10% and between infusion 12 of epoch 1 and infusion 1 of IGSC, 20% for subjects under IGSC, 16%. Epoch 2: between infusion 21 and infusion 22 of IGSC, 20%.

End point values	SC 1 Week	SC 2 Weeks	IV 3 Weeks	IV 4 Weeks
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	2	3	16
Units: g/L				
median (full range (min-max))				
Cmax	10.9 (4.42 to 13.18)	10.17 (8.42 to 11.92)	15.17 (14.78 to 20.47)	15.37 (11.7 to 21.24)
Cmin	8.77 (3.37 to 11.89)	8.76 (7.42 to 10.09)	10.5 (6.26 to 12.98)	6.59 (4.27 to 11.66)

End point values	SC 20% 1 Week			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: g/L				
median (full range (min-max))				
Cmax	9.8 (5.9 to 20.69)			
Cmin	8.04 (4.42 to 16.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum concentration (Tmax) for IgG total by treatment

End point title	Time to maximum concentration (Tmax) for IgG total by treatment

End point description:

Assessments were performed in subjects 12 years and older. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

Epoch 1: between infusion 3 and infusion 4 for subjects under IGIV, 10% and between infusion 12 of epoch 1 and infusion 1 of IGSC, 20% for subjects under IGSC, 16%. Epoch 2: between infusion 21 and infusion 22 of IGSC, 20%.

End point values	SC 1 Week	SC 2 Weeks	IV 3 Weeks	IV 4 Weeks
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	2	3	16
Units: hours				
median (full range (min-max))	25.05 (22.98 to 170.85)	167.38 (121.75 to 213)	24.33 (23.83 to 27.8)	4.58 (1.97 to 101.83)

End point values	SC 20% 1 Week			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: hours				
median (full range (min-max))	73.92 (19.78 to 192.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual rate of infections per subject (all infections; sinus infections)

End point title	Annual rate of infections per subject (all infections; sinus infections)

End point description:

Rate = Number of infections divided by the total number of subject-years under treatment

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: Rate				
number (not applicable)				
IV - All infections	6.29			
IV - Sinus bacterial	0.59			
IV - Sinusitis	0.12			
SC - All infections	8.92			
SC - Acute sinusitis	0.54			
SC 20% - All infections	4.38			
SC 20% - Sinusitis	0.15			
SC 20% - Acute sinusitis	0.09			
SC 20% - Chronic sinusitis	0.02			
SC 20% - Sinusitis bacterial	0.02			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual rate of fever episodes per subject

End point title	Annual rate of fever episodes per subject

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Rate				
number (not applicable)	0.95	0.88	2.16	

Statistical analyses

No statistical analyses for this end point

Secondary: Days off school or work

End point title	Days off school or work

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Days	90	710	187	

Statistical analyses

No statistical analyses for this end point

Secondary: Days on antibiotics

End point title	Days on antibiotics

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:
From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Days	165	827	201	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hospitalizations

End point title	Number of hospitalizations

End point description:
The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:
From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Days	1	7	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Length of stay in hospital (in days)

End point title	Length of stay in hospital (in days)

End point description:
The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:
From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Days	1	76	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of acute physician visits

End point title	Number of acute physician visits

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Number of visits	43	172	28	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of related AEs (including and excluding infections) divided by the number of subjects

End point title	Number of related AEs (including and excluding infections) divided by the number of subjects

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Percent				
number (not applicable)				
Including infections	21.2	41.7	31.3	
Excluding infections	21.2	41.7	31.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of related AEs (including and excluding infections) divided by the number of infusions

End point title	Number of related AEs (including and excluding infections) divided by the number of infusions

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Percent				
number (not applicable)				
Including infections	12.2	7.8	5	
Excluding infections	12.2	7.8	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Annual rate of SAEs, related and not related

End point title	Annual rate of SAEs, related and not related

End point description:

Rate per year = number of AEs divided by the total number of subject-years under treatment.
The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Rate per year				
number (not applicable)				
Unrelated	0.24	0.18	0.54	
Related	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGIV treatment divided by the number of subjects

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGIV treatment divided by the number of subjects

End point description:

Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Rate per Subject				
number (not applicable)				
Local AEs - Non-serious - Mild	0.121			
Systemic AEs incl. inf. - Non-serious - Mild	3.606			
Systemic AEs incl. inf. - Non-serious - Moderate	0.879			
Systemic AEs incl. inf. - Serious - Moderate	0.061			
Systemic AEs excl. inf. - Non-serious - Mild	2.455			
Systemic AEs excl. inf. - Non-serious - Moderate	0.424			
Systemic AEs excl. inf. - Serious - Moderate	0.061			

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGSC treatment divided by the number of subjects

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGSC treatment divided by the number of subjects

End point description:

Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: Rate per subject				
number (not applicable)				
Local AEs - Non-serious - Mild	0.125			
Systemic AEs incl. inf. - Non-serious - Mild	3			
Systemic AEs incl. inf. - Non-serious - Moderate	1.063			
Systemic AEs incl. inf. - Serious - Moderate	0.125			
Systemic AEs excl. inf. - Non-serious - Mild	1.438			
Systemic AEs excl. inf. - Non-serious - Moderate	0.625			
Systemic AEs excl. inf. - Serious - Moderate	0.063			

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGSC 20% treatment divided by the number of subjects

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGSC 20% treatment divided by the number of subjects

End point description:

Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: Rate per subject				
number (not applicable)				
Local AEs - Non-serious - Mild	3.667			
Local AEs - Non-serious - Moderate	0.042			
Systemic AEs incl. inf. - Non-serious - Mild	8.646			
Systemic AEs incl. inf. - Non-serious - Moderate	2.604			
Systemic AEs incl. inf. - Serious - Mild	0.021			
Systemic AEs incl. inf. - Serious - Moderate	0.104			
Systemic AEs incl. inf. - Serious - Severe	0.042			
Systemic AEs excl. inf. - Non-serious - Mild	5.479			
Systemic AEs excl. inf. - Non-serious - Moderate	1.708			
Systemic AEs excl. inf. - Non-serious - Severe	0.042			
Systemic AEs excl. inf. - Serious - Mild	0.021			
Systemic AEs excl. inf. - Serious - Moderate	0.063			
Systemic AEs excl. inf. - Serious - Severe	0.042			

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGIV treatment divided by the number of infusions

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGIV treatment divided by the number of infusions

End point description:

Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Rate per infusion				
number (not applicable)				
Local AEs - Non-serious - Mild	0.029			
Systemic AEs incl. inf. - Non-serious - Mild	0.856			
Systemic AEs incl. inf. - Non-serious - Moderate	0.209			
Systemic AEs incl. inf. - Serious - Moderate	0.014			
Systemic AEs excl. inf. - Non-serious - Mild	0.583			
Systemic AEs excl. inf. - Non-serious - Moderate	0.101			
Systemic AEs excl. inf. - Serious - Moderate	0.014			

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGSC treatment divided by the number of infusions

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGSC treatment divided by the number of infusions
End point description:	
Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections	
End point type	Secondary
End point timeframe:	
From first infusion until the end of the study, approximately 15 months per subject	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: Rate per infusion				
number (not applicable)				
Local AEs - Non-serious - Mild	0.011			
Systemic AEs incl. inf. - Non-serious - Mild	0.265			
Systemic AEs incl. inf. - Non-serious - Moderate	0.094			
Systemic AEs incl. inf. - Serious - Moderate	0.011			
Systemic AEs excl. inf. - Non-serious - Mild	0.127			

Systemic AEs excl. inf. - Non-serious - Moderate	0.055			
Systemic AEs excl. inf. - Serious - Moderate	0.006			

Statistical analyses

No statistical analyses for this end point

Secondary: Rates of AEs (including and excluding infections) defined as number of AEs under IGSC 20% treatment divided by the number of infusions

End point title	Rates of AEs (including and excluding infections) defined as number of AEs under IGSC 20% treatment divided by the number of infusions

End point description:

Note: Abbreviations: incl. inf. = including infections; excl. inf. = excluding infections. Rate per infusion for systemic AEs including infections - Serious - Mild: 0.001 entered instead of <0.001. Rate per infusion for systemic AEs excluding infections - Serious - Mild: 0.001 entered instead of <0.001.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: Rate per infusion				
number (not applicable)				
Local AEs - Non-serious - Mild	0.075			
Local AEs - Non-serious - Moderate	0.001			
Systemic AEs incl. inf. - Non-serious - Mild	0.177			
Systemic AEs incl. inf. - Non-serious - Moderate	0.053			
Systemic AEs incl. inf. - Serious - Mild	0.001			
Systemic AEs incl. inf. - Serious - Moderate	0.002			
Systemic AEs incl. inf. - Serious - Severe	0.001			
Systemic AEs excl. inf. - Non-serious - Mild	0.112			
Systemic AEs excl. inf. - Non-serious - Moderate	0.035			
Systemic AEs excl. inf. - Non-serious - Severe	0.001			
Systemic AEs excl. inf. - Serious - Mild	0.001			
Systemic AEs excl. inf. - Serious - Moderate	0.001			
Systemic AEs excl. inf. - Serious - Severe	0.001			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of infusions associated with one or more related non-serious AE (including and excluding infections)

End point title	Proportion of infusions associated with one or more related non-serious AE (including and excluding infections)

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Proportion of infusions				
number (not applicable)				
Including infections	12.2	7.8	5	
Excluding infections	12.2	7.8	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects reporting one or more related non-serious AE (including and excluding infections)

End point title	Proportion of subjects reporting one or more related non-serious AE (including and excluding infections)

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Proportion of subjects				
number (not applicable)				
Including Infections	21.2	41.7	31.3	
Excluding infection	21.2	41.7	31.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of temporally associated AEs (including and excluding infections) divided by the number of subjects

End point title	Number of temporally associated AEs (including and excluding infections) divided by the number of subjects

End point description:

Temporally associated AEs are defined as AEs occurring during or within 72 hours of infusion completion. Rate per subject = total number of AEs divided by the total number of subjects under treatment. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Rate per subject				
number (not applicable)				
Including infections	1.303	9.458	1.938	
Excluding infections	1.212	7.917	1.25	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of temporally associated AEs (including and excluding infections) divided by the number of infusions

End point title	Number of temporally associated AEs (including and excluding infections) divided by the number of infusions

End point description:

Temporally associated AEs are defined as AEs occurring during or within 72 hours of infusion completion. Rate per infusion = total number of AEs divided by the total number of infusions under treatment. The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Rate per infusion				
number (not applicable)				
Including infections	0.309	0.193	0.171	
Excluding infections	0.288	0.162	0.11	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of infusions for which the infusion rate was reduced and/or the infusion interrupted or stopped for tolerability concerns or for AEs

End point title	Proportion of infusions for which the infusion rate was reduced and/or the infusion interrupted or stopped for tolerability concerns or for AEs

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Percentage of infusions				
number (not applicable)	0.7	0.2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects for whom the infusion rate was reduced and/or the infusion interrupted or stopped for tolerability concerns or for AEs

End point title	Proportion of subjects for whom the infusion rate was reduced and/or the infusion interrupted or stopped for tolerability concerns or for AEs

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Percentage of subjects				
number (not applicable)	3	4.2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of infusions tolerated

End point title	Proportion of infusions tolerated

End point description:

The analysis was conducted on subjects in the Safety Analysis Dataset.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	IGIV	IGSC 20%	IGSC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	48	16	
Units: Percentage of infusions				
number (not applicable)	100	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of adults and adolescents who experienced potential hemolysis (a decline in hemoglobin of 2.0 g/dL or more)

End point title	Number of adults and adolescents who experienced potential hemolysis (a decline in hemoglobin of 2.0 g/dL or more)

End point description:

Adults and adolescent subjects in the study (36) were evaluated pre- and post infusion for hemolysis. Further testing was performed when there was a decline in hemoglobin of 2.0 g/dL or more.

The analysis was conducted on subjects in the Safety Analysis Dataset.
Note: Six subjects experienced a decline in hemoglobin of 2.0 g/dL or more. None of the incidences of a fall in hemoglobin was assessed to be due to a hemolytic reaction.

End point type	Secondary

End point timeframe:

From first infusion until the end of the study, approximately 15 months per subject

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	36			
Units: Number of subjects	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the study period of 2 years and 11 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0
Reporting groups	
Reporting group title	IGIV
Reporting group description: Subjects treated with Kiovig	
Reporting group title	IGSC 20%
Reporting group description: Subjects treated with Immune Globulin Subcutaneous (Human) (IGSC), 20%	
Reporting group title	IGSC
Reporting group description: Subjects treated with Subcuvia	

Serious adverse events	IGIV	IGSC 20%	IGSC
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 33 (6.06%)	6 / 48 (12.50%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Forearm fracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 48 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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

Ventricular fibrillation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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
Nervous system disorders			
Brain stem infarction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 48 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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
Respiratory, thoracic and mediastinal disorders			
Nasal septum deviation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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
Rhinorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			

subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	0 / 16 (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: 5 %

Non-serious adverse events	IGIV	IGSC 20%	IGSC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 33 (78.79%)	46 / 48 (95.83%)	16 / 16 (100.00%)
Investigations			
Body temperature increased			
subjects affected / exposed	3 / 33 (9.09%)	0 / 48 (0.00%)	0 / 16 (0.00%)
occurrences (all)	4	0	0

Injury, poisoning and procedural
complpR soning and procedural

subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infusion site pruritus			
subjects affected / exposed	0 / 33 (0.00%)	6 / 48 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	29	1
Malaise			
subjects affected / exposed	0 / 33 (0.00%)	2 / 48 (4.17%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Infusion site erythema			
subjects affected / exposed	0 / 33 (0.00%)	9 / 48 (18.75%)	0 / 16 (0.00%)
occurrences (all)	0	53	0
Infusion site swelling			
subjects affected / exposed	0 / 33 (0.00%)	4 / 48 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	46	0
Infusion site pain			
subjects affected / exposed	1 / 33 (3.03%)	6 / 48 (12.50%)	0 / 16 (0.00%)
occurrences (all)	4	12	0
Infusion site discomfort			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	11	0
Injection site pain			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	11	0
Pyrexia			
subjects affected / exposed	0 / 33 (0.00%)	4 / 48 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Gastrointestinal disorders			
Diarrhoe			
subjects affected / exposed	6 / 33 (18.18%)	12 / 48 (25.00%)	1 / 16 (6.25%)
occurrences (all)	7	68	1
Vomiting			
subjects affected / exposed	6 / 33 (18.18%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	6	4	0

Nausea			
subjects affected / exposed	3 / 33 (9.09%)	3 / 48 (6.25%)	1 / 16 (6.25%)
occurrences (all)	3	3	1
Abdominal pain upper			
subjects affected / exposed	2 / 33 (6.06%)	3 / 48 (6.25%)	1 / 16 (6.25%)
occurrences (all)	2	15	2
Toothache			
subjects affected / exposed	2 / 33 (6.06%)	1 / 48 (2.08%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Enteritis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	1	1	2
Abdominal pain			
subjects affected / exposed	1 / 33 (3.03%)	3 / 48 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	5	1
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	3 / 33 (9.09%)	2 / 48 (4.17%)	0 / 16 (0.00%)
occurrences (all)	4	3	0
Cough			
subjects affected / exposed	3 / 33 (9.09%)	11 / 48 (22.92%)	0 / 16 (0.00%)
occurrences (all)	3	18	0
Oropharyngeal pain			
subjects affected / exposed	0 / 33 (0.00%)	5 / 48 (10.42%)	2 / 16 (12.50%)
occurrences (all)	0	6	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 33 (9.09%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	5	10	0

Musculoskeletal chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 33 (15.15%)	7 / 48 (14.58%)	0 / 16 (0.00%)
occurrences (all)	7	16	0
Sinusitis bacterial			
subjects affected / exposed	2 / 33 (6.06%)	1 / 48 (2.08%)	0 / 16 (0.00%)
occurrences (all)	5	1	0
Viral rhinitis			
subjects affected / exposed	4 / 33 (12.12%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	5	4	0
Bacterial rhinitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 48 (0.00%)	0 / 16 (0.00%)
occurrences (all)	4	0	0
Viral infection			
subjects affected / exposed	3 / 33 (9.09%)	2 / 48 (4.17%)	0 / 16 (0.00%)
occurrences (all)	3	2	0
Viral pharyngitis			
subjects affected / exposed	2 / 33 (6.06%)	5 / 48 (10.42%)	0 / 16 (0.00%)
occurrences (all)	3	5	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 33 (6.06%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	3	1	1
Bronchitis			
subjects affected / exposed	2 / 33 (6.06%)	7 / 48 (14.58%)	2 / 16 (12.50%)
occurrences (all)	2	14	2
Respiratory tract infection viral			
subjects affected / exposed	2 / 33 (6.06%)	3 / 48 (6.25%)	1 / 16 (6.25%)
occurrences (all)	2	3	2
Rhinitis			
subjects affected / exposed	2 / 33 (6.06%)	11 / 48 (22.92%)	0 / 16 (0.00%)
occurrences (all)	2	11	0
Upper respiratory tract infection			

subjects affected / exposed	2 / 33 (6.06%)	18 / 48 (37.50%)	7 / 16 (43.75%)
occurrences (all)	2	46	8
Lower respiratory tract infection			
subjects affected / exposed	1 / 33 (3.03%)	2 / 48 (4.17%)	3 / 16 (18.75%)
occurrences (all)	1	4	3
Tinea pedis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	0	1	3
Acute sinusitis			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Conjunctivitis			
subjects affected / exposed	1 / 33 (3.03%)	4 / 48 (8.33%)	1 / 16 (6.25%)
occurrences (all)	2	6	2
Oral herpes			
subjects affected / exposed	0 / 33 (0.00%)	2 / 48 (4.17%)	2 / 16 (12.50%)
occurrences (all)	0	7	2
Enteritis infectious			
subjects affected / exposed	1 / 33 (3.03%)	5 / 48 (10.42%)	1 / 16 (6.25%)
occurrences (all)	2	9	1
Influenza			
subjects affected / exposed	0 / 33 (0.00%)	2 / 48 (4.17%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Otitis media			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	6 / 48 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	8	1
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vaginal infection			
subjects affected / exposed	1 / 33 (3.03%)	1 / 48 (2.08%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Viral tonsillitis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 33 (3.03%)	5 / 48 (10.42%)	0 / 16 (0.00%)
occurrences (all)	1	7	0
Bronchitis bacterial			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Otitis media acute			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Ear infection			
subjects affected / exposed	0 / 33 (0.00%)	3 / 48 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 33 (0.00%)	0 / 48 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2

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