Clinical trial results:
A Multicenter Extension Study of the Efficacy, Tolerability, and Safety of Immune Globulin Subcutaneous (Human) IgPro20 in Subjects with Primary Immunodeficiency (IgPro20 EU Extension Study)

Summary

EudraCT number	2008-000830-30
Trial protocol	DE ES FR SE GB
Global end of trial date	21 December 2011

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	ZLB07_002CR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00751621
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring AG
Sponsor organisation address	Wankdorfstrasse 10, Bern 22, Switzerland, 3000
Public contact	Trial Registration Co-ordinator, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Trial Registration Co-ordinator, CSL Behring, clinicaltrials@cslbehring.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	10 April 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is a continuation of the study ZLB06_001CR with the objective of assessing efficacy, tolerability, safety of IgPro, as well as long-term health-related quality of life in patients with PID.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, the Declaration of Helsinki (version of 1996), and standard operating procedures for clinical research and development at CSL Behring and the Clinical Research Organizations involved. The study was conducted under a protocol reviewed and approved by an IEC/IRB. The study was conducted by scientifically and medically qualified persons. The benefits of the study were in proportion to the risks; the rights and welfare of the subjects were respected; the physicians conducting the study did not find the hazards to outweigh the potential benefits; the results reported are accurate; and each subject or subject's parent or legal guardian gave his or her written informed consent before any protocol-driven tests or evaluations were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 August 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	Poland: 7
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Romania: 10
Worldwide total number of subjects	40
EEA total number of subjects	39

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)	15
Adolescents (12-17 years)	7
Adults (18-64 years)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who had previously participated in the pivotal study ZLB06_001CR (NCT00542997) were enrolled in the extension study ZLB07_002CR.

Pre-assignment

Screening details:

The number of subjects and sites was dependent on the subjects' and sites' interest to continue the IgPro20 treatment following the pivotal study ZLB06_001CR.

Period 1

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

Arms

Arm title	IgPro20

Arm description:

Subcutaneous (SC) administration by the subject/parent/guardian with the planned weekly dose of IgPro20 to be the same as the subject's last dose recommended by the investigator in study ZLB06_001CR.

Arm type	Experimental
Investigational medicinal product name	IgPro20
Investigational medicinal product code	
Other name	IgG with Proline (IgPro), Hizentra
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

IgPro20 is a liquid formulation of normal human IgG at a concentration of 20% administered as a SC infusion at weekly intervals. Subcutaneous administration by the subject/parent/guardian with the planned weekly dose of IgPro20 to be the same as the subject's last dose recommended by the investigator in study ZLB06_001CR.

Number of subjects in period 1	IgPro20
Started	40
Completed	36
Not completed	4
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Subject moved to another country	1
Poor adherence to asthma treatment	1

Baseline characteristics

Reporting groups	
Reporting group title	IgPro20
Reporting group description:	
Subcutaneous (SC) administration by the subject/parent/guardian with the planned weekly dose of IgPro20 to be the same as the subject's last dose recommended by the investigator in study ZLB06_001CR.	

Reporting group values	IgPro20	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	15	15	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	21.6		
standard deviation	± 15.31	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	28	28	

End points

End points reporting groups

Reporting group title	IgPro20

Reporting group description:

Subcutaneous (SC) administration by the subject/parent/guardian with the planned weekly dose of IgPro20 to be the same as the subject's last dose recommended by the investigator in study ZLB06_001CR.

Subject analysis set title	HRQL - At Baseline
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Baseline values for those subjects in the Full-Analysis health related quality of life (HRQL) data set (defined as all subjects entered into the study who complete a baseline and at least 1 follow-up HRQL assessment), who were at least 15 years of age.

Subject analysis set title	HRQL - At End of Study
Subject analysis set type	Sub-group analysis

Subject analysis set description:

End of study values for subjects in the Full-Analysis HRQL data set (defined as all subjects entered into the study who complete a baseline and at least 1 follow-up HRQL assessment), who were at least 15 years of age.

Primary: Total Serum IgG Trough Levels

End point title	Total Serum IgG Trough Levels[1]

End point description:

The IgG trough values per subject were aggregated to a median value, and then median values across subjects were summarized using descriptive statistics.

The full analysis/intent to treat (ITT) dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Primary

End point timeframe:

Up to 42 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Variables were summarized using descriptive statistics.

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[2]			
Units: g/L				
arithmetic mean (standard deviation)	7.97 (± 1.171)			

Notes:

[2] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Clinically Documented Serious Bacterial Infections (SBIs)

End point title	Annualized Rate of Clinically Documented Serious Bacterial Infections (SBIs)

End point description:

The annualized rate was based on the total number of SBIs and the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

Potential SBIs included bacterial pneumonia, bacteremia and septicemia, osteomyelitis/septic arthritis, bacterial meningitis, and visceral abscess. If an adverse event (AE) was identified as a potential SBI, the AE was adjudicated by the Medical Monitor and Investigator to determine if the event fulfilled the predefined criteria for SBIs.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[3]			
Units: SBIs per subject year				
number (not applicable)	0.048			

Notes:

[3] - Number of subject study days analyzed: 38208

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Infection Episodes

End point title	Annualized Rate of Infection Episodes

End point description:

The annualized rate was based on the total number of infection episodes occurring during the study divided by the total number of subject study days for all subjects in the specified analysis population and adjusted to 365 days.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[4]			
Units: infection episodes per subject year				
number (confidence interval 95%)	3.334 (2.993 to 3.703)			

Notes:

[4] - ITT population.
Number of Subject Study Days Analyzed: 38208

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Infection Episodes

End point title	Number of Infection Episodes

End point description:

Total number of infections for the ITT population.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[5]			
Units: infection episodes	349			

Notes:

[5] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Days Out of Work / School / Kindergarten / Day Care or Unable to Perform Normal Activities Due to Infections

End point title	Annualized Rate of Days Out of Work / School / Kindergarten / Day Care or Unable to Perform Normal Activities Due to Infections

End point description:

The annualized rate was based on the total number of days out of work / school / kindergarten / day care or inability to perform normal activities due to infection, and the total number of subject diary days for all subjects in the ITT population and adjusted to 365 days.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[6]			
Units: days per subject year				
number (not applicable)	6.773			

Notes:

[6] - ITT population
Number of Subject Diary Days Analyzed: 38045

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days Out of Work / School / Kindergarten / Day Care or Unable to Perform Normal Activities Due to Infections

End point title	Number of Days Out of Work / School / Kindergarten / Day Care or Unable to Perform Normal Activities Due to Infections

End point description:

Number of Days Out of Work / School / Kindergarten / Day Care or Unable to Perform Normal Activities Due to Infections.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[7]			
Units: days	706			

Notes:

[7] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Hospitalization Due to Infections

End point title	Annualized Rate of Hospitalization Due to Infections

End point description:

The annualized rate was based on the total number of days of hospitalization due to infections and the total number of subject diary days for all subjects in the specified analysis population and adjusted to 365 days.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[8]			
Units: days per subject year				
number (not applicable)	1.055			

Notes:

[8] - ITT population.
Number of Subject Diary Days Analyzed: 38045

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of Hospitalization Due to Infections

End point title	Number of Days of Hospitalization Due to Infections

End point description:

Total number of days of hospitalization due to infections for the ITT population.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[9]			
Units: days	110			

Notes:

[9] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Use of Antibiotics for Infection Prophylaxis and Treatment

End point title	Use of Antibiotics for Infection Prophylaxis and Treatment

End point description:

Annualized rate of days with antibiotics for infection prophylaxis and treatment. The annualized rate was based on the total number of days of antibiotic use for infection prophylaxis and treatment in the efficacy period, and the total number of subject study days for all subjects in the ITT population, and adjusted to 365 days.

The full analysis/ITT dataset comprised all subjects treated with IgPro20 and for whom any efficacy data was available.

End point type	Secondary

End point timeframe:

up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[10]			
Units: days per subject year				
number (not applicable)	72.13			

Notes:

[10] - ITT population
Number of Subject Study Days Analyzed: 38208

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (Short Form 36 Health Survey)

End point title	Health Related Quality of Life (Short Form 36 Health Survey)

End point description:

The Short Form 36 Health Survey is a 36-item questionnaire that measures generic health concepts that are relevant across age, disease, and treatment groups. The questions are grouped into eight domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Scores range from 0 to 100, with higher scores indicating a better health state.

End point type	Secondary

End point timeframe:

At baseline and at the last available post-baseline observation for each subject (up to 42 months)

End point values	HRQL - At Baseline	HRQL - At End of Study		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: units on a scale				
median (full range (min-max))				
Physical Functioning	95 (75 to 100)	100 (20 to 100)		
Role-physical	100 (18.8 to 100)	100 (37.5 to 100)		
Role-emotional	100 (25 to 100)	100 (25 to 100)		
Social Functioning	100 (62.5 to 100)	100 (37.5 to 100)		
Bodily Pain	84 (22 to 100)	84 (22 to 100)		
Mental Health	85 (55 to 95)	80 (35 to 95)		
Vitality	65.6 (31.3 to 81.3)	75 (18.8 to 100)		
General Health	52 (15 to 82)	54.5 (20 to 92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Relevant Changes in Vital Signs From Baseline to the Completion Visit

End point title	Clinically Relevant Changes in Vital Signs From Baseline to the Completion Visit

End point description:

The total number of subjects with clinically relevant changes in vital signs from baseline to the completion visit. Vital signs included heart rate, systolic blood pressure, diastolic blood pressure, and body temperature.

The 'All Treated' (AT) safety data set included all subjects treated with study drug.

End point type	Secondary

End point timeframe:

At baseline (data either from Infusion 40 or the completion visit of study ZLB06_001CR), and at completion (up to 42 months)

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	39[11]			
Units: participants	0			

Notes:

[11] - AT population, reporting subjects with data collected at both baseline and completion

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Significant Abnormal Changes in Routine Laboratory Parameters Between Baseline and the Completion Visit

End point title	Clinically Significant Abnormal Changes in Routine Laboratory Parameters Between Baseline and the Completion Visit

End point description:

The total number of subjects with clinically significant abnormal changes in routine laboratory parameters between baseline and the completion visit. Routine laboratory parameters included haematology, serum chemistry and urinalysis.

The AT safety data set included all subjects treated with study drug.

End point type	Secondary

End point timeframe:

At baseline (data either from Infusion 40 or the completion visit of study ZLB06_001CR), and at completion (up to 42 months)

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[12]			
Units: participants				
Haematology	3			
Serum Chemistry	1			
Urinalysis	0			

Notes:

[12] - AT population, reporting subjects with data collected at both baseline and completion

Statistical analyses

No statistical analyses for this end point

Secondary: Rate, Severity and Relatedness of Any Adverse Events (AEs) Per Infusion

End point title	Rate, Severity and Relatedness of Any Adverse Events (AEs) Per Infusion

End point description:

The rate of AEs was the number of AEs over the number of infusions administered. Mild AE: Did not interfere with routine activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities. At least possibly related AEs included possibly related AEs, probably related AEs, and related AEs.

The AT safety data set included all subjects treated with study drug.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	IgPro20			
Subject group type	Reporting group			
Number of subjects analysed	40[13]			
Units: AEs per infusion				
number (not applicable)				
Total AEs	0.0936			
Mild AEs	0.0685			
Moderate AEs	0.0231			
Severe AEs	0.002			
At least possibly related AEs	0.0026			
Serious AEs	0.0033			
At least possibly related and serious AEs	0			

Notes:

[13] - AT population.
Number of Infusions Analyzed: 5405

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected for the duration of the study, up to 42 months.

Adverse event reporting additional description:

A total of 5405 weekly infusions of IgPro20 were administered to 40 subjects in this study. Three subjects received fewer than 100 infusions. The AT safety data set comprised all subjects treated with IgPro20 during any study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	IgPro20

Reporting group description:

Subcutaneous administration by the subject/parent/guardian with the planned weekly dose of IgPro20 to be the same as the subject's last dose recommended by the investigator in study ZLB06_001CR.

Serious adverse events	IgPro20		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 40 (35.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal column injury			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenic purpura			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Agranulocytosis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coeliac disease			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	IgPro20		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Investigations			
Weight increased			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	5		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Ligament sprain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Surgical and medical procedures			

Wisdom teeth removal subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 3 2 / 40 (5.00%) 6 2 / 40 (5.00%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all)	 4 / 40 (10.00%) 6 2 / 40 (5.00%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Aphthous stomatitis subjects affected / exposed occurrences (all) Constipation	 3 / 40 (7.50%) 5 4 / 40 (10.00%) 9 3 / 40 (7.50%) 3		

subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Gastritis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 40 (27.50%)		
occurrences (all)	34		
Bronchiectasis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Productive cough			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	4		
Rhinorrhoea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Infections and infestations			
Bronchitis			
subjects affected / exposed	21 / 40 (52.50%)		
occurrences (all)	51		

Upper respiratory tract infection				
subjects affected / exposed	18 / 40 (45.00%)			
occurrences (all)	49			
Sinusitis				
subjects affected / exposed	13 / 40 (32.50%)			
occurrences (all)	31			
Nasopharyngitis				
subjects affected / exposed	12 / 40 (30.00%)			
occurrences (all)	19			
Rhinitis				
subjects affected / exposed	9 / 40 (22.50%)			
occurrences (all)	15			
Febrile infection				
subjects affected / exposed	6 / 40 (15.00%)			
occurrences (all)	10			
Acute sinusitis				
subjects affected / exposed	5 / 40 (12.50%)			
occurrences (all)	5			
Pharyngitis				
subjects affected / exposed	5 / 40 (12.50%)			
occurrences (all)	10			
Influenza				
subjects affected / exposed	4 / 40 (10.00%)			
occurrences (all)	4			
Viral infection				
subjects affected / exposed	4 / 40 (10.00%)			
occurrences (all)	4			
Viral upper respiratory tract infection				
subjects affected / exposed	4 / 40 (10.00%)			
occurrences (all)	5			
Conjunctivitis infective				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	11			
Ear infection				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	6			

Enteritis infectious				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	12			
Lower respiratory tract infection				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	6			
Oral herpes				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	8			
Otitis media				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	8			
Pneumonia				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	2			
Urinary tract infection				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences (all)	6			
Acute tonsillitis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	3			
Diarrhoea infectious				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	3			
Enterobiasis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	3			
Gastroenteritis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	2			
Laryngitis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	6			
Otitis externa				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	2			

Otitis media acute subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2009	This protocol amendment included the change of the supervising investigator for Germany (Leiter der klinischen Prüfung according to German drug law) and the biometrics service provider as well as several minor editorial changes.
13 January 2009	This was a country-specific amendment applicable for study sites in the UK. To fulfill the requirements of the MHRA, the study duration was defined as exactly 30 months.
13 January 2009	This was a country-specific amendment applicable for study sites in Sweden. To fulfill the requirements of the Swedish Competent Authorities (Läkemedelsverket), the study duration was defined as exactly 30 months. Additionally, the investigators were advised to contact subjects by telephone between the 6 monthly visits.
06 July 2009	This amendment included an increase in the maximum storage temperature of IgPro20, a switch from 50 mL IgPro20 bottles to 20 mL bottles, and a clarification concerning calculation of the visit intervals.
06 December 2010	This was a country-specific amendment applicable for all study sites, except the UK. The individual study duration depended on the time between last infusion within study ZLB06_001CR and the availability of IgPro20 on the European market, and could vary from country to country. The study duration was originally expected to not exceed 30 months, but was defined as not exceeding 42 months by this amendment.
14 March 2011	This was a country-specific amendment applicable for study sites in the UK. Study duration was previously defined as exactly 30 months in Substantial Amendment 3.0 and was prolonged to 36 months in this protocol amendment to satisfy MHRA request of better defining the study duration.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24412910