Clinical trial results:
A Multicenter Study on the Efficacy and Safety of Vivaglobin® in Previously Untreated Patients (PUPs) with Primary Immunodeficiency (PID)

Summary

EudraCT number	2006-006522-25
Trial protocol	DE GB BE GR IT ES
Global end of trial date	31 October 2008

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	ZLB06_005CR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00520494
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring AG
Sponsor organisation address	Wankdorfstrasse 10, Berne 22, Switzerland, CH-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	03 March 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to assess the efficacy and safety of Vivaglobin in PUPs with PID common variable immunodeficiency (CVID) or X-linked agammaglobulinemia (XLA), who were free of serious bacterial infections (SBIs) at initiation of therapy.

The primary efficacy objective of this open-label study was to assess whether subcutaneous immunoglobulin (SCIG) treatment with a loading dose of Vivaglobin of 100 mg/kg bw for 5 consecutive days resulted in an immunoglobulin G (IgG) increase to ≥5 g/L as measured on Day 12 after initiation of SCIG therapy.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines, and standard operating procedures for clinical research and development at CSL Behring (CSLB). The study protocol and all amendments were approved by the Independent Ethics Committee(s) (IECs) / Institutional Review Board(s) (IRBs) of the participating centers. Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study.

The investigator may cease study treatment and withdraw the subject, or the subject may withdraw himself from participation in the study at any time. If a subject is withdrawn from the study or further participation is declined, the subject will continue to have access to medical care and will be treated according to routine medical practice, but will no longer receive the investigational medicinal product (IMP).

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	15 March 2007
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	Spain: 2
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Canada: 6
Worldwide total number of subjects	18
EEA total number of subjects	12

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)	6
Adolescents (12-17 years)	2
Adults (18-64 years)	8
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

6 sites in Canada, Germany, Italy, and Spain included a total of 18 patients screened and enrolled for this study.

Period 1

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

Arms

Arm title	Vivaglobin

Arm description:

Vivaglobin: 16% (160 mg/mL) liquid formulation of human IgG for subcutaneous (SC) use. Loading dose: 100 mg/kg for 5 consecutive days; maintenance dose: 100 mg/kg 1 to 2 times a week for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Human normal immunoglobulin G (IgG) for subcutaneous (SC) use
Investigational medicinal product code	CE1200
Other name	Vivaglobin®
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosage form: Glycine-buffered pasteurized liquid containing 16% IgG for SC infusion

Number of subjects in period 1	Vivaglobin
Started	18
Completed	17
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	18	18	
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)	6	6	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	8	8	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	25.9		
standard deviation	± 21.85	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	10	10	

End points

End points reporting groups

Reporting group title	Vivaglobin

Reporting group description:

Vivaglobin: 16% (160 mg/mL) liquid formulation of human IgG for subcutaneous (SC) use. Loading dose: 100 mg/kg for 5 consecutive days; maintenance dose: 100 mg/kg 1 to 2 times a week for 24 weeks.

Primary: Proportion of Subjects Achieving Immunoglobulin G (IgG) Levels ≥ 5 g/L on Day 12

End point title	Proportion of Subjects Achieving Immunoglobulin G (IgG) Levels ≥ 5 g/L on Day 12[1]

End point description:

End point type	Primary

End point timeframe:

Day 12

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: Primary end point data analysis consisted of the calculation of a proportion and a 2-sided 95% confidence interval as per protocol; no statistical hypothesis was planned or conducted.

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[2]			
Units: proportion of subjects				
number (confidence interval 95%)	0.944 (0.7271 to 0.9986)			

Notes:

[2] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving IgG Levels ≥ 5 g/L on Day 19

End point title	Proportion of Subjects Achieving IgG Levels ≥ 5 g/L on Day 19

End point description:

End point type	Secondary

End point timeframe:

Day 19

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[3]			
Units: proportion of subjects				
number (confidence interval 95%)	0.944 (0.7271 to 0.9986)			

Notes:

[3] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving IgG Levels ≥ 5 g/L on Day 26

End point title	Proportion of Subjects Achieving IgG Levels ≥ 5 g/L on Day 26

End point description:

End point type	Secondary

End point timeframe:

Day 26

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[4]			
Units: proportion of subjects				
number (confidence interval 95%)	1 (0.8147 to 1)			

Notes:

[4] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: IgG Increase (Change From Baseline) on Day 12

End point title	IgG Increase (Change From Baseline) on Day 12

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 12

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	17[5]			
Units: g/L				
arithmetic mean (standard deviation)	3.941 (± 0.7466)			

Notes:

[5] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Rate of Infections

End point title	Overall Rate of Infections

End point description:

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

Infections were defined as all AEs with the system organ classification of "infections and infestations."

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[6]			
Units: infections per subject year				
number (confidence interval 95%)	2.785 (1.785 to 4.144)			

Notes:

[6] - Intent-to-treat data set
Number of infections analyzed: 24

Statistical analyses

No statistical analyses for this end point

Secondary: Total Serum IgG Trough Levels on Day 12

End point title	Total Serum IgG Trough Levels on Day 12

End point description:

End point type	Secondary

End point timeframe:

Day 12

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[7]			
Units: g/L				
arithmetic mean (standard deviation)	7.466 (± 1.4592)			

Notes:

[7] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Total Serum IgG Trough Levels at Week 25

End point title	Total Serum IgG Trough Levels at Week 25

End point description:

End point type	Secondary

End point timeframe:

Week 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	17[8]			
Units: g/L				
arithmetic mean (standard deviation)	8.039 (± 1.1793)			

Notes:

[8] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Specific IgGs Against Cytomegalovirus, Tetanus, and Measles on Day 12

End point title	Serum Concentrations of Specific IgGs Against Cytomegalovirus, Tetanus, and Measles on Day 12

End point description:

End point type	Secondary

End point timeframe:

Day 12

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	16[9]			
Units: IU/mL				
arithmetic mean (standard deviation)				
Cytomegalovirus	3.182 (± 0.8025)			
Tetanus	1.399 (± 0.3846)			
Measles	0.743 (± 0.3681)			

Notes:

[9] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Specific IgGs Against Cytomegalovirus, Tetanus, and Measles at Week 25

End point title	Serum Concentrations of Specific IgGs Against Cytomegalovirus, Tetanus, and Measles at Week 25

End point description:

End point type	Secondary

End point timeframe:

Week 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	15[10]			
Units: IU/mL				
arithmetic mean (standard deviation)				
Cytomegalovirus	3.638 (± 2.2649)			
Tetanus	1.623 (± 0.9344)			
Measles	0.879 (± 0.8993)			

Notes:

[10] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Specific IgGs Against H. Influenzae Type B and S. Pneumoniae On Day 12

End point title	Serum Concentrations of Specific IgGs Against H. Influenzae Type B and S. Pneumoniae On Day 12

End point description:

End point type	Secondary

End point timeframe:

Day 12

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	16[11]			
Units: mg/L				
arithmetic mean (standard deviation)				
H. influenzae	1.023 (± 0.3141)			
S. pneumoniae	18.588 (± 9.4659)			

Notes:

[11] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Specific IgGs Against H. Influenzae Type B and S. Pneumoniae at Week 25

End point title	Serum Concentrations of Specific IgGs Against H. Influenzae Type B and S. Pneumoniae at Week 25

End point description:

End point type	Secondary

End point timeframe:

Week 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	15[12]			
Units: mg/L				
arithmetic mean (standard deviation)				
H. influenzae	1.671 (± 0.7796)			
S. pneumoniae	26.985 (± 22.2594)			

Notes:

[12] - Intent-to-treat data set

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:

Number of subjects using antibiotics for infection prophylaxis and treatment. Medications were classified as antibiotics according to the anatomic therapeutic chemical code.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[13]			
Units: subjects				
Prophylaxis	1			
Treatment	8			

Notes:

[13] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life as Measured by the Adapted Short Form-36 Health Survey (SF-36; Age ≥ 14 Years)

End point title	Quality of Life as Measured by the Adapted Short Form-36 Health Survey (SF-36; Age ≥ 14 Years)

End point description:

The SF-36 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 study completion, approximately Week 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	10[14]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical functioning	75.5 (± 33.948)			

Role-physical	70.63 (± 37.038)			
Bodily pain	65.6 (± 37.262)			
General health	56.4 (± 27.097)			
Vitality	54.4 (± 28.575)			
Social functioning	80 (± 30.162)			
Role-emotional	79.17 (± 33.158)			
Mental health	74.5 (± 23.268)			

Notes:

[14] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life as Measured by the Child Health Questionnaire Parent Form-50 (CHQ-PF50; Age ≤ 13 Years)

End point title	Quality of Life as Measured by the Child Health Questionnaire Parent Form-50 (CHQ-PF50; Age ≤ 13 Years)

End point description:

The CHQ-PF50 is a 50-item questionnaire that measures generic health concepts and is suitable for patients younger than 14 years of age. The questions are grouped into 15 domains: global health, physical functioning, role/social limitations - emotional/behavioral, role/social limitations - physical, bodily pain, behavior, global behavior, mental health, self esteem, general health perceptions, change in health, parental impact - emotional, parental impact - time, family activities, and family cohesion. Scores range from 0 to 100, with higher scores indicating a better health state.

End point type	Secondary

End point timeframe:

At study completion, approximately Week 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	8[15]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Global health	82.5 (± 15.353)			
Physical functioning	97.91 (± 4.135)			
Role/social limitations - emotional/behavioral	100 (± 0)			
Role/social limitations - physical	95.84 (± 11.773)			
Bodily pain	82.5 (± 24.349)			
Behavior	74.06 (± 13.899)			

Global behavior	75.63 (± 12.939)			
Mental health	83.13 (± 13.871)			
Self esteem	90.64 (± 6.948)			
General health perceptions	61.66 (± 22.791)			
Change in health	84.38 (± 18.601)			
Parental impact - emotional	64.58 (± 39.53)			
Parental impact - time	88.9 (± 15.698)			
Family activities	86.98 (± 17.457)			
Family cohesion	77.5 (± 15.353)			

Notes:

[15] - Intent-to-treat data set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) by Severity and Relatedness

End point title	Number of Subjects With Adverse Events (AEs) by Severity and Relatedness

End point description:

Mild AE: Did not interfere with activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

Not related: Explained by factors not involving the drug, no temporal relationship; Possibly related: Occurred within a reasonable time of administration, could also be explained by concurrent disease or other drugs; Probably related: Compelling temporal relationship, could not be explained concurrent disease/other drugs; Related AE: Compelling temporal relationship, known/suspected response to the drug confirmed by improvement on stopping.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[16]			
Units: subjects				
Total AEs	14			
Mild AEs	14			
Moderate AEs	5			
Severe AEs	2			
Not related AEs	14			
Possibly related AEs	3			

Probably related AEs	4			
Related AEs	5			

Notes:

[16] - Safety data set

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of AEs by Severity and Relatedness

End point title	Rate of AEs by Severity and Relatedness

End point description:

The rate was the number of AEs over the number of infusions administered.

Mild AE: Did not interfere with activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

Not related: Explained by factors not involving the drug, no temporal relationship; Possibly related: Occurred within a reasonable time of administration, could also be explained by concurrent disease or other drugs; Probably related: Compelling temporal relationship, could not be explained concurrent disease/other drugs; Related AE: Compelling temporal relationship, known/suspected response to the drug confirmed by improvement on stopping.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[17]			
Units: AEs per infusion				
number (not applicable)				
Total AEs	0.305			
Mild AEs	0.263			
Moderate AEs	0.034			
Severe AEs	0.007			
Not related AEs	0.2			
Possibly related AEs	0.013			
Probably related AEs	0.018			
Related AEs	0.074			

Notes:

[17] - Safety data set
Number of infusions analyzed: 551

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Local Reactions by Severity and Relatedness

End point title	Number of Subjects With Local Reactions by Severity and Relatedness

End point description:

Local reactions included: infusion site erythema, infusion site pain, infusion site pruritus, infusion site rash, infusion site reaction, infusion site swelling, injection site bruising, injection site erythema, injection site irritation, injection site pruritus, injection site swelling, edema peripheral, tenderness, erythema, pruritus, and skin swelling.

Mild AE: Did not interfere with activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

Not related: Explained by factors not involving the drug, no temporal relationship; Possibly related: Occurred within a reasonable time of administration, could also be explained by concurrent disease or other drugs; Probably related: Compelling temporal relationship, could not be explained concurrent disease/other drugs; Related AE: Compelling temporal relationship, known/suspected response to the drug confirmed by improvement on stopping.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[18]			
Units: participants				
Total local reactions	6			
Mild local reactions	6			
Moderate local reactions	0			
Severe local reactions	0			
Not related local reactions	1			
Possibly related local reactions	0			
Probably related local reactions	1			
Related local reactions	5			

Notes:

[18] - Safety data set

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Local Reactions by Severity and Relatedness

End point title	Rate of Local Reactions by Severity and Relatedness

End point description:

The rate was the number of local reactions over the number of infusions administered.

Local reactions included: infusion site: erythema, pain, pruritus, rash, reaction, swelling; injection site: bruising, erythema, irritation, pruritus, swelling; edema peripheral; tenderness; erythema; pruritus; and skin swelling.

Mild AE: Did not interfere with activities; Moderate AE: Interfered somewhat with routine activities; Severe AE: Impossible to perform routine activities.

Not related: Explained by factors not involving the drug, no temporal relationship; Possibly related: Occurred within a reasonable time of administration, could also be explained by concurrent disease or other drugs; Probably related: Compelling temporal relationship, could not be explained concurrent

disease/other drugs; Related AE: Compelling temporal relationship, known/suspected response to the drug confirmed by improvement on stopping.

End point type	Secondary

End point timeframe:

For the duration of the study, up to approximately 25 weeks

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[19]			
Units: local reactions per infusion				
number (not applicable)				
Total local reactions	0.076			
Mild local reactions	0.076			
Moderate local reactions	0			
Severe local reactions	0			
Not related local reactions	0.004			
Possibly related local reactions	0.004			
Probably related local reactions	0.009			
Related local reactions	0.064			

Notes:

[19] - Safety data set
Number of infusions analyzed: 551

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Relevant Changes in Routine Laboratory Parameters

End point title	Number of Subjects With Clinically Relevant Changes in Routine Laboratory Parameters

End point description:

Laboratory parameters included hematology, serum chemistry, and urinalysis parameters, and were assessed at screening, Week 12 (hematology and serum chemistry) and at the completion visit (approximately Week 25).

End point type	Secondary

End point timeframe:

Weeks 12 and 25

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[20]			
Units: participants	0			

Notes:

[20] - Safety data set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Relevant Changes in Vital Signs

End point title	Number of Subjects With Clinically Relevant Changes in Vital Signs

End point description:

Vital signs included heart rate, systolic blood pressure, diastolic blood pressure, and body temperature.

End point type	Secondary

End point timeframe:

At the screening visit, before and after infusions (Days 1 to 5), and at the completion visit (Week 25)

End point values	Vivaglobin			
Subject group type	Reporting group			
Number of subjects analysed	18[21]			
Units: participants	0			

Notes:

[21] - Safety data set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
For the duration of the study, up to approximately 25 weeks.	
Adverse event reporting additional description:	
Safety data set: all treated subjects.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	Vivaglobin
Reporting group description:	
Vivaglobin: 16% (160 mg/mL) liquid formulation of human IgG for SC use. Loading dose: 100 mg/kg for 5 consecutive days; maintenance dose: 100 mg/kg 1 to 2 times a week for 24 weeks.	

Serious adverse events	Vivaglobin		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Meningitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonal bacteraemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemophilus infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonas bronchitis			
subjects affected / exposed	1 / 18 (5.56%)		
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	Vivaglobin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 18 (77.78%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Infusion site erythema			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	7		
Infusion site pain			

subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	4			
Injection site bruising				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	2			
Injection site erythema				
subjects affected / exposed	3 / 18 (16.67%)			
occurrences (all)	5			
Injection site pruritus				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	3			
Injection site swelling				
subjects affected / exposed	4 / 18 (22.22%)			
occurrences (all)	9			
Oedema peripheral				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	3			
Pyrexia				
subjects affected / exposed	5 / 18 (27.78%)			
occurrences (all)	11			
Chills				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Feeling hot				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Infusion site pruritus				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Infusion site rash				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Infusion site reaction				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Infusion site swelling				

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	3		
Injection site irritation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Tenderness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
Dysphonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nasal discomfort			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pharyngeal oedema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Throat tightness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Thoracic vertebral fracture			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	13		
Disturbance in attention			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Migraine subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1		
Blood and lymphatic system disorders Haemolysis subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		
Eye disorders Eye swelling subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Cheilitis subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Enteritis subjects affected / exposed occurrences (all) Gastritis subjects affected / exposed occurrences (all) Oral pain	 4 / 18 (22.22%) 6 2 / 18 (11.11%) 2 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 1 / 18 (5.56%) 2		

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Stomach discomfort			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Swollen tongue			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Dermatitis allergic			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pruritus generalised			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rosacea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Skin swelling subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Renal and urinary disorders Renal failure acute subjects affected / exposed occurrences (all) Renal pain subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 2 / 18 (11.11%) 2 1 / 18 (5.56%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Candidiasis subjects affected / exposed occurrences (all) Ear infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Otitis media subjects affected / exposed occurrences (all)	 2 / 18 (11.11%) 5 3 / 18 (16.67%) 4 1 / 18 (5.56%) 1 1 / 18 (5.56%) 2 1 / 18 (5.56%) 3 1 / 18 (5.56%) 1		

Respiratory tract infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 2 1 / 18 (5.56%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2008	This amendment specified the sample size in more detail, defined further secondary efficacy endpoints, specified the per protocol efficacy data set in more detail, and updated the number of study sites and location. Further editorial changes to reflect recent change in sponsor name and staff, reporting of SAEs and shipment of samples were incorporated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported