Clinical trial results:
A Phase 3, Pivotal, Open-label, Multicenter Study to Assess the Efficacy and Safety of BIVV009 in Patients With Primary Cold Agglutinin Disease Who Have a Recent History of Blood Transfusion

Summary

EudraCT number	2017-003538-10
Trial protocol	AT GB DE NO ES BE NL IT
Global end of trial date	05 October 2021

Results information

Result version number	v1 (current)
This version publication date	20 October 2022
First version publication date	20 October 2022

Trial information

Trial identification

Sponsor protocol code	BIVV009-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03347396
WHO universal trial number (UTN)	-
Other trial identifiers	Sanofi study ID: EFC16215, Study name: Cardinal, IND #: 128,190

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Bioverativ, a Sanofi company, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Bioverativ, a Sanofi company, Contact-US@sanofi.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	29 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A: The primary objective of Part A was to determine whether BIVV009 administration results in a greater than or equal to (>=) 2 grams per decilitre (g/dL) increase in hemoglobin (Hgb) levels or increases Hgb to >=12 g/dL and obviates the need for blood transfusion during treatment in subjects with cold agglutinin disease (CAD) who had a recent history of blood transfusion.

Part B:
The primary objective of Part B was to evaluate the long-term safety and tolerability of BIVV009 in subjects with primary CAD.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2018
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	Norway: 3
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	24
EEA total number of subjects	15

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	18
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 16 active sites in 8 countries. Out of 42 screened subjects, a total of 24 subjects were enrolled from 05 March 2018 to 10 Jan 2019. This was a single arm study, consisted of 2 Parts: Part A and Part B.

Pre-assignment

Screening details:

Subjects were stratified based on baseline body weight to receive BIVV009 6.5 grams (g) (if <75 kg) or 7.5 g (if >=75 kg). As planned, data presented as: 1) Dose-wise (2 dose cohorts: BIVV009 6.5 g & BIVV009 7.5 g) for sections, 'disposition, baseline characteristics, safety endpoints & AEs'. 2) combined population (BIVV009) for efficacy endpoints.

Period 1

Period 1 title	Part A (Week 26)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BIVV009 6.5 g

Arm description:

Subjects with primary CAD and body weight less than (<)75 kilograms (kg) with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an intravenous (IV) infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.

Arm type	Experimental
Investigational medicinal product name	BIVV009
Investigational medicinal product code	
Other name	Sutimlimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with body weight <75 kg received fixed doses of BIVV009 6.5 g as IV infusion on Day 0 and Day 7 and every 14 days thereafter up to Week 25.

Arm title	BIVV009 7.5 g

Arm description:

Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.

Arm type	Experimental
Investigational medicinal product name	BIVV009
Investigational medicinal product code	
Other name	Sutimlimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with body weight >=75 kg received fixed doses of BIVV009 7.5 g as IV infusion on Day 0 and Day 7 and every 14 days thereafter up to Week 25.

Number of subjects in period 1	BIVV009 6.5 g	BIVV009 7.5 g
Started	17	7
Completed	16	6
Not completed	1	1
Death	-	1
Adverse event	1	-

Period 2

Period 2 title	Part B (149 weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BIVV009 6.5 g

Arm description:

Subjects with primary CAD and body weight <75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.

Arm type	Experimental
Investigational medicinal product name	BIVV009
Investigational medicinal product code	
Other name	Sutimlimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with body weight <75 kg received fixed doses of BIVV009 6.5 g as IV infusion every 2 weeks starting at Week 27 during Part B up to 143 weeks.

Arm title	BIVV009 7.5 g

Arm description:

Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue

to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.

Arm type	Experimental
Investigational medicinal product name	BIVV009
Investigational medicinal product code	
Other name	Sutimlimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with body weight >=75 kg received fixed doses of BIVV009 7.5 g as IV infusion every 2 weeks starting at Week 27 during Part B up to 149 weeks.

Number of subjects in period 2	BIVV009 6.5 g	BIVV009 7.5 g
Started	16	6
Completed	14	5
Not completed	2	1
Death	1	-
Adverse event	1	1

Baseline characteristics

Reporting groups	
Reporting group title	BIVV009 6.5 g
Reporting group description:	
Subjects with primary CAD and body weight less than (<)75 kilograms (kg) with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an intravenous (IV) infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.	
Reporting group title	BIVV009 7.5 g
Reporting group description:	
Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.	

Reporting group values	BIVV009 6.5 g	BIVV009 7.5 g	Total
Number of subjects	17	7	24
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	71.8	70.1	
standard deviation	± 9.05	± 6.01	-
Gender categorical Units: Subjects			
Female	11	4	15
Male	6	3	9
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	0	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	1	3
More than one race	0	0	0
Unknown or Not Reported	12	6	18

End points

End points reporting groups

Reporting group title	BIVV009 6.5 g

Reporting group description:

Subjects with primary CAD and body weight less than (<)75 kilograms (kg) with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an intravenous (IV) infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.

Reporting group title	BIVV009 7.5 g

Reporting group description:

Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.

Reporting group title	BIVV009 6.5 g

Reporting group description:

Subjects with primary CAD and body weight <75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.

Reporting group title	BIVV009 7.5 g

Reporting group description:

Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.

Subject analysis set title	BIVV009
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects with primary CAD who had a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to enrollment) received an IV infusion of BIVV009 6.5 g (if body weight was <75 kg) or BIVV009 7.5 g (if body weight was >=75 kg) on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25. Subjects who completed Part A per protocol through the end of treatment visit (Week 26) were eligible to be enrolled and continue to receive BIVV009 in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks.

Primary: Part A: Percentage of Subjects With Response to Treatment

End point title	Part A: Percentage of Subjects With Response to Treatment[1]

End point description:

A subject was considered responder: if he or she did not receive blood transfusion from Week 5 through Week 26 (end of treatment in Part A) and did not receive treatment for CAD beyond what was permitted per protocol. Additionally, subject's hemoglobin (Hgb) level had to meet either of the following criteria: Hgb level >=12 g/dL at treatment assessment endpoint (defined as average of values from Week 23, 25, and 26 visits), or Hgb increased >=2 g/dL from baseline (defined as last Hgb value before administration of first dose of study drug) at treatment assessment endpoint. Percentage of responders was calculated together with a 95% exact Clopper-Pearson confidence interval (CI). Analysis was performed on Part A- full analysis set (FAS) which included all subjects who received at least 1 dose (including partial dose) of study drug. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Primary

End point timeframe:

From Week 5 through Week 26

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: percentage of subjects				
number (confidence interval 95%)	54.2 (32.8 to 74.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Part B: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)[2]

End point description:

An Adverse Event (AE): any untoward medical occurrence in subject who received study drug and did not necessarily had to have a causal relationship with treatment. TESAEs was defined as any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. TEAEs: AEs that developed, worsened or became serious during treatment-emergent (TE) period (from the first investigational medicinal product [IMP] administration in Part B to the last IMP administration + 9 weeks follow up [FU] period). Part B safety analysis set (SAS) which included all subjects who received at least 1 dose (including partial dose) of study drug in Part B. Data for this endpoint was planned to be collected and analysed for dose-wise reporting groups (BIVV009 6.5 g and BIVV009 7.5 g).

End point type	Primary

End point timeframe:

Part B, 6.5 g cohort: From first dose (Week 27) up to 143 weeks of treatment + 9 weeks of FU (i.e., up to Week 179); Part B, 7.5 g cohort: From first dose (Week 27) up to 149 weeks of treatment + 9 weeks of FU (i.e., up to Week 185)

Notes:

[2] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	BIVV009 6.5 g	BIVV009 7.5 g		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: subjects				
TEAEs	16	6		
TESAEs	10	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Mean Change From Baseline in Bilirubin Levels at the Treatment Assessment Timepoint

End point title	Part A: Mean Change From Baseline in Bilirubin Levels at the Treatment Assessment Timepoint

End point description:

Mean change from baseline (Week 0) in bilirubin levels at the treatment assessment timepoint is reported in this endpoint. Treatment assessment timepoint was defined as the average of the values from the Week 23, 25, and 26 visits. Least squares (LS) mean and 95% confidence interval (CI) was assessed by Mixed Model for Repeated Measures (MMRM) approach using heterogeneous Toeplitz (TOEPH) covariance matrix with change from baseline as the dependent variable and baseline value and visits as independent variables. Baseline was defined as the last non-missing value prior to the first administration of study drug. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

Baseline (Week 0), treatment assessment timepoint (i.e., average of Week 23, 25 and 26)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: micromoles per Litre (mcmol/L)				
least squares mean (confidence interval 95%)	-38.18 (-42.52 to -33.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Mean Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score (Quality of Life) at Treatment Assessment Timepoint

End point title	Part A: Mean Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score (Quality of Life) at Treatment Assessment Timepoint

End point description:

FACIT-Fatigue scale consists of 13 questions assessed using a 5-point scale (0=not at all; 1 = a little bit, 2 = somewhat, 3 = quite a bit and 4 = very much). Responses to each question were added to obtain a total score. Total score ranged from 0 to 52, with higher score indicating more fatigue. Treatment assessment timepoint was defined as the average of the values from the Week 23, 25, and 26 visits. LS mean and 95% CI was assessed by MMRM approach using TOEPH covariance matrix with change from baseline (Week 0) as the dependent variable and baseline value and visits as independent variables. Baseline was defined as the last non-missing value prior to the first administration of study drug. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

Baseline (Week 0), treatment assessment timepoint (i.e., average of Week 23, 25 and 26)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: score on a scale				
least squares mean (confidence interval 95%)	10.85 (8.00 to 13.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Mean Change From Baseline in Lactate Dehydrogenase (LDH) at the Treatment Assessment Timepoint

End point title	Part A: Mean Change From Baseline in Lactate Dehydrogenase (LDH) at the Treatment Assessment Timepoint

End point description:

Mean change from baseline (Week 0) in LDH at the treatment assessment timepoint is reported in this endpoint. Treatment assessment timepoint was defined as the average of the values from the Week 23, 25, and 26 visits. LS mean and 95% CI was assessed by MMRM approach using TOEPH covariance matrix with change from baseline as the dependent variable and baseline value and visits as independent variables. Baseline was defined as the last non-missing value prior to the first administration of study drug. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

Baseline (Week 0), treatment assessment timepoint (i.e., average of Week 23, 25 and 26)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: units per litre				
least squares mean (confidence interval 95%)	-126.95 (-218.47 to -35.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Blood Transfusions Per Subject

End point title	Part A: Number of Blood Transfusions Per Subject

End point description:

A subject was to receive a transfusion if his or her Hgb level met either of the following criteria: Hgb was <9 g/dL and the subject had symptoms of anemia or Hgb was <7 g/dL and the subject was asymptomatic. Number of transfusions after the first 5 weeks of study drug administration and up to Week 26 were reported in this endpoint. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

From Week 5 up to Week 26

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: blood transfusions per subject				
arithmetic mean (standard deviation)	0.9 (± 2.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Blood Units Transfused Per Subject

End point title	Part A: Number of Blood Units Transfused Per Subject

End point description:

A subject was to receive a transfusion if his or her Hgb level met either of the following criteria: Hgb was <9 g/dL and the subject had symptoms of anemia or Hgb was <7 g/dL and the subject was asymptomatic. Number of blood units transfused after the first 5 weeks of study drug administration and up to Week 26 were reported in this endpoint. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with at least 1 transfusion. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

From Week 5 up to Week 26

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: blood units transfused per subject				
arithmetic mean (standard deviation)	5.8 (± 8.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Mean Change From Baseline in Hemoglobin (Hgb) Level at the Treatment Assessment Timepoint

End point title	Part A: Mean Change From Baseline in Hemoglobin (Hgb) Level at the Treatment Assessment Timepoint

End point description:

Mean change from baseline (Week 0) in Hgb at treatment assessment timepoint is reported in this endpoint. Treatment assessment timepoint was defined as the average of the values from the Week 23, 25, and 26 visits. LS mean and 95% CI was assessed by MMRM approach using TOEPH covariance matrix with change from baseline as the dependent variable and baseline value and visits as independent variables. Baseline was defined as the last non-missing value prior to the first administration of study drug. Analysis was performed on Part A-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

Baseline (Week 0), treatment assessment timepoint (i.e., average of Week 23, 25 and 26)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: g/dL				
least squares mean (confidence interval 95%)	2.60 (0.74 to 4.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Hemoglobin (Hgb) Level at Each Specified Time Points

End point title	Part B: Change From Baseline in Hemoglobin (Hgb) Level at Each Specified Time Points

End point description:

Change from baseline (Week 0) in Hgb levels at each specified time points is reported in this endpoint. Baseline was defined as the last non-missing value prior to the first administration of study drug in Part A. End of treatment (ET) visit/safety follow up (SFU) visit was 9 weeks after administration of last dose (i.e., up to Week 185). Analysis was performed on Part B-FAS which included all subjects who enrolled in Part B study and received at least 1 dose (including partial dose) of study drug. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here,

'99999' is used as a space filler and denotes that standard deviation (SD) was not estimable since only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 27, 29,31,33,35,37,39,41,43,45,47,49, 51,53,55,57,59,61,63,65,67,69,71,73,75,77,79,83,87,91, 95,99,103,107,111,115,119, 123,127,131,135,139,143, 147,151, 155,159,163,167,171,175 and ET/SFU Visit (up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: g/dL				
arithmetic mean (standard deviation)				
Week 27 (n=22)	2.76 (± 2.20)			
Week 29 (n=22)	2.77 (± 2.20)			
Week 31 (n=22)	2.74 (± 1.96)			
Week 33 (n=22)	2.87 (± 1.97)			
Week 35 (n=21)	2.82 (± 2.10)			
Week 37 (n=21)	2.71 (± 2.08)			
Week 39 (n=21)	2.72 (± 2.26)			
Week 41 (n=21)	2.76 (± 2.24)			
Week 43 (n=21)	2.73 (± 2.06)			
Week 45 (n=21)	2.84 (± 2.21)			
Week 47 (n=21)	2.74 (± 1.95)			
Week 49 (n=21)	2.73 (± 2.09)			
Week 51 (n=22)	2.71 (± 1.97)			
Week 53 (n=22)	2.66 (± 1.97)			
Week 55 (n=21)	2.73 (± 1.96)			
Week 57 (n=21)	3.01 (± 2.36)			
Week 59 (n=21)	2.81 (± 2.10)			
Week 61 (n=21)	2.88 (± 2.37)			
Week 63 (n=21)	2.99 (± 2.33)			
Week 65 (n=21)	2.53 (± 2.18)			
Week 67 (n=20)	2.52 (± 2.20)			
Week 69 (n=20)	2.96 (± 2.08)			
Week 71 (n=19)	2.86 (± 2.31)			
Week 73 (n=20)	2.79 (± 2.25)			
Week 75 (n=21)	2.70 (± 2.18)			
Week 77 (n=21)	2.93 (± 2.59)			
Week 79 (n=19)	3.13 (± 2.23)			
Week 83 (n=20)	2.89 (± 2.47)			
Week 87 (n=18)	2.63 (± 2.36)			
Week 91 (n=20)	3.23 (± 2.17)			
Week 95 (n=19)	3.12 (± 2.06)			
Week 99 (n=20)	2.98 (± 2.01)			
Week 103 (n=21)	2.92 (± 2.09)			
Week 107 (n=21)	2.60 (± 2.10)			
Week 111 (n=21)	2.82 (± 2.17)			
Week 115 (n=19)	2.96 (± 2.25)			

Week 119 (n=20)	2.79 (± 2.57)			
Week 123 (n=20)	2.82 (± 2.35)			
Week 127 (n=19)	2.89 (± 1.99)			
Week 131 (n=19)	3.03 (± 2.19)			
Week 135 (n=19)	3.35 (± 1.99)			
Week 139 (n=13)	3.42 (± 2.14)			
Week 143 (n=11)	3.43 (± 2.31)			
Week 147 (n=8)	3.75 (± 2.38)			
Week 151 (n=8)	3.43 (± 1.91)			
Week 155 (n=8)	3.74 (± 1.94)			
Week 159 (n=6)	5.20 (± 1.65)			
Week 163 (n=4)	4.18 (± 1.14)			
Week 167 (n=2)	4.80 (± 0.42)			
Week 171 (n=1)	4.80 (± 99999)			
Week 175 (n=1)	4.40 (± 99999)			
ET/SFU Visit (n=20)	1.21 (± 1.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Bilirubin Levels at Each Specified Time Points

End point title	Part B: Change From Baseline in Bilirubin Levels at Each Specified Time Points

End point description:

Change from baseline (Week 0) in bilirubin levels at each specified time point is reported in this endpoint. Baseline was defined as the last non-missing value prior to the first administration of study drug in Part A. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Analysis was performed on Part B-FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, '99999' is used as a space filler and denotes that SD was not estimable since only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 27, 29,31,33,35,37,39,41,43,45,47,49, 51,53,55,57,59,61,63,65,67,69,71,73,75,77,79,83,87,91, 95,99,103,107,111,115,119, 123,127,131,135,139,143, 147,151, 155,159,163,167,171,175 and ET/SFU Visit (up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: mcmol/L				
arithmetic mean (standard deviation)				
Week 27 (n=19)	-34.96 (± 18.31)			
Week 29 (n=19)	-34.92 (± 15.78)			

Week 31 (n=19)	-32.58 (± 17.07)			
Week 33 (n=19)	-32.67 (± 17.52)			
Week 35 (n=19)	-32.25 (± 22.39)			
Week 37 (n=19)	-33.24 (± 15.53)			
Week 39 (n=13)	-35.92 (± 13.17)			
Week 41 (n=18)	-35.03 (± 13.71)			
Week 43 (n=16)	-36.46 (± 17.25)			
Week 45 (n=18)	-34.81 (± 15.76)			
Week 47 (n=18)	-34.57 (± 16.53)			
Week 49 (n=18)	-32.36 (± 19.50)			
Week 51 (n=16)	-34.88 (± 15.90)			
Week 53 (n=19)	-35.25 (± 18.32)			
Week 55 (n=18)	-34.79 (± 16.70)			
Week 57 (n=18)	-36.32 (± 16.54)			
Week 59 (n=18)	-35.77 (± 17.73)			
Week 61 (n=18)	-36.39 (± 16.14)			
Week 63 (n=17)	-38.25 (± 15.43)			
Week 65 (n=17)	-35.46 (± 16.84)			
Week 67 (n=17)	-35.74 (± 18.37)			
Week 69 (n=17)	-33.88 (± 16.83)			
Week 71 (n=17)	-32.54 (± 23.01)			
Week 73 (n=14)	-33.03 (± 21.82)			
Week 75 (n=16)	-30.55 (± 21.68)			
Week 77 (n=18)	-30.95 (± 22.83)			
Week 79 (n=17)	-35.51 (± 14.79)			
Week 83 (n=16)	-38.60 (± 13.90)			
Week 87 (n=15)	-37.45 (± 16.29)			
Week 91 (n=16)	-35.19 (± 16.07)			
Week 95 (n=15)	-33.57 (± 15.93)			
Week 99 (n=15)	-28.71 (± 21.98)			
Week 103 (n=18)	-32.04 (± 22.45)			

Week 107 (n=18)	-34.46 (± 15.27)			
Week 111 (n=15)	-37.67 (± 14.28)			
Week 115 (n=16)	-36.41 (± 16.76)			
Week 119 (n=16)	-34.65 (± 13.71)			
Week 123 (n=17)	-29.99 (± 24.96)			
Week 127 (n=17)	-35.57 (± 17.83)			
Week 131 (n=16)	-35.03 (± 18.72)			
Week 135 (n=15)	-36.88 (± 14.71)			
Week 139 (n=11)	-37.60 (± 14.59)			
Week 143 (n=8)	-44.50 (± 15.96)			
Week 147 (n=6)	-44.82 (± 15.12)			
Week 151 (n=6)	-46.53 (± 10.80)			
Week 155 (n=6)	-50.32 (± 12.63)			
Week 159 (n=5)	-46.30 (± 13.90)			
Week 163 (n=4)	-46.13 (± 11.86)			
Week 167 (n=2)	-36.30 (± 12.59)			
Week 171 (n=1)	-32.50 (± 99999)			
Week 175 (n=1)	-29.10 (± 99999)			
ET/SFU Visit (n=17)	-9.98 (± 18.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score (Quality of Life) at Each Specified Time Points

End point title	Part B: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score (Quality of Life) at Each Specified Time Points

End point description:

FACIT-Fatigue scale consists of 13 questions assessed using a 5-point scale (0=not at all; 1 = a little bit, 2 = somewhat, 3 = quite a bit and 4 = very much). Responses to each question were added to obtain a total score. The Total score ranged from 0 to 52, with higher score indicating more fatigue. Baseline (Week 0) was defined as the last non-missing value prior to the first administration of study drug in Part A. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Analysis was performed on Part B-FAS. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, '99999' is used as a space filler and denotes that SD was not estimable due to only one subject being available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 39, 51, 63, 75, 87, 99, 111, 123, 135, 147,159, 171 and ET Visit/SFU visit (i.e., up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39 (n=19)	9.37 (± 16.00)			
Week 51 (n=20)	10.50 (± 12.05)			
Week 63 (n=19)	10.21 (± 11.88)			
Week 75 (n=19)	11.00 (± 11.51)			
Week 87 (n=18)	10.39 (± 13.41)			
Week 99 (n=17)	9.94 (± 8.19)			
Week 111 (n=18)	9.11 (± 12.35)			
Week 123 (n=19)	6.79 (± 11.28)			
Week 135 (n=14)	11.71 (± 13.85)			
Week 147 (n=7)	13.29 (± 13.39)			
Week 159 (n=4)	24.75 (± 10.24)			
Week 171 (n=1)	32.00 (± 99999)			
ET/SFU Visit (n=19)	1.05 (± 8.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in 12-Item Short-Form Survey (SF-12) Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores at Each Specified Time Points

End point title	Part B: Change From Baseline in 12-Item Short-Form Survey (SF-12) Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores at Each Specified Time Points

End point description:

SF-12: 12 item-questionnaire contained 12 items, categorised into 8 domains (subscales) of functioning & well-being: physical functioning, role-physical, role emotional, mental health, bodily pain, general health, vitality & social functioning, with each domain score ranged from 0 (poor health) to 100 (better health). Higher scores = good health condition. These 8 domains were further summarised into 2 summary scores, PCS and MCS for which score ranged from 0 (poor health) to 100 (better health). Higher scores = better HRQOL. Baseline (Week 0): last non-missing value prior to first administration of study drug in Part A. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Part B-FAS. Here, 'n' = subjects with available data. Data for this endpoint was planned to be

collected & analysed for combined population (i.e., either 6.5 g or 7.5 g). '99999' = space filler which denotes SD was not estimable since only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 39, 51, 63, 75, 87, 99, 111, 123, 135 and ET Visit/SFU visit (i.e., up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39-PCS (n=16)	7.813 (± 10.486)			
Week 39-MCS (n=16)	5.859 (± 10.249)			
Week 51-PCS (n=18)	6.677 (± 9.925)			
Week 51-MCS (n=18)	3.912 (± 9.493)			
Week 63-PCS (n=19)	8.318 (± 7.148)			
Week 63-MCS (n=19)	2.385 (± 9.777)			
Week 75-PCS (n=18)	6.580 (± 9.214)			
Week 75-MCS (n=18)	3.102 (± 9.881)			
Week 87-PCS (n=18)	6.398 (± 9.021)			
Week 87-MCS (n=18)	1.611 (± 10.336)			
Week 99-PCS (n=14)	9.054 (± 5.803)			
Week 99-MCS (n=14)	2.581 (± 9.169)			
Week 111-PCS (n=8)	11.958 (± 3.832)			
Week 111-MCS (n=8)	2.523 (± 12.585)			
Week 123-PCS (n=6)	4.743 (± 6.900)			
Week 123-MCS (n=6)	3.810 (± 14.071)			
Week 135-PCS (n=1)	10.450 (± 99999)			
Week 135-MCS (n=1)	27.900 (± 99999)			
ET/SFU Visit-PCS (n=1)	-8.920 (± 99999)			
ET/SFU Visit-MCS (n=1)	-1.180 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in 5-level European Quality of Life 5-Dimensions 5-Level Questionnaire (EQ-5D-5L) Health State Utility Index and VAS Scores at Each Specified Time Points

End point title	Part B: Change From Baseline in 5-level European Quality of Life 5-Dimensions 5-Level Questionnaire (EQ-5D-5L) Health State Utility Index and VAS Scores at Each Specified Time Points

End point description:

EQ-5D-5L: subject-rated questionnaire included 2 components: health state utility index (descriptive) & Visual Analog Scale (VAS). EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response option: no, slight, moderate, severe & extreme problems measured with Likert scale. EQ-5D-5L responses converted into single index utility score between 0 to 1. Higher score=better health . EQ-5D-5L VAS rated subject's current health state on scale from 0(worst imaginable health) to 100 (best imaginable health). Baseline (Week 0): last non-missing value prior to first administration of study drug in Part A. ET visit/SFU visit: 9 weeks after administration of last dose (i.e., up to Week 185). Part B FAS. Data was planned to be collected & analysed for combined population. 'n'= subjects with available data. '99999'; space filler which denotes that SD was not estimable since only 1 subject was available.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 39, 51, 63, 75, 87, 99, 111, 123, 135, 147, 159, 171 and ET Visit/SFU visit (i.e., up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39 - Index score (n=18)	0.067 (± 0.264)			
Week 39 - VAS score (n=18)	18.111 (± 20.642)			
Week 51 - Index score (n=20)	0.078 (± 0.194)			
Week 51 - VAS score (n=20)	14.500 (± 19.050)			
Week 63 - Index score (n=19)	0.092 (± 0.166)			
Week 63 - VAS score (n=19)	18.053 (± 16.844)			
Week 75 - Index score (n=19)	0.069 (± 0.211)			
Week 75 - VAS score (n=19)	17.842 (± 16.604)			
Week 87 - Index score (n=19)	0.022 (± 0.226)			
Week 87 - VAS score (n=19)	14.421 (± 20.815)			
Week 99 - Index Score (n=17)	0.060 (± 0.136)			
Week 99 - VAS Score (n=17)	14.059 (± 13.818)			

Week 111 - Index score (n=18)	0.099 (± 0.174)			
Week 111 - VAS score (n=18)	18.889 (± 15.408)			
Week 123 - Index Score (n=19)	0.009 (± 0.190)			
Week 123 - VAS score (n=19)	8.842 (± 18.765)			
Week 135 - Index score (n=15)	0.085 (± 0.233)			
Week 135 - VAS score (n=15)	17.067 (± 21.608)			
Week 147 - Index score (n=7)	0.143 (± 0.131)			
Week 147 - VAS score (n=7)	17.857 (± 20.178)			
Week 159 - Index Score (n=4)	0.250 (± 0.145)			
Week 159 - VAS Score (n=4)	36.250 (± 14.930)			
Week 171 - Index score (n=1)	0.535 (± 99999)			
Week 171 - VAS score (n=1)	35.000 (± 99999)			
ET/SFU - Index score (n=19)	-0.025 (± 0.173)			
ET/SFU - VAS score (n=19)	1.263 (± 19.287)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Subjects With Response to Participant's Global Impression of (Fatigue) Severity (PGIS) Questionnaire at Each Specified Time Points

End point title	Part B: Number of Subjects With Response to Participant's Global Impression of (Fatigue) Severity (PGIS) Questionnaire at Each Specified Time Points

End point description:

The PGIS is a self-reported scale. The PGIS is a 1-item questionnaire designed to assess subject’s impression of disease severity using a 5-point scale ranging from 1 to 5, where 1=none, 2=mild, 3=moderate, 4=severe, 5=very severe. Higher scores indicated greater severity. Analysis was performed on Part B-FAS population. Here, ‘n’ = subjects with available data for each specified category. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

At Weeks 39, 51, 63, 75, 87, 99, 111, 123, 135, 147,159, 171 and at ET Visit/SFU visit (i.e., up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: subjects				
Week 39 - None (n=18)	5			
Week 39 - Mild (n=18)	8			
Week 39 - Moderate (n=18)	4			
Week 39 - Severe (n=18)	1			
Week 39 - Very severe (n=18)	0			
Week 51 - None (n=21)	5			
Week 51 - Mild (n=21)	13			
Week 51 - Moderate (n=21)	3			
Week 51 - Severe (n=21)	0			
Week 51 - Very severe (n=21)	0			
Week 63 - None (n=20)	4			
Week 63 - Mild (n=20)	12			
Week 63 - Moderate (n=20)	3			
Week 63 - Severe (n=20)	1			
Week 63 - Very severe (n=20)	0			
Week 75 - None (n=20)	3			
Week 75 - Mild (n=20)	12			
Week 75 - Moderate (n=20)	5			
Week 75 - Severe (n=20)	0			
Week 75 - Very severe (n=20)	0			
Week 87 - None (n=19)	5			
Week 87 - Mild (n=19)	9			
Week 87 - Moderate (n=19)	3			
Week 87 - Severe (n=19)	2			
Week 87 - Very severe (n=19)	0			
Week 99 - None (n=18)	4			
Week 99 - Mild (n=18)	10			
Week 99 - Moderate (n=18)	4			
Week 99 - Severe (n=18)	0			
Week 99 - Very severe (n=18)	0			
Week 111 - None (n=19)	7			
Week 111 - Mild (n=19)	6			
Week 111 - Moderate (n=19)	6			
Week 111 - Severe (n=19)	0			
Week 111 - Very severe (n=19)	0			
Week 123 - None (n=20)	4			
Week 123 - Mild (n=20)	7			
Week 123 - Moderate (n=20)	7			
Week 123 - Severe (n=20)	2			
Week 123 - Very severe (n=20)	0			
Week 135 - None (n=15)	4			
Week 135 - Mild (n=15)	8			
Week 135 - Moderate (n=15)	3			
Week 135 - Severe (n=15)	0			
Week 135 - Very severe (n=15)	0			
Week 147 - None (n=7)	3			
Week 147 - Mild (n=7)	3			

Week 147 - Moderate (n=7)	1			
Week 147 - Severe (n=7)	0			
Week 147 - Very severe (n=7)	0			
Week 159 - None (n=4)	3			
Week 159 - Mild (n=4)	1			
Week 159 - Moderate (n=4)	0			
Week 159 - Severe (n=4)	0			
Week 159 - Very severe (n=4)	0			
Week 171 - None (n=1)	0			
Week 171 - Mild (n=1)	1			
Week 171 - Moderate (n=1)	0			
Week 171 - Severe (n=1)	0			
Week 171 - Very severe (n=1)	0			
ET/SFU - None (n=20)	4			
ET/SFU - Mild (n=20)	6			
ET/SFU - Moderate (n=20)	4			
ET/SFU - Severe (n=20)	5			
ET/SFU - Very severe (n=20)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Subjects With Response to Participant's Global Impression of Change (PGIC) Questionnaire at Each Specified Time Points

End point title	Part B: Number of Subjects With Response to Participant's Global Impression of Change (PGIC) Questionnaire at Each Specified Time Points

End point description:

PGIC is a self-administered questionnaire to evaluate the improvement or worsening compared to the start of the study. PGIC was assessed on a 7-point Likert scale ranged from 1 (greatly improved) to 7 (greatly worsened). Categories were defined based on the PGIC scores as follows: 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse and 7=very much worsen. Higher scores indicated greater severity. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Analysis was performed on Part B-FAS. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

At Weeks 39, 51, 63, 75, 87, 99, 111, 123, 135, 147,159, 171 and at ET Visit/SFU visit (i.e., up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: subjects				
Week 39 - Very much improved (n=19)	9			
Week 39 - Much improved (n=19)	5			

Week 39 - Minimally improved (n=19)	3			
Week 39 - No change (n=19)	1			
Week 39 - Minimally worse (n=19)	0			
Week 39 - Much worse (n=19)	1			
Week 39 - Very much worse (n=19)	0			
Week 51 - Very much improved (n=21)	6			
Week 51 - Much improved (n=21)	13			
Week 51 - Minimally improved (n=21)	2			
Week 51 - No change (n=21)	0			
Week 51 - Minimally worse (n=21)	0			
Week 51 - Much worse (n=21)	0			
Week 51- Very much worse (n=21)	0			
Week 63 - Very much improved (n=20)	8			
Week 63 - Much improved (n=20)	9			
Week 63 - Minimally improved (n=20)	1			
Week 63 - No change (n=20)	1			
Week 63 - Minimally worse (n=20)	1			
Week 63 - Much worse (n=20)	0			
Week 63 - Very much worse (n=20)	0			
Week 75 - Very much improved (n=20)	5			
Week 75 - Much improved (n=20)	11			
Week 75 - Minimally improved (n=20)	1			
Week 75 - No change (n=20)	2			
Week 75 - Minimally worse (n=20)	1			
Week 75 - Much worse (n=20)	0			
Week 75 - Very much worse (n=20)	0			
Week 87 - Very much improved (n=19)	5			
Week 87 - Much improved (n=19)	11			
Week 87 - Minimally improved (n=19)	2			
Week 87 - No change (n=19)	1			
Week 87 - Minimally worse (n=19)	0			
Week 87 - Much worse (n=19)	0			
Week 87 - Very much worse (n=19)	0			
Week 99 - Very much improved (n=18)	4			
Week 99 - Much improved (n=18)	10			
Week 99 - Minimally improved (n=18)	3			
Week 99 - No Change (n=18)	1			
Week 99 - Minimally worse (n=18)	0			
Week 99 - Much worse (n=18)	0			
Week 99 - Very much worse (n=18)	0			
Week 111 - Very much improved (n=19)	7			
Week 111 - Much improved (n=19)	7			
Week 111 - Minimally improved (n=19)	5			
Week 111 - No change (n=19)	0			
Week 111 - Minimally worse (n=19)	0			
Week 111 - Much worse (n=19)	0			
Week 111 - Very much worse (n=19)	0			
Week 123 - Very much improved (n=20)	8			
Week 123 - Much improved (n=20)	6			
Week 123 - Minimally improved (n=20)	6			

Week 123 - No change (n=20)	0			
Week 123 - Minimally worse (n=20)	0			
Week 123 - Much worse (n=20)	0			
Week 123 - Very much worse (n=20)	0			
Week 135 - Very much improved (n=15)	5			
Week 135 - Much improved (n=15)	6			
Week 135 - Minimally improved (n=15)	2			
Week 135 - No change (n=15)	1			
Week 135 - Minimally worse (n=15)	1			
Week 135 - Much worse (n=15)	0			
Week 135 - Very much worse (n=15)	0			
Week 147 - Very much improved (n=7)	4			
Week 147 - Much improved (n=7)	2			
Week 147 - Minimally improved (n=7)	1			
Week 147 - No change (n=7)	0			
Week 147 - Minimally worse (n=7)	0			
Week 147 - Much worse (n=7)	0			
Week 147 - Very much worse (n=7)	0			
Week 159 - Very much improved (n=4)	4			
Week 159 - Much improved (n=4)	0			
Week 159 - Minimally improved (n=4)	0			
Week 159 - No change (n=4)	0			
Week 159 - Minimally worse (n=4)	0			
Week 159 - Much worse (n=4)	0			
Week 159 - Very much worse (n=4)	0			
Week 171 - Very much improved (n=1)	1			
Week 171 - Much improved (n=1)	0			
Week 171 - Minimally improved (n=1)	0			
Week 171 - No Change (n=1)	0			
Week 171 - Minimally worse (n=1)	0			
Week 171 - Much worse (n=1)	0			
Week 171 - Very much worse (n=1)	0			
ET/SFU Visit- Very much improved (n=20)	3			
ET/SFU Visit- Much improved (n=20)	8			
ET/SFU Visit- Minimally improved (n=20)	2			
ET/SFU Visit- No Change (n=20)	4			
ET/SFU Visit- Minimally worse (n=20)	2			
ET/SFU Visit- Much worse (n=20)	0			
ET/SFU Visit- Very much worse (n=20)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Mean Change From Baseline in Lactate Dehydrogenase (LDH) Level at Each Specified Time Points

End point title	Part B: Mean Change From Baseline in Lactate Dehydrogenase (LDH) Level at Each Specified Time Points

End point description:

Mean change from baseline (Week 0) in LDH levels at each specified time points (i.e., Weeks 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 83, 87, 91, 95, 99, 103, 107, 111, 115, 119, 123, 127, 131, 135, 139, 143, 147, 151, 155, 159, 163, 167, 171, 175 and ET/SFU Visit) is reported in this endpoint. Baseline was defined as the last non-missing value prior to the first administration of study drug in Part A. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Analysis was performed on Part B-FAS. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, '99999' is used as a space filler and denotes that SD was not estimable since only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 27,29,31,33,35,37,39,41,43,45,47,49,51,53,55,57,59,61,63,65,67,69, 71,73,75,77,79,83,87,91,95,99,103,107,111,115,119,123,127,131,135,139,143,147,151,155, 159,163,167,171,175 and ET/SFU Visit (up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: units per litre				
arithmetic mean (standard deviation)				
Week 27 (n=22)	-111.59 (± 327.80)			
Week 29 (n=21)	-129.76 (± 331.91)			
Week 31 (n=22)	-95.27 (± 319.25)			
Week 33 (n=21)	-82.19 (± 330.04)			
Week 35 (n=22)	-126.64 (± 346.75)			
Week 37 (n=21)	-151.57 (± 307.15)			
Week 39 (n=15)	-49.27 (± 172.53)			
Week 41 (n=21)	-116.10 (± 305.11)			
Week 43 (n=19)	-150.26 (± 271.72)			
Week 45 (n=21)	-85.48 (± 308.01)			
Week 47 (n=21)	-79.81 (± 286.13)			
Week 49 (n=21)	-104.38 (± 313.66)			
Week 51 (n=19)	-76.84 (± 344.60)			
Week 53 (n=21)	-87.00 (± 299.09)			
Week 55 (n=21)	-68.29 (± 305.09)			
Week 57 (n=21)	-101.71 (± 273.44)			
Week 59 (n=21)	-97.71 (± 296.74)			

Week 61 (n=21)	-89.48 (± 298.05)			
Week 63 (n=20)	-94.20 (± 288.34)			
Week 65 (n=20)	-91.05 (± 305.75)			
Week 67 (n=19)	-106.32 (± 327.48)			
Week 69 (n=19)	-75.00 (± 333.47)			
Week 71 (n=18)	-52.39 (± 378.82)			
Week 73 (n=17)	-70.35 (± 348.56)			
Week 75 (n=19)	-18.68 (± 323.02)			
Week 77 (n=21)	-64.67 (± 335.73)			
Week 79 (n=20)	-54.10 (± 338.58)			
Week 83 (n=19)	-87.21 (± 344.88)			
Week 87 (n=18)	-89.17 (± 392.80)			
Week 91 (n=19)	-78.47 (± 349.15)			
Week 95 (n=16)	-132.75 (± 301.36)			
Week 99 (n=18)	-13.83 (± 155.04)			
Week 103 (n=20)	106.40 (± 309.44)			
Week 107 (n=20)	-85.45 (± 312.50)			
Week 111 (n=19)	-107.58 (± 286.18)			
Week 115 (n=19)	-107.84 (± 293.61)			
Week 119 (n=19)	-63.68 (± 310.56)			
Week 123 (n=20)	-58.90 (± 339.49)			
Week 127 (n=18)	-57.72 (± 400.26)			
Week 131 (n=19)	-113.63 (± 344.53)			
Week 135 (n=17)	-97.06 (± 339.41)			
Week 139 (n=13)	-1.00 (± 256.65)			
Week 143 (n=10)	180.70 (± 318.62)			
Week 147 (n=7)	-10.29 (± 196.90)			
Week 151 (n=8)	-24.13 (± 146.79)			
Week 155 (n=8)	-17.38 (± 146.80)			
Week 159 (n=4)	-126.00 (± 150.38)			
Week 163 (n=4)	-31.50 (± 35.49)			

Week 167 (n=2)	-48.50 (± 68.59)			
Week 171 (n=1)	-23.00 (± 99999)			
Week 175 (n=1)	6.00 (± 99999)			
ET/SFU visit (n=20)	-107.50 (± 249.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Blood Transfusions Per Subject

End point title	Part B: Number of Blood Transfusions Per Subject

End point description:

A subject was to receive a transfusion if his or her Hgb level met either of the following criteria: Hgb was <9 g/dL and the subject had symptoms of anemia or Hgb was <7 g/dL and the subject was asymptomatic. Analysis was performed on Part B-FAS. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

From Week 27 up to 149 weeks of treatment (i.e., up to Week 176)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: blood transfusions per subject				
arithmetic mean (standard deviation)	2.86 (± 6.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Blood Units Transfused Per Subject

End point title	Part B: Number of Blood Units Transfused Per Subject

End point description:

A subject was to receive a transfusion if his or her Hgb level met either of the following criteria: Hgb was <9 g/dL and the subject had symptoms of anemia or Hgb was <7 g/dL and the subject was asymptomatic. Analysis was performed on Part B-FAS. Here, 'number of subjects analysed' = subjects with at least 1 transfusion. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either at 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

From Week 27 up to 149 weeks of treatment (i.e., up to Week 176)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: blood units transfused per subject				
arithmetic mean (standard deviation)	16.57 (± 16.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Haptoglobin Values at Each Specified Time Points

End point title	Part B: Change From Baseline in Haptoglobin Values at Each Specified Time Points

End point description:

Change from baseline (Week 0) in haptoglobin values at each specified time points (i.e., Weeks 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 83, 87, 91, 95, 99, 103, 107, 111, 115, 119, 123, 127, 131, 135, 139, 143, 147, 151, 155, 159, 163, 167, 171, 175 and ET/SFU Visit) is reported in this endpoint. Baseline was defined as the last non-missing value prior to thez first administration of study drug in Part A. ET visit/SFU visit was 9 weeks after administration of last dose (i.e., up to Week 185). Haptoglobin values <0.2 were imputed as 0.2. Part B-FAS. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either at 6.5 g or 7.5 g]). Here, '99999' is used as a space filler and denotes that standard deviation was not estimable since only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 27, 29,31,33,35,37,39,41,43,45,47,49, 51,53,55,57,59,61,63,65,67,69,71,73,75,77,79,83,87,91, 95,99,103,107,111,115,119, 123,127,131,135,139,143, 147,151, 155,159,163,167,171,175 and ET/SFU Visit (up to Week 185)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: grams per litre				
arithmetic mean (standard deviation)				
Week 27 (n=22)	0.21 (± 0.38)			
Week 29 (n=21)	0.21 (± 0.45)			
Week 31 (n=22)	0.21 (± 0.43)			
Week 33 (n=22)	0.28 (± 0.53)			
Week 35 (n=22)	0.25 (± 0.41)			
Week 37 (n=21)	0.14 (± 0.28)			
Week 39 (n=17)	0.27 (± 0.49)			
Week 41 (n=20)	0.39 (± 0.59)			
Week 43 (n=18)	0.29 (± 0.47)			

Week 45 (n=21)	0.16 (± 0.26)			
Week 47 (n=20)	0.15 (± 0.35)			
Week 49 (n=21)	0.21 (± 0.41)			
Week 51 (n=19)	0.20 (± 0.37)			
Week 53 (n=22)	0.23 (± 0.46)			
Week 55 (n=20)	0.26 (± 0.45)			
Week 57 (n=20)	0.26 (± 0.43)			
Week 59 (n=21)	0.29 (± 0.44)			
Week 61 (n=21)	0.23 (± 0.43)			
Week 63 (n=20)	0.38 (± 0.50)			
Week 65 (n=20)	0.25 (± 0.41)			
Week 67 (n=19)	0.25 (± 0.42)			
Week 69 (n=20)	0.24 (± 0.47)			
Week 71 (n=19)	0.19 (± 0.33)			
Week 73 (n=19)	0.13 (± 0.29)			
Week 75 (n=20)	0.13 (± 0.24)			
Week 77 (n=21)	0.17 (± 0.29)			
Week 79 (n=20)	0.09 (± 0.22)			
Week 83 (n=20)	0.14 (± 0.25)			
Week 87 (n=18)	0.35 (± 0.53)			
Week 91 (n=19)	0.17 (± 0.28)			
Week 95 (n=20)	0.19 (± 0.33)			
Week 99 (n=18)	0.21 (± 0.37)			
Week 103 (n=21)	0.15 (± 0.25)			
Week 107 (n=21)	0.26 (± 0.40)			
Week 111 (n=19)	0.22 (± 0.33)			
Week 115 (n=18)	0.21 (± 0.35)			
Week 119 (n=19)	0.16 (± 0.31)			
Week 123 (n=20)	0.19 (± 0.45)			
Week 127 (n=20)	0.14 (± 0.23)			
Week 131 (n=19)	0.18 (± 0.38)			
Week 135 (n=18)	0.18 (± 0.35)			
Week 139 (n=13)	0.10 (± 0.17)			
Week 143 (n=11)	0.07 (± 0.16)			
Week 147 (n=8)	0.06 (± 0.16)			
Week 151 (n=8)	0.12 (± 0.24)			
Week 155 (n=8)	0.09 (± 0.22)			
Week 159 (n=5)	0.15 (± 0.34)			
Week 163 (n=4)	0.30 (± 0.35)			
Week 167 (n=2)	0.00 (± 0.00)			
Week 171 (n=1)	0.00 (± 99999)			
Week 175 (n=1)	0.00 (± 99999)			
ET/SFU visit (n=20)	0.02 (± 0.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Healthcare Visits by Type

End point title	Part B: Number of Healthcare Visits by Type

End point description:

In this endpoint, number of healthcare visits which included non-study healthcare resource utilisation visit (consisted mainly of extra visits to the office of the study doctor, visit to a generalist doctor or visit to a specialist doctor), hospitalisation visit and visit to hospital emergency is reported. Analysis was performed on Part B-FAS. Data for this endpoint was planned to be collected and analysed for combined population (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]).

End point type	Secondary

End point timeframe:

From Week 27 up to 149 weeks of treatment (i.e., up to Week 176)

End point values	BIVV009			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: visits				
number (not applicable)				
Non-study healthcare resource utilisation visits	16			
Hospitalisation	8			
Visit to a hospital emergency room	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: From first dose (Day 0) up to Week 26; Part B: 6.5 g cohort: From first dose (Week 27) up to 143 weeks of treatment + 9 weeks FU (i.e., up to Week 179); 7.5 g cohort: From first dose up to 149 weeks of treatment + 9 weeks FU (i.e., up to Week 185)

Adverse event reporting additional description:

Reported AEs and SAEs including fatal AEs were TEAEs that developed/worsened or became serious during on-treatment period. Analysis was performed on SAS.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Part A: BIVV009 6.5 g

Reporting group description:

Subjects with primary CAD and body weight <75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 6.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

Reporting group title	Part A: BIVV009 7.5 g

Reporting group description:

Subjects with primary CAD and body weight >=75 kg with a recent history of blood transfusion (defined as at least 1 transfusion during the last 6 months prior to screening in this study) received an IV infusion of BIVV009 7.5 g on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

Reporting group title	Part B: BIVV009 6.5 g

Reporting group description:

Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 6.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 143 weeks. All subjects who completed Part A elected to continue in Part B.

Reporting group title	Part B: BIVV009 7.5 g

Reporting group description:

Subjects who completed Part A per protocol through the end of treatment visit (Week 26) could continue to receive BIVV009 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks. All subjects who completed Part A elected to continue in Part B.

Serious adverse events	Part A: BIVV009 6.5 g	Part A: BIVV009 7.5 g	Part B: BIVV009 6.5 g
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 17 (23.53%)	3 / 7 (42.86%)	10 / 16 (62.50%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic Cancer			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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 / 1	0 / 0

Meningioma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Renal Cell Carcinoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubular Breast Carcinoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Vascular disorders			
Cyanosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Vascular Disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Artery Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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

Injury, poisoning and procedural complications			
Femoral Neck Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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			
Angina Pectoris			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Coronary Artery Stenosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (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
Stress Cardiomyopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Nervous system disorders			
Parkinsonism			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (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
Transient Global Amnesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (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
Cold Type Haemolytic Anaemia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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 / 1
Haemolytic Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (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
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous Haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Haemorrhoids			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Inguinal Hernia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Hepatobiliary disorders			
Cholecystitis Acute			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Biliary Colic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Cholelithiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (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
Infections and infestations			
Asymptomatic Covid-19			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Covid-19 Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Herpes Zoster			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Pneumococcal Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Klebsiella			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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 / 1
Respiratory Tract Infection			

subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (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
Viral Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection Staphylococcal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	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

Serious adverse events	Part B: BIVV009 7.5 g		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic Cancer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Meningioma				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Cell Carcinoma				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubular Breast Carcinoma				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Cyanosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral Vascular Disorder				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral Artery Thrombosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Inflammation				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-Cardiac Chest Pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Femoral Neck Fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary Artery Stenosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stress Cardiomyopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Parkinsonism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient Global Amnesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cold Type Haemolytic Anaemia			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemolytic Anaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Iridocyclitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal Detachment				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Uveitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vitreous Haemorrhage				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal Pain Upper				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal Hernia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis Acute			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biliary Colic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Asymptomatic Covid-19			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Covid-19 Pneumonia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia Sepsis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal Sepsis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Klebsiella				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal Sepsis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection Bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound Infection Staphylococcal				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Part A: BIVV009 6.5 g	Part A: BIVV009 7.5 g	Part B: BIVV009 6.5 g
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)	6 / 7 (85.71%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Bowen's Disease			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Myelodysplastic Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Seborrhoeic Keratosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vascular disorders			
Fibromuscular Dysplasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Essential Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cyanosis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	3	0	3
Circulatory Collapse			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Air Embolism			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	1	0	6
Hot Flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	4
Catheter Site Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Drug Intolerance			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Device Related Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chest Discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mucosal Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Influenza Like Illness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Facial Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	1	0	3
Feeling Cold			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Oedema Peripheral			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Peripheral Swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	3 / 16 (18.75%)
occurrences (all)	0	1	4
Temperature Intolerance			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Seasonal Allergy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Autoinflammatory Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Intermenstrual Bleeding			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ovarian Cyst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pelvic Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Bronchial Irritation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Dyspnoea Exertional			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	7	0	6
Restrictive Pulmonary Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory Tract Congestion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Productive Cough			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Pleural Effusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Nasal Congestion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sputum Discoloured			

subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Anxiety Disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Confusional State			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	1	1	3
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Adjustment Disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mental Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood Immunoglobulin G Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood Pressure Increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
C-Reactive Protein Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Chest X-Ray Abnormal			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Computerised Tomogram Head Abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Serum Ferritin Decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Weight Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Arthropod Bite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Back Injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Bone Contusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Contusion			

subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Exposure To Extreme Temperature			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye Contusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hand Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	3	1	1
Infusion Related Reaction			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Joint Injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Limb Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Procedural Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Road Traffic Accident			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin Abrasion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Spinal Column Injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Stress Fracture			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tendon Rupture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Aortic Valve Incompetence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Aortic Valve Sclerosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Aortic Valve Stenosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Atrial Fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Cardiac Failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Coronary Artery Disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Sinus Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mitral Valve Incompetence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Stress Cardiomyopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Supraventricular Extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tricuspid Valve Incompetence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ventricular Extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Carotid Artery Stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cerebrovascular Disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	3
Dizziness Postural			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Multiple Sclerosis Relapse			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Parkinsonism			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	5 / 16 (31.25%)
occurrences (all)	0	3	11
Haemolysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haemolytic Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cold Type Haemolytic Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Increased Tendency To Bruise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Monoclonal B-Cell Lymphocytosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Meniere's Disease			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Dry Eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Macular Degeneration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ocular Discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Photopsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Visual Field Defect			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Visual Impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			

subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Abdominal Tenderness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	2 / 16 (12.50%)
occurrences (all)	1	1	3
Ascites			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	1	0	3
Dental Caries			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 7 (14.29%)	2 / 16 (12.50%)
occurrences (all)	1	1	4
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dysphagia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	3
Gastritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastritis Erosive			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrooesophageal Reflux Disease			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	2 / 17 (11.76%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	2
Oral Mucosal Blistering			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	1	0	3
Periodontal Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Biliary Colic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cholelithiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Drug Eruption			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Actinic Keratosis			

subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Nodular Vasculitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Panniculitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rash Maculo-Papular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin Induration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin Lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin Irritation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Stasis Dermatitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin Ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	4	0	0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chronic Kidney Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haemoglobinuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal Failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal Impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Coccydynia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Intervertebral Disc Calcification			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	3
Neck Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Osteoporosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pain In Extremity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	3
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Systemic Scleroderma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Temporomandibular Joint Syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Trigger Finger			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Abdominal Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Bacteriuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	7
Asymptomatic Covid-19			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cystitis Bacterial			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Herpes Simplex Viraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	3
Fungal Skin Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Nasopharyngitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 7 (0.00%)	4 / 16 (25.00%)
occurrences (all)	2	0	6
Oral Herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Otitis Externa			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Otitis Externa Bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash Pustular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Root Canal Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin Candida			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tinea Pedis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	3
Tooth Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2

Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	4	0	1
Urinary Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	3 / 16 (18.75%)
occurrences (all)	1	0	13
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Viral Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 7 (14.29%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Decreased Appetite			
subjects affected / exposed	1 / 17 (5.88%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Iron Deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Hypoalbuminaemia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Magnesium Deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vitamin B12 Deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	0 / 17 (0.00%)	0 / 7 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	Part B: BIVV009 7.5 g		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bowen's Disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myelodysplastic Syndrome			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Seborrhoeic Keratosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Fibromuscular Dysplasia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Essential Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cyanosis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Circulatory Collapse			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Air Embolism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	3		
Hot Flush			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Catheter Site Haematoma			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Drug Intolerance				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Device Related Thrombosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Chest Discomfort				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Non-Cardiac Chest Pain				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Mucosal Inflammation				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Malaise				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Influenza Like Illness				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Facial Pain				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Fatigue				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	5			
Feeling Cold				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oedema Peripheral				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Peripheral Swelling				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Temperature Intolerance			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Seasonal Allergy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Autoinflammatory Disease			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Intermenstrual Bleeding			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ovarian Cyst			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pelvic Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchial Irritation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chronic Obstructive Pulmonary			

Disease				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Cough				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dyspnoea Exertional				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Dyspnoea				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Epistaxis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Restrictive Pulmonary Disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Respiratory Tract Congestion				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Productive Cough				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Pleural Effusion				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nasal Congestion				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Sputum Discoloured				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Sleep Apnoea Syndrome				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			

Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety Disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Confusional State			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Adjustment Disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Mental Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood Creatinine Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood Immunoglobulin G Decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood Pressure Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
C-Reactive Protein Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest X-Ray Abnormal			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Computerised Tomogram Head Abnormal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Serum Ferritin Decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Weight Increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Arthropod Bite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back Injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone Contusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Concussion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Exposure To Extreme Temperature			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Eye Contusion			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hand Fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infusion Related Reaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Joint Injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Limb Injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Procedural Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Road Traffic Accident			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin Abrasion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Spinal Column Injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Stress Fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Tendon Rupture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cardiac disorders			

Aortic Valve Incompetence				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Aortic Valve Sclerosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Aortic Valve Stenosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Atrial Fibrillation				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Atrioventricular Block First Degree				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Cardiac Failure				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Coronary Artery Disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Sinus Bradycardia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Mitral Valve Incompetence				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Stress Cardiomyopathy				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Supraventricular Extrasystoles				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Tricuspid Valve Incompetence				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Ventricular Extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Carotid Artery Stenosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cerebrovascular Disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dizziness Postural			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Multiple Sclerosis Relapse			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Parkinsonism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Seizure			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Haemolysis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	3		
Haemolytic Anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cold Type Haemolytic Anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Increased Tendency To Bruise			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Monoclonal B-Cell Lymphocytosis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Meniere's Disease			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Tinnitus			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vertigo			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry Eye			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Macular Degeneration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ocular Discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Photopsia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Visual Field Defect			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Visual Impairment			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal Tenderness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal Pain Upper			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	8			
Ascites				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Dental Caries				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	4			
Dyspepsia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Haemorrhoidal Haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastritis Erosive				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastrooesophageal Reflux Disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oral Mucosal Blistering				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	5		
Periodontal Disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hepatobiliary disorders			
Biliary Colic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cholelithiasis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Drug Eruption			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Actinic Keratosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nodular Vasculitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperkeratosis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Panniculitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash Maculo-Papular			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin Induration			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin Lesion			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Skin Irritation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Stasis Dermatitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin Ulcer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Acute Kidney Injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Chronic Kidney Disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Haemoglobinuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Renal Failure subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Renal Impairment subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Back Pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Arthralgia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3		
Coccydynia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Intervertebral Disc Calcification subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Neck Pain			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle Spasms			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain In Extremity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Systemic Scleroderma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Temporomandibular Joint Syndrome			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Trigger Finger			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abdominal Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bacteriuria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Bronchitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Cystitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Asymptomatic Covid-19				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Cystitis Bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Herpes Simplex Viraemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Fungal Skin Infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Eye Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Escherichia Urinary Tract Infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oral Herpes				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Otitis Externa				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Otitis Externa Bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash Pustular				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Respiratory Tract Infection Viral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Root Canal Infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Skin Candida				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Skin Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Tinea Pedis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Tooth Infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Upper Respiratory Tract Infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Urinary Tract Infection				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	6			

Urinary Tract Infection Bacterial			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Decreased Appetite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Iron Deficiency			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Magnesium Deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vitamin B12 Deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2018	Following changes were done: • Changed urine pregnancy testing to serum or urine pregnancy testing beginning on Day 0. • Clarified that subjects who received a transfusion in Part A would not be withdrawn and would still be eligible to participate in Part B. • Excluded from Part B subjects who received prohibited medications in Part A. • Changed the collection of pharmacokinetic (PK), pharmacodynamic (PD), and antidrug antibody (ADA) samples from 6 to 9 weeks after the last dose of study drug in subjects who discontinue early and those who had a hematologic breakthrough event. • Changed inclusion criterion to "Ferritin above the lower limit of normal. Concurrent treatment with iron supplementation was permitted if the subject has been on a stable dose for the previous 4 weeks." • Extended the requirement for highly effective contraception from 6 weeks following the last administration of study drug to 9 weeks. • Modified the exclusion criterion "Clinical diagnosis of systemic lupus erythematosus or other autoimmune disorders with antinuclear antibodies at Screening" to add that antinuclear antibodies of long-standing duration without associated clinical symptoms were to be adjudicated on a case-by-case basis. • Added total healthcare resource utilisation as an exploratory efficacy endpoint in Part A and as an efficacy endpoint in Part B. • Specified that vaccinations were to be administered in accordance with regional guidelines. • Added the occurrence of clinically significant hematologic breakthrough events attributable to the development of ADA and/or the development of positive SLE autoantibody titers as a criterion for the removal of a subject from study participation if, in the opinion of the Investigator, it could jeopardise the safety of the subject. • Clarified that subjects must be monitored for allergic reactions and anaphylaxis rather than infusion-related reactions. • Added solicited symptomatic anemia as a study assessment.
09 March 2018	Following changes were done: • Subjects requiring treatment with permitted concomitant medications and/or transfusions were not to be discontinued from the study. Subjects in Part B were transfused per the Transfusion Criteria. • Modified exclusion criterion "Clinical diagnosis of SLE or other autoimmune disorders with antinuclear antibodies at Screening" to add that antinuclear antibodies of longstanding duration without associated clinical symptoms were adjudicated on a case-by-case basis. • Extended the SFU visit for collection of AE data, PK, PD, and ADA samples from 6 weeks to 9 weeks after the last administration of study drug in subjects who discontinued early. • Increased the frequency of pregnancy testing (serum or urine). • Extended the recording period for AEs from 6 to 9 weeks after administration of the last dose of study drug. • Extended the reported period for SAEs from 6 to 9 weeks after the last dose of study drug or through the final study visit, whichever occurred later. • Increased the frequency of pregnancy testing (serum or urine).

19 December 2019	Following changes were done:• Added information regarding CAD. • Added an exploratory objective to evaluate the immunogenicity of sutimlimab and specified immunogenicity assessments evaluation, and conditions for ADA testing using available pre-dose PD back-up samples. • Added assessment in Part B of satisfaction with home infusion after first home infusion and after fourth home infusion. • Specified for subjects with home infusions, safety assessments were to include AEs with onset within 24 hours of infusion. • Added conditions for which subjects undergoing home infusions with study drug were to return to bi-weekly dosing, and which they may return to home infusions. • Specified collection of PK samples pre-dose and 1 hour(+-15 minutes) post-dose at 3-month intervals during the first year of treatment in Part B and then at 6-month intervals for the remainder of the time on study. • Specified collection of PD samples pre-dose and 1 hour(+-15 minutes) post-dose at 3-month intervals during the first year of treatment in Part B and then at 6-month intervals for the remainder of the time on study. • Increased the planned total study duration per subject to approximately 2.5 to 3.5 years. The duration of dosing in Part B was to last from 2 - 3 years. Part B was to run for 2 years following completion of LPO in Part A. Added SLE panel testing and ADA against sutimlimab for Part B Extension Phase. • Specified that immunisation review/vaccination was to be assessed during entire study. Revaccination with booster doses were to be given according to regional guidelines for subjects with persistent complement deficiency and in accordance with respective labels. • Added that in subjects who consented to the use of their blood samples for future research, PD back-up samples could be used to assay ADA. • Added that the hematology panel and clinical chemistry panel were to be performed every 2 weeks until Week 79 and then every 4 weeks after. •Removed "iron" from chemistry panel.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported