Clinical trial results:
A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF BIVV009 IN PATIENTS WITH PRIMARY COLD AGGLUTININ DISEASE WITHOUT A RECENT HISTORY OF BLOOD TRANSFUSION

Summary

EudraCT number	2017-003539-12
Trial protocol	AT GB DE NO ES BE NL IT
Global end of trial date	03 December 2021

Results information

Result version number	v1 (current)
This version publication date	16 December 2022
First version publication date	16 December 2022

Trial information

Trial identification

Sponsor protocol code	EFC16216

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03347422
WHO universal trial number (UTN)	-
Other trial identifiers	IND #: 128,190, STUDY NAME: Cadenza

Notes:

Sponsors

Sponsor organisation name	Sanofi-aventis Recherche & Développement
Sponsor organisation address	1, Avenue Pierre Brossolette, Chilly Mazarin, France, 91385
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	25 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of Part A was to determine whether sutimlimab administration results in a greater than or equal to (>=)1.5 grams per decilitre (g/dL) increase in hemoglobin (Hgb) level and avoidance of transfusion in subjects with primary cold agglutinin disease (CAD) without a recent history of blood transfusion. The purpose of Part B was to evaluate the long-term safety and tolerability of sutimlimab 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	17 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	Netherlands: 4
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	United States: 5

Worldwide total number of subjects	42
EEA total number of subjects	25

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)	18
From 65 to 84 years	22
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 27 sites in 13 countries. Out of 66 screened subjects, a total of 42 subjects were enrolled and randomised from 17 March 2018 to 30 March 2020. This 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 and BIVV009 7.5 g) for safety endpoints and adverse events (AEs). 2) combined population (BIVV009 at any dose) for efficacy endpoints.

Period 1

Period 1 title	Part A (26 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	BIVV009

Arm description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an intravenous (IV) infusion of BIVV009 6.5 g (for subjects less than [<]75 kilograms [kg]) or 7.5 g dose (for subjects >=75 kg) on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

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 received fixed doses of BIVV009 6.5 g or 7.5 g based on body weight, as IV infusion on Day 0 and Day 7 and every 14 days thereafter up to Week 25.

Arm title	Placebo

Arm description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

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

Dosage and administration details:

Subjects received fixed doses of placebo matched to BIVV009 (6.5 g or 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	Placebo
Started	22	20
Completed	19	20
Not completed	3	0
Adverse event, non-fatal	3	-

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/BIVV009

Arm description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of BIVV009 6.5 g (for subjects <75 kg) or 7.5 g dose (for subjects >=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), received placebo on Week 26 and continued to receive BIVV009 6.5 or 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks (for 6.5 g) or 121 weeks (for 7.5 g). 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 (for 6.5 g) and body weight >=75 kg (for 7.5 g) received placebo on Week 26 and continued to receive fixed doses of BIVV009 6.5 g or 7.5 g as IV infusion every 2 weeks starting at Week 27 for up to an additional 149 weeks (for 6.5 g) or 121 weeks (for 7.5 g).

Arm title	Placebo/BIVV009

Arm description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 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) received BIVV009 6.5 (if <75 kg) or 7.5 g (if >=75 kg) in Part B, on Week 26 and Week 27 and every 2 weeks thereafter for up to an additional 123 weeks (for 6.5 g) or 137 weeks (for 7.5 g). 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 (for 6.5 g) and body weight >=75 kg (for 7.5 g) received fixed doses of BIVV009 6.5 g or 7.5 g as IV infusion on Week 26 and Week 27 and every 2 weeks thereafter for up to an additional 123 weeks (for 6.5 g) or 137 weeks (for 7.5 g).

Number of subjects in period 2	BIVV009/BIVV009	Placebo/BIVV009
Started	19	20
Completed	16	16
Not completed	3	4
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	1
Unspecified	1	-
Lack of efficacy	1	2

Baseline characteristics

Reporting groups	
Reporting group title	BIVV009
Reporting group description:	
Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an intravenous (IV) infusion of BIVV009 6.5 g (for subjects less than [<]75 kilograms [kg]) or 7.5 g dose (for subjects >=75 kg) on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.	
Reporting group title	Placebo
Reporting group description:	
Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.	

Reporting group values	BIVV009	Placebo	Total
Number of subjects	22	20	42
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65.3	68.2	
standard deviation	± 10.9	± 10.1	-
Gender categorical Units: Subjects			
Female	17	16	33
Male	5	4	9
Race Units: Subjects			
Asian	5	2	7
White	0	4	4
Black or African American	0	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
More than one race	0	0	0
Unknown or Not Reported	17	14	31

End points

End points reporting groups

Reporting group title	BIVV009

Reporting group description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an intravenous (IV) infusion of BIVV009 6.5 g (for subjects less than [<]75 kilograms [kg]) or 7.5 g dose (for subjects >=75 kg) on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

Reporting group title	Placebo

Reporting group description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 on Day 0 and Day 7 and every 14 days thereafter in Part A up to Week 25.

Reporting group title	BIVV009/BIVV009

Reporting group description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of BIVV009 6.5 g (for subjects <75 kg) or 7.5 g dose (for subjects >=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), received placebo on Week 26 and continued to receive BIVV009 6.5 or 7.5 g in Part B, every 2 weeks starting at Week 27 for up to an additional 149 weeks (for 6.5 g) or 121 weeks (for 7.5 g). All subjects who completed Part A elected to continue in Part B.

Reporting group title	Placebo/BIVV009

Reporting group description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 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) received BIVV009 6.5 (if <75 kg) or 7.5 g (if >=75 kg) in Part B, on Week 26 and Week 27 and every 2 weeks thereafter for up to an additional 123 weeks (for 6.5 g) or 137 weeks (for 7.5 g). All subjects who completed Part A elected to continue in Part B.

Subject analysis set title	Part B: BIVV009 6.5 g
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who completed Part A per protocol through the end of treatment visit (Week 26) were eligible to be enrolled in Part B where they were treated for up to an additional 149 weeks. Subjects who received placebo in Part A received BIVV009 6.5 g on Week 26, Week 27 and every 2 weeks thereafter; subjects who received BIVV009 6.5 g in Part A received placebo on Week 26, BIVV009 6.5 g on Week 27 and every 2 weeks thereafter for up to an additional 149 weeks.

Subject analysis set title	Part B: BIVV009 7.5 g
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who completed Part A per protocol through the end of treatment visit (Week 26) were eligible to be enrolled in Part B where they were treated for up to an additional 137 weeks. Subjects who received placebo in Part A received BIVV009 7.5 g on Week 26, Week 27 and every 2 weeks thereafter; subjects who received BIVV009 7.5 g in Part A received placebo on Week 26, BIVV009 7.5 g on Week 27 and every 2 weeks thereafter for up to an additional 137 weeks.

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

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

End point description:

A subject was considered a responder: if he or she did not receive blood transfusion from Week 5 through Week 26 (end of treatment) and did not receive treatment for CAD beyond what was permitted per protocol. Additionally, subject’s hemoglobin (Hgb) level must have increased to >=1.5 g/dL from baseline (defined as last Hgb value before administration of first dose of study drug) at treatment assessment timepoint (defined as average of values from the Week 23, 25, and 26 visits). Percentage of responders was calculated together with 95% exact Clopper-Pearson confidence interval (CI). Analysed on Part A-full analysis set (FAS) which included all subjects who received at least 1 dose (including

partial dose) of study drug (BIVV009 or placebo). Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., all subjects who received BIVV009 [either at 6.5 or 7.5 g] and placebo in Part A.

End point type	Primary

End point timeframe:

From Week 5 through Week 26

End point values	BIVV009	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: percentage of subjects				
number (confidence interval 95%)	72.7 (49.8 to 89.3)	15.0 (3.2 to 37.9)		

Statistical analyses

Statistical analysis title	BIVV009 versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoints were reported and continued when primary endpoint was statistically significant at two-sided 0.05 level.

Comparison groups	BIVV009 v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	15.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.88
upper limit	88.04

Notes:

[1] - Stratified by baseline hemoglobin (< median versus >=median) and geographic region (Asia/Other, North America, and Europe).

[2] - Threshold for significance was 0.05.

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

End point title	Part B: Number of Subjects With Treatment-emergent Adverse Events (AEs) and Serious AEs (SAEs)[3]

End point description:

Adverse Event (AE): any untoward medical occurrence in a subject who received study drug and did not necessarily have to have a causal relationship with the 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 congenital anomaly/birth defect, was medically important event. TEAEs: AEs that developed, worsened or became serious during the treatment-emergent (TE) period (from first

investigational medicinal product [IMP] administration in Part B to last IMP administration + 9 weeks follow-up period). Analysed on 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 separately for each dose (BIVV009 6.5 g and 7.5 g).

End point type	Primary

End point timeframe:

Part B, 6.5 g cohort: From first dose (Week 26) up to 149 weeks of treatment + 9 weeks of follow-up (i.e., up to Week 184); Part B, 7.5 g cohort: From first dose (Week 26) up to 137 weeks of treatment + 9 weeks of follow-up (i.e., up to Week 172)

Notes:

[3] - 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 provided.

End point values	Part B: BIVV009 6.5 g	Part B: BIVV009 7.5 g		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	7		
Units: subjects				
TEAEs	29	7		
TESAEs	6	1		

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 Hemoglobin (Hgb) 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. Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]) and placebo in Part A.

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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: gram per decilitre				
least squares mean (confidence interval 95%)	2.66 (2.09 to 3.22)	0.09 (-0.50 to 0.68)		

Statistical analyses

Statistical analysis title	BIVV009 versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoint were reported and continued when previous endpoint was statistically significant at two-sided 0.05 level.

Comparison groups	BIVV009 v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Mixed model for repeated measures
Parameter estimate	LS Mean Difference
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.75
upper limit	3.38
Variability estimate	Standard error of the mean
Dispersion value	0.408

Notes:

[4] - Threshold of significance at 0.05 level.

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

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

End point description:

Mean change from baseline (Week 0) in total bilirubin 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. 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 of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]) and placebo in Part A.

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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: micromoles per litre				
arithmetic mean (standard deviation)	-22.881 (± 10.401)	-1.388 (± 13.901)		

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 at the Treatment Assessment Timepoint

End point title	Part A: Mean Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale Score at the 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. Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]) and placebo in Part A.

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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: score on a scale				
least squares mean (confidence interval 95%)	10.83 (7.45 to 14.22)	1.91 (-1.65 to 5.46)		

Statistical analyses

Statistical analysis title	BIVV009 versus Placebo

Statistical analysis description:

A hierarchical testing procedure was used to control the overall type I error. Testing was then performed sequentially in order the endpoint were reported and continued when previous endpoint was statistically significant at two-sided 0.05 level.

Comparison groups	BIVV009 v Placebo

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Mixed model for repeated measures
Parameter estimate	LS Mean Difference
Point estimate	8.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	13.85
Variability estimate	Standard error of the mean
Dispersion value	2.45

Notes:

[5] - Threshold of significance at 0.05 level.

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. 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 of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]) and placebo in Part A.

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	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: units per litre				
arithmetic mean (standard deviation)	-150.833 (± 160.824)	7.600 (± 212.690)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With Solicited Symptomatic Anemia at Week 26

End point title	Part A: Percentage of Subjects With Solicited Symptomatic Anemia at Week 26

End point description:

Symptomatic anemia was defined as having following symptoms: i. Fatigue; ii. Weakness; iii. Shortness of breath; iv. Palpitations, fast heart beat; v. Light headedness and/or vi. Chest pain. Percentage of subjects with solicited symptomatic anemia symptoms was 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 of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]) and placebo in Part A.

End point type	Secondary

End point timeframe:

Week 26

End point values	BIVV009	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: percentage of subjects				
number (not applicable)				
Fatigue	31.6	68.4		
Weakness	5.3	31.6		
Shortness of breath	5.3	36.8		
Palpitations	0	15.8		
Light headedness	5.3	15.8		
Chest pain	0	5.3		

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. Early Termination (ET) visit/safety follow up (SFU) visit was 9 weeks after administration of last dose (i.e., up to Week 184). Analysis was performed on Part B-FAS which included all subjects who enrolled in Part B and received at least 1 dose (including partial dose) of study drug (BIVV009). Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, '99999' is used as space filler which denotes that standard deviation (SD) was not estimable since only one subject was available for analysis and "9999 & 99999" denotes no subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), every 2 weeks starting from Week 27 till Week 175 and at ET/SFU visit (i.e., up to Week 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: grams per decilitre				
arithmetic mean (standard deviation)				
Week 27 (n=19,20)	2.647 (± 1.348)	1.125 (± 1.545)		
Week 29 (n=17,18)	2.507 (± 1.669)	1.947 (± 1.467)		
Week 31 (n=18,19)	2.490 (± 1.550)	2.358 (± 1.471)		
Week 33 (n=18,19)	2.519 (± 1.520)	1.987 (± 2.054)		
Week 35 (n=17,19)	2.611 (± 1.522)	1.977 (± 2.010)		
Week 37 (n=18,19)	2.197 (± 1.461)	2.469 (± 1.550)		
Week 39 (n=17,18)	2.528 (± 1.607)	2.368 (± 1.835)		
Week 41 (n=19,19)	2.162 (± 1.636)	2.074 (± 1.825)		
Week 43 (n=17,19)	2.436 (± 1.103)	2.182 (± 1.643)		
Week 45 (n=18,20)	2.644 (± 1.688)	2.249 (± 1.858)		
Week 47 (n=16,19)	2.335 (± 1.108)	2.315 (± 2.129)		
Week 49 (n=16,18)	2.531 (± 1.280)	2.121 (± 1.883)		
Week 51 (n=16,19)	2.349 (± 1.260)	2.394 (± 1.870)		
Week 53 (n=16,18)	2.346 (± 1.182)	2.411 (± 1.786)		
Week 55 (n=17,18)	2.438 (± 1.396)	2.539 (± 1.403)		
Week 57 (n=16,17)	2.531 (± 1.446)	2.250 (± 1.774)		
Week 59 (n=17,17)	2.590 (± 1.397)	2.008 (± 2.615)		
Week 61 (n=17,18)	4.073 (± 6.761)	2.059 (± 1.911)		
Week 63 (n=17,17)	2.382 (± 1.546)	2.102 (± 1.780)		
Week 65 (n=16,17)	2.925 (± 1.447)	2.311 (± 1.986)		
Week 67 (n=17,17)	4.170 (± 6.509)	2.534 (± 2.036)		
Week 69 (n=16,17)	2.777 (± 1.411)	2.505 (± 2.093)		
Week 71 (n=14,15)	2.654 (± 1.495)	2.357 (± 1.758)		
Week 73 (n=15,16)	2.800 (± 2.132)	2.197 (± 1.989)		
Week 75 (n=15,16)	2.391 (± 1.700)	2.175 (± 2.151)		
Week 77 (n=14,16)	3.074 (± 2.088)	2.451 (± 1.878)		
Week 79 (n=13,15)	2.614 (± 1.874)	2.419 (± 2.247)		

Week 81 (n=14,17)	2.598 (± 1.801)	2.458 (± 1.579)		
Week 83 (n=14,13)	2.469 (± 1.777)	2.762 (± 1.539)		
Week 85 (n=12,15)	2.755 (± 1.942)	2.489 (± 1.375)		
Week 87 (n=13,15)	2.477 (± 1.779)	2.765 (± 1.605)		
Week 89 (n=12,13)	2.551 (± 1.835)	2.482 (± 2.004)		
Week 91 (n=11,12)	2.380 (± 2.084)	2.556 (± 1.538)		
Week 93 (n=11,12)	2.931 (± 2.386)	2.655 (± 2.033)		
Week 95 (n=11,12)	2.262 (± 2.014)	2.578 (± 1.970)		
Week 97 (n=11,12)	2.413 (± 2.262)	2.551 (± 1.544)		
Week 99 (n=11,13)	2.019 (± 1.799)	2.412 (± 1.822)		
Week 101 (n=11,12)	2.276 (± 1.986)	2.171 (± 1.852)		
Week 103 (n=11,13)	2.378 (± 2.342)	2.527 (± 1.807)		
Week 105 (n=11,12)	2.291 (± 1.719)	2.321 (± 1.805)		
Week 107 (n=11,13)	2.319 (± 1.511)	2.560 (± 1.858)		
Week 109 (n=11,11)	2.509 (± 1.772)	2.645 (± 1.608)		
Week 111 (n=11,12)	2.416 (± 1.908)	2.750 (± 1.707)		
Week 113 (n=11,12)	2.860 (± 1.832)	2.268 (± 1.497)		
Week 115 (n=10,10)	2.622 (± 1.986)	2.326 (± 1.809)		
Week 117 (n=9,11)	3.135 (± 1.598)	2.474 (± 1.808)		
Week 119 (n=9,10)	3.106 (± 1.493)	2.608 (± 2.045)		
Week 121 (n=9,8)	3.388 (± 1.616)	2.325 (± 2.223)		
Week 123 (n=9,9)	3.255 (± 1.346)	2.878 (± 2.667)		
Week 125 (n=8,7)	3.197 (± 1.366)	1.700 (± 2.684)		
Week 127 (n=7,8)	3.371 (± 1.551)	2.102 (± 3.211)		
Week 129 (n=7,7)	3.171 (± 1.566)	2.129 (± 2.739)		
Week 131 (n=6,6)	3.453 (± 1.823)	1.423 (± 3.184)		
Week 133 (n=5,4)	3.520 (± 1.707)	2.025 (± 1.167)		
Week 135 (n=5,5)	3.611 (± 1.458)	3.048 (± 1.620)		
Week 137 (n=4,3)	4.074 (± 2.392)	2.400 (± 1.808)		
Week 139 (n=5,3)	3.929 (± 1.889)	3.334 (± 2.669)		
Week 141 (n=3,3)	3.500 (± 0.656)	2.733 (± 1.674)		

Week 143 (n=4,3)	3.220 (± 1.064)	2.985 (± 1.904)		
Week 145 (n=2,3)	3.350 (± 0.636)	3.467 (± 2.108)		
Week 147 (n=3,2)	3.202 (± 0.591)	2.300 (± 0.566)		
Week 149 (n=1,2)	2.900 (± 99999)	2.550 (± 0.778)		
Week 151 (n=2,1)	2.961 (± 0.370)	3.000 (± 99999)		
Week 153 (n=1,1)	2.800 (± 99999)	2.800 (± 99999)		
Week 155 (n=1,1)	2.700 (± 99999)	3.600 (± 99999)		
Week 157 (n=1,1)	2.700 (± 99999)	3.000 (± 99999)		
Week 159 (n=1,1)	3.300 (± 99999)	2.300 (± 99999)		
Week 161 (n=1,1)	4.100 (± 99999)	2.400 (± 99999)		
Week 163 (n=1,1)	4.100 (± 99999)	2.600 (± 99999)		
Week 165 (n=1,0)	3.800 (± 99999)	9999 (± 99999)		
Week 167 (n=1,0)	4.700 (± 99999)	9999 (± 99999)		
Week 169 (n=1,0)	4.300 (± 99999)	9999 (± 99999)		
Week 171 (n=1,0)	4.200 (± 99999)	9999 (± 99999)		
Week 173 (n=1,0)	4.000 (± 99999)	9999 (± 99999)		
Week 175 (n=1,0)	2.500 (± 99999)	9999 (± 99999)		
ET/SFU Visit (n=17,18)	0.149 (± 2.073)	0.359 (± 1.872)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change from baseline (Week 0) in total 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 184). 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 of BIVV009 (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 and "9999 & 99999" denotes no subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), every 2 weeks starting from Week 27 till Week 175 and at ET/SFU visit (i.e., up to

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	18		
Units: micromoles per litre				
arithmetic mean (standard deviation)				
Week 27 (n=17,18)	-22.965 (± 9.899)	-18.761 (± 13.353)		
Week 29 (n=16,18)	-20.119 (± 12.170)	-19.889 (± 14.500)		
Week 31 (n=16,17)	-21.675 (± 11.025)	-22.153 (± 14.962)		
Week 33 (n=15,16)	-19.860 (± 11.527)	-24.263 (± 15.169)		
Week 35 (n=15,16)	-20.540 (± 10.557)	-21.888 (± 13.930)		
Week 37 (n=16,15)	-21.350 (± 13.234)	-22.527 (± 16.315)		
Week 39 (n=15,15)	-23.493 (± 11.425)	-21.173 (± 15.901)		
Week 41 (n=16,16)	-18.694 (± 12.189)	-21.138 (± 16.150)		
Week 43 (n=15,16)	-20.593 (± 11.449)	-21.544 (± 16.603)		
Week 45 (n=16,18)	-18.556 (± 11.213)	-20.156 (± 16.757)		
Week 47 (n=14,18)	-20.400 (± 9.803)	-20.250 (± 15.536)		
Week 49 (n=14,17)	-21.450 (± 10.271)	-21.024 (± 13.630)		
Week 51 (n=14,16)	-19.686 (± 11.072)	-19.444 (± 15.942)		
Week 53 (n=15,17)	-19.107 (± 11.267)	-20.335 (± 17.126)		
Week 55 (n=13,16)	-19.354 (± 12.209)	-23.481 (± 12.300)		
Week 57 (n=13,15)	-21.708 (± 10.467)	-18.953 (± 15.825)		
Week 59 (n=14,15)	-19.979 (± 9.706)	-19.820 (± 16.209)		
Week 61 (n=13,15)	-18.254 (± 10.541)	-21.073 (± 17.457)		
Week 63 (n=15,15)	-21.587 (± 9.680)	-21.753 (± 16.663)		
Week 65 (n=14,14)	-20.400 (± 9.866)	-20.950 (± 19.833)		
Week 67 (n=15,14)	-22.680 (± 10.317)	-20.150 (± 20.250)		
Week 69 (n=14,15)	-21.279 (± 9.423)	-17.827 (± 22.194)		
Week 71 (n=12,13)	-19.008 (± 8.255)	-20.585 (± 21.125)		
Week 73 (n=12,15)	-23.058 (± 7.766)	-20.080 (± 17.803)		

Week 75 (n=12,14)	-21.492 (± 7.453)	-20.771 (± 20.261)		
Week 77 (n=12,14)	-23.267 (± 8.972)	-19.814 (± 19.337)		
Week 79 (n=12,15)	-21.125 (± 12.701)	-21.027 (± 19.830)		
Week 81 (n=11,13)	-19.255 (± 9.478)	-22.331 (± 20.117)		
Week 83 (n=12,11)	-16.567 (± 12.565)	-25.091 (± 13.838)		
Week 85 (n=11,13)	-18.045 (± 12.183)	-23.292 (± 12.976)		
Week 87 (n=10,11)	-19.990 (± 12.043)	-21.473 (± 14.444)		
Week 89 (n=10,11)	-17.790 (± 11.036)	-24.782 (± 13.390)		
Week 91 (n=9,11)	-16.944 (± 13.476)	-23.091 (± 14.949)		
Week 93 (n=9,10)	-18.300 (± 11.132)	-24.970 (± 13.852)		
Week 95 (n=8,11)	-18.613 (± 12.265)	-23.564 (± 11.122)		
Week 97 (n=9,9)	-18.656 (± 11.462)	-26.122 (± 11.870)		
Week 99 (n=9,11)	-17.389 (± 10.932)	-23.700 (± 12.919)		
Week 101 (n=9,10)	-18.411 (± 10.175)	-25.940 (± 12.309)		
Week 103 (n=9,11)	-18.178 (± 11.156)	-22.655 (± 11.308)		
Week 105 (n=9,10)	-19.422 (± 8.444)	-26.920 (± 10.996)		
Week 107 (n=9,11)	-18.100 (± 9.955)	-23.018 (± 12.755)		
Week 109 (n=9,9)	-18.456 (± 10.606)	-25.422 (± 14.100)		
Week 111 (n=9,10)	-19.767 (± 9.992)	-24.380 (± 12.298)		
Week 113 (n=9,10)	-19.389 (± 9.192)	-23.940 (± 15.514)		
Week 115 (n=9,9)	-19.622 (± 8.194)	-21.533 (± 14.215)		
Week 117 (n=8,8)	-22.088 (± 10.247)	-22.225 (± 15.256)		
Week 119 (n=8,8)	-20.038 (± 8.529)	-22.713 (± 14.859)		
Week 121 (n=8,6)	-22.063 (± 7.215)	-21.183 (± 10.750)		
Week 123 (n=8,7)	-21.438 (± 8.058)	-22.029 (± 12.421)		
Week 125 (n=7,5)	-20.657 (± 8.889)	-19.560 (± 12.997)		
Week 127 (n=6,6)	-20.550 (± 9.782)	-21.433 (± 15.850)		
Week 129 (n=6,5)	-22.883 (± 11.291)	-19.020 (± 11.749)		
Week 131 (n=5,5)	-19.420 (± 12.936)	-23.100 (± 15.797)		
Week 133 (n=4,4)	-27.600 (± 7.477)	-17.450 (± 16.917)		
Week 135 (n=4,5)	-29.500 (± 7.816)	-21.900 (± 19.552)		

Week 137 (n=3,2)	-28.833 (± 8.615)	-11.650 (± 18.173)		
Week 139 (n=4,3)	-25.800 (± 9.081)	-24.733 (± 17.470)		
Week 141 (n=2,3)	-34.400 (± 2.404)	-13.833 (± 16.669)		
Week 143 (n=3,3)	-26.967 (± 9.235)	-20.033 (± 22.861)		
Week 145 (n=2,3)	-32.900 (± 3.677)	-18.100 (± 27.217)		
Week 147 (n=3,2)	-29.300 (± 7.418)	-3.300 (± 34.083)		
Week 149 (n=1,2)	-31.700 (± 99999)	-7.300 (± 28.284)		
Week 151 (n=2,1)	-21.500 (± 0.566)	0.300 (± 99999)		
Week 153 (n=1,1)	-30.800 (± 99999)	-11.400 (± 99999)		
Week 155 (n=1,1)	-35.300 (± 99999)	0.700 (± 99999)		
Week 157 (n=1,1)	-32.400 (± 99999)	-0.100 (± 99999)		
Week 159 (n=1,1)	-32.500 (± 99999)	4.700 (± 99999)		
Week 161 (n=1,1)	-36.800 (± 99999)	5.500 (± 99999)		
Week 163 (n=1,1)	-37.100 (± 99999)	13.000 (± 99999)		
Week 165 (n=1,0)	-36.300 (± 99999)	9999 (± 99999)		
Week 167 (n=1,0)	-34.300 (± 99999)	9999 (± 99999)		
Week 169 (n=1,0)	-32.700 (± 99999)	9999 (± 99999)		
Week 171 (n=1,0)	-33.100 (± 99999)	9999 (± 99999)		
Week 173 (n=1,0)	-32.100 (± 99999)	9999 (± 99999)		
Week 175 (n=1,0)	-28.400 (± 99999)	9999 (± 99999)		
ET/SFU Visit (n=17,17)	1.976 (± 9.444)	1.165 (± 18.773)		

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 184). 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 of BIVV009 (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 and "9999 & 99999" denotes no 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, 147, 159, 171 and ET Visit/SFU visit (i.e., up to Week 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39 (n=18,18)	11.048 (± 12.333)	7.958 (± 12.003)		
Week 51 (n=15,16)	10.080 (± 11.506)	6.354 (± 9.680)		
Week 63 (n=16,16)	10.672 (± 13.225)	8.499 (± 11.146)		
Week 75 (n=13,14)	9.861 (± 12.953)	10.304 (± 9.722)		
Week 87 (n=13,15)	11.015 (± 13.972)	8.483 (± 11.323)		
Week 99 (n=11,13)	12.109 (± 14.786)	8.788 (± 10.985)		
Week 111 (n=11,12)	11.563 (± 13.411)	10.688 (± 11.768)		
Week 123 (n=9,9)	10.806 (± 13.736)	6.583 (± 16.613)		
Week 135 (n=5,5)	16.683 (± 18.953)	12.650 (± 15.243)		
Week 147 (n=2,2)	9.208 (± 1.120)	0.500 (± 2.121)		
Week 159 (n=1,1)	20.000 (± 99999)	10.000 (± 99999)		
Week 171 (n=1,0)	15.000 (± 99999)	9999 (± 99999)		
ET/SFU Visit (n=19,18)	-1.257 (± 10.399)	-1.551 (± 12.840)		

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 and well-being: physical functioning, role-physical, role emotional, mental health, bodily pain, general health, vitality and social functioning, with each domain score ranged from 0 (poor health) to 100 (better health). Higher scores = good health condition. The 8 domains were further summarised into 2 summary scores, PCS and MCS that 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: 9 weeks after administration of last dose (i.e., up to Week 184). Part B-FAS. Here, 'n' = subjects with available data. Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., either 6.5 g or 7.5 g). '99999'=1 subject thus SD was not estimable & '99999' & '9999' = no 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, 147,159, 171 and ET Visit/SFU visit (i.e., up to Week 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39-PCS (n=18,18)	4.814 (± 8.830)	6.745 (± 11.255)		
Week 39-MCS (n=18,18)	8.543 (± 9.155)	1.151 (± 11.591)		
Week 51-PCS (n=14,16)	5.320 (± 6.913)	5.654 (± 8.527)		
Week 51-MCS (n=14,16)	8.461 (± 6.754)	1.704 (± 8.813)		
Week 63-PCS (n=16,16)	5.840 (± 6.916)	6.216 (± 9.514)		
Week 63-MCS (n=16,16)	8.117 (± 9.955)	1.722 (± 10.175)		
Week 75-PCS (n=12,15)	5.723 (± 7.563)	7.661 (± 10.418)		
Week 75-MCS (n=12,15)	7.932 (± 9.279)	3.519 (± 7.891)		
Week 87-PCS (n=12,15)	5.226 (± 8.196)	8.778 (± 12.405)		
Week 87-MCS (n=12,15)	6.058 (± 10.981)	2.219 (± 9.111)		
Week 99-PCS (n=10,13)	3.945 (± 7.463)	8.262 (± 12.534)		
Week 99-MCS (n=10,13)	7.136 (± 11.850)	4.682 (± 7.698)		
Week 111-PCS (n=10,12)	4.800 (± 7.985)	8.080 (± 12.302)		
Week 111-MCS (n=10,12)	8.705 (± 7.777)	4.411 (± 10.249)		
Week 123-PCS (n=9,9)	4.147 (± 7.110)	7.973 (± 13.200)		
Week 123-MCS (n=9,9)	8.650 (± 8.323)	-2.538 (± 13.136)		
Week 135-PCS (n=5,4)	6.660 (± 9.096)	6.070 (± 13.819)		

Week 135-MCS (n=5,4)	8.860 (± 9.817)	2.790 (± 6.170)		
Week 147-PCS (n=2,2)	-1.655 (± 3.769)	-3.740 (± 1.824)		
Week 147-MCS (n=2,2)	11.220 (± 6.095)	-1.110 (± 0.679)		
Week 159-PCS (n=1,1)	5.620 (± 99999)	-10.410 (± 99999)		
Week 159-MCS (n=1,1)	16.400 (± 99999)	9.590 (± 99999)		
Week 171-PCS (n=1,0)	11.980 (± 99999)	9999 (± 99999)		
Week 171-MCS (n=1,0)	0.250 (± 99999)	9999 (± 99999)		
ET/SFU Visit-PCS (n=18,18)	-3.478 (± 10.875)	-0.429 (± 10.922)		
ET/SFU Visit-MCS (n=18,18)	1.835 (± 11.882)	-2.137 (± 10.148)		

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 included 2 components: health state utility index (descriptive system) & 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 184). Part B FAS. Data was planned to be collected & analysed for combined population of BIVV009(6.5g or 7.5g). 'n'=subjects with available data. '99999'=only 1 subject SD was not estimable and 9999 and 99999=no subject 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 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 39 - Index score (n=17,18)	0.020 (± 0.165)	0.054 (± 0.135)		

Week 51 - Index score (n=15,16)	0.075 (± 0.173)	-0.008 (± 0.197)		
Week 63 - Index score (n=16,16)	0.060 (± 0.214)	0.015 (± 0.157)		
Week 75 - Index score (n=13,15)	-0.004 (± 0.144)	0.063 (± 0.152)		
Week 87 - Index score (n=13,15)	-0.034 (± 0.240)	0.059 (± 0.158)		
Week 99 - Index score (n=11,13)	-0.058 (± 0.216)	0.058 (± 0.146)		
Week 111 - Index score (n=11,12)	-0.033 (± 0.205)	0.050 (± 0.194)		
Week 123- Index score (n=9,9)	-0.020 (± 0.235)	0.031 (± 0.221)		
Week 135- Index score (n=5,5)	0.008 (± 0.351)	0.094 (± 0.245)		
Week 147- Index score (n=2,2)	0.054 (± 0.037)	-0.087 (± 0.222)		
Week 159- Index score (n=1,1)	0.174 (± 99999)	0.087 (± 99999)		
Week 171- Index score (n=1,0)	0.053 (± 99999)	-9999 (± 99999)		
ET/SFU - Index score (n=19,18)	-0.108 (± 0.238)	-0.077 (± 0.169)		
Week 39 - VAS score (n=17,18)	20.647 (± 16.871)	12.000 (± 17.146)		
Week 51 - VAS score (n=15,16)	14.800 (± 27.589)	9.125 (± 21.112)		
Week 63 - VAS score (n=15,16)	19.867 (± 21.603)	14.375 (± 15.573)		
Week 75 - VAS score (n=13,15)	16.846 (± 22.120)	18.933 (± 20.243)		
Week 87 - VAS score (n=13,15)	14.077 (± 25.221)	16.867 (± 17.912)		
Week 99 - VAS score (n=11,13)	19.364 (± 20.796)	18.385 (± 20.706)		
Week 111 - VAS score (n=11,12)	18.273 (± 19.463)	22.833 (± 20.621)		
Week 123- VAS score (n=9,9)	21.667 (± 18.371)	18.000 (± 30.389)		
Week 135- VAS score (n=5,5)	26.000 (± 20.433)	23.400 (± 27.574)		
Week 147- VAS score (n=2,2)	17.500 (± 17.678)	3.500 (± 26.163)		
Week 159- VAS score (n=1,1)	40.000 (± 99999)	27.000 (± 99999)		
Week 171- VAS score (n=1,0)	35.000 (± 99999)	-9999 (± 99999)		
ET/SFU - VAS score (n=19,18)	1.526 (± 17.976)	-2.056 (± 14.957)		

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 184). Data for this endpoint was planned to be collected and analysed for combined population of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, n=0 denotes no subject was available for analysis.

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 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: subjects				
Week 39 - None (n=17,17)	7	5		
Week 39 - Mild (n=17,17)	8	7		
Week 39 - Moderate (n=17,17)	1	5		
Week 39 - Severe (n=17,17)	1	0		
Week 39 - Very Severe (n=17,17)	0	0		
Week 51 - None (n=15,16)	5	4		
Week 51 - Mild (n=15,16)	8	7		
Week 51 - Moderate (n=15,16)	2	5		
Week 51 - Severe (n=15,16)	0	0		
Week 51 - Very Severe (n=15,16)	0	0		
Week 63 - None (n=17,16)	6	4		
Week 63 - Mild (n=17,16)	8	7		
Week 63 - Moderate (n=17,16)	3	5		
Week 63 - Severe (n=17,16)	0	0		
Week 63 - Very Severe (n=17,16)	0	0		
Week 75 - None (n=13,15)	5	6		
Week 75 - Mild (n=13,15)	6	6		
Week 75 - Moderate (n=13,15)	2	3		
Week 75 - Severe (n=13,15)	0	0		
Week 75 - Very Severe (n=13,15)	0	0		
Week 87 - None (n=13,15)	6	7		
Week 87 - Mild (n=13,15)	5	4		
Week 87 - Moderate (n=13,15)	1	3		
Week 87 - Severe (n=13,15)	1	1		
Week 87 - Very Severe (n=13,15)	0	0		
Week 99 - None (n=11,13)	5	8		
Week 99 - Mild (n=11,13)	5	3		
Week 99 - Moderate (n=11,13)	1	2		
Week 99 - Severe (n=11,13)	0	0		
Week 99 - Very Severe (n=11,13)	0	0		

Week 111 - None (n=11,12)	5	7		
Week 111 - Mild (n=11,12)	4	3		
Week 111 - Moderate (n=11,12)	2	2		
Week 111 - Severe (n=11,12)	0	0		
Week 111 - Very Severe (n=11,12)	0	0		
Week 123 - None (n=9,9)	2	5		
Week 123 - Mild (n=9,9)	6	2		
Week 123 - Moderate (n=9,9)	1	2		
Week 123 - Severe (n=9,9)	0	0		
Week 123 - Very Severe (n=9,9)	0	0		
Week 135 - None (n=5,5)	0	2		
Week 135 - Mild (n=5,5)	3	1		
Week 135 - Moderate (n=5,5)	2	2		
Week 135 - Severe (n=5,5)	0	0		
Week 135 - Very Severe (n=5,5)	0	0		
Week 147 - None (n=2,2)	0	1		
Week 147 - Mild (n=2,2)	1	0		
Week 147 - Moderate (n=2,2)	1	1		
Week 147 - Severe (n=2,2)	0	0		
Week 147 - Very Severe (n=2,2)	0	0		
Week 159 - None (n=1,1)	0	0		
Week 159 - Mild (n=1,1)	0	0		
Week 159 - Moderate (n=1,1)	1	1		
Week 159 - Severe (n=1,1)	0	0		
Week 159 - Very Severe (n=1,1)	0	0		
Week 171 - None (n=1,0)	0	0		
Week 171 - Mild (n=1,0)	1	0		
Week 171 - Moderate (n=1,0)	0	0		
Week 171 - Severe (n=1,0)	0	0		
Week 171 - Very Severe (n=1,0)	0	0		
ET/SFU - None (n=19,18)	2	4		
ET/SFU - Mild (n=19,18)	5	3		
ET/SFU - Moderate (n=19,18)	7	5		
ET/SFU - Severe (n=19,18)	3	5		
ET/SFU - Very Severe (n=19,18)	2	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 184). 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 of BIVV009 (i.e., all subjects who received BIVV009 [either 6.5 g or 7.5 g]). Here, n=0 denotes no subject was available for analysis.

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 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: subjects				
Week 39 - Very much improved (n=17,16)	4	3		
Week 39 - Much improved (n=17,16)	8	6		
Week 39 - Minimally improved (n=17,16)	2	6		
Week 39 - No Change (n=17,16)	2	1		
Week 39 - Minimally worse (n=17,16)	1	0		
Week 39 - Much worse (n=17,16)	0	0		
Week 39 - Very much worse (n=17,16)	0	0		
Week 51 - Very much improved (n=15,16)	5	3		
Week 51 - Much improved (n=15,16)	3	6		
Week 51 - Minimally improved (n=15,16)	2	4		
Week 51 - No Change (n=15,16)	5	2		
Week 51 - Minimally worse (n=15,16)	0	0		
Week 51 - Much worse (n=15,16)	0	1		
Week 51 - Very much worse (n=15,16)	0	0		
Week 63 - Very much improved (n=17,16)	5	3		
Week 63 - Much improved (n=17,16)	8	4		
Week 63 - Minimally improved (n=17,16)	0	5		
Week 63 - No change (n=17,16)	4	3		
Week 63 - Minimally worse (n=17,16)	0	0		
Week 63 - Much worse (n=17,16)	0	1		
Week 63 - Very much worse (n=17,16)	0	0		
Week 75 - Very much improved (n=13,15)	6	6		
Week 75 - Much improved (n=13,15)	2	3		
Week 75 - Minimally improved (n=13,15)	1	5		
Week 75 - No Change (n=13,15)	4	1		
Week 75 - Minimally worse (n=13,15)	0	0		
Week 75 - Much worse (n=13,15)	0	0		
Week 75 - Very much worse (n=13,15)	0	0		
Week 87 - Very much improved (n=13,15)	7	7		
Week 87 - Much improved (n=13,15)	0	3		

Week 87 - Minimally improved (n=13,15)	2	1		
Week 87 - No Change (n=13,15)	2	3		
Week 87 - Minimally worse (n=13,15)	1	1		
Week 87 - Much worse (n=13,15)	1	0		
Week 87 - Very much worse (n=13,15)	0	0		
Week 99 - Very much improved (n=11,13)	3	8		
Week 99 - Much improved (n=11,13)	3	2		
Week 99 - Minimally improved (n=11,13)	1	3		
Week 99 - No change (n=11,13)	3	0		
Week 99 - Minimally worse (n=11,13)	1	0		
Week 99 - Much worse (n=11,13)	0	0		
Week 99 - Very much worse (n=11,13)	0	0		
Week 111 - Very much improved (n=11,12)	3	6		
Week 111 - Much improved (n=11,12)	5	4		
Week 111 - Minimally improved (n=11,12)	1	1		
Week 111 - No Change (n=11,12)	2	1		
Week 111 - Minimally worse (n=11,12)	0	0		
Week 111 - Much worse (n=11,12)	0	0		
Week 111 - Very much worse (n=11,12)	0	0		
Week 123 - Very much improved (n=9,9)	3	4		
Week 123 - Much improved (n=9,9)	3	3		
Week 123 - Minimally improved (n=9,9)	2	1		
Week 123 - No Change (n=9,9)	1	1		
Week 123 - Minimally worse (n=9,9)	0	0		
Week 123 - Much worse (n=9,9)	0	0		
Week 123 - Very much worse (n=9,9)	0	0		
Week 135 - Very much improved (n=5,5)	2	2		
Week 135 - Much improved (n=5,5)	2	1		
Week 135 - Minimally improved (n=5,5)	0	1		
Week 135 - No Change (n=5,5)	0	1		
Week 135 - Minimally worse (n=5,5)	1	0		
Week 135 - Much worse (n=5,5)	0	0		
Week 135 - Very much worse (n=5,5)	0	0		
Week 147 - Very much improved (n=2,2)	1	0		
Week 147 - Much improved (n=2,2)	0	1		
Week 147 - Minimally improved (n=2,2)	0	1		
Week 147 - No Change (n=2,2)	1	0		
Week 147 - Minimally worse (n=2,2)	0	0		
Week 147 - Much worse (n=2,2)	0	0		
Week 147 - Very much worse (n=2,2)	0	0		
Week 159 - Very much improved (n=1,1)	1	0		
Week 159 - Much improved (n=1,1)	0	0		
Week 159 - Minimally improved (n=1,1)	0	1		
Week 159 - No Change (n=1,1)	0	0		
Week 159 - Minimally worse (n=1,1)	0	0		
Week 159 - Much worse (n=1,1)	0	0		

Week 159 - Very much worse (n=1,1)	0	0		
Week 171- Very much improved (n=1,0)	1	0		
Week 171- Much improved (n=1,0)	0	0		
Week 171- Minimally improved (n=1,0)	0	0		
Week 171- No Change (n=1,0)	0	0		
Week 171- Minimally worse (n=1,0)	0	0		
Week 171- Much worse (n=1,0)	0	0		
Week 171- Very much worse (n=1,0)	0	0		
ET/SFU Visit- Very much improved (n=19,18)	3	3		
ET/SFU Visit- Much improved (n=19,18)	5	6		
ET/SFU Visit- Minimally improved (n=19,18)	4	1		
ET/SFU Visit- No Change (n=19,18)	3	3		
ET/SFU Visit- Minimally worse (n=19,18)	1	2		
ET/SFU Visit- Much worse (n=19,18)	3	3		
ET/SFU Visit- Very much worse (n=19,18)	0	0		

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 is reported in this endpoint. Baseline was defined as 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 184). Analysed 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 of BIVV009 (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 and "9999 & 99999" denotes no subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), every 2 weeks starting from Week 27 till Week 175 and at ET/SFU visit (i.e., up to Week 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: units per litre				
arithmetic mean (standard deviation)				
Week 27 (n=19,20)	-151.000 (± 184.640)	0.650 (± 208.051)		

Week 29 (n=18,19)	-115.944 (± 226.913)	11.000 (± 222.383)		
Week 31 (n=18,17)	-85.111 (± 247.506)	38.882 (± 211.386)		
Week 33 (n=17,16)	-66.176 (± 324.145)	4.813 (± 203.939)		
Week 35 (n=18,16)	-64.667 (± 261.431)	-19.313 (± 142.989)		
Week 37 (n=16,17)	4.438 (± 398.843)	25.765 (± 219.679)		
Week 39 (n=16,16)	-88.500 (± 271.941)	27.313 (± 210.705)		
Week 41 (n=18,17)	23.778 (± 342.195)	-6.000 (± 173.810)		
Week 43 (n=17,17)	-22.118 (± 310.381)	-21.706 (± 181.668)		
Week 45 (n=17,18)	26.529 (± 329.717)	-13.500 (± 190.460)		
Week 47 (n=15,18)	-22.600 (± 302.511)	-24.944 (± 153.580)		
Week 49 (n=16,18)	-29.250 (± 289.392)	15.722 (± 193.630)		
Week 51 (n=16,18)	-12.563 (± 290.489)	-9.556 (± 155.646)		
Week 53 (n=16,17)	-16.938 (± 299.788)	12.529 (± 206.642)		
Week 55 (n=14,16)	-89.500 (± 219.634)	-11.250 (± 177.647)		
Week 57 (n=15,16)	-78.200 (± 285.140)	64.188 (± 266.395)		
Week 59 (n=16,17)	-84.438 (± 220.376)	31.647 (± 226.128)		
Week 61 (n=17,17)	-74.353 (± 215.414)	20.588 (± 263.984)		
Week 63 (n=17,17)	-98.235 (± 185.259)	38.059 (± 325.329)		
Week 65 (n=16,15)	-97.438 (± 212.335)	-16.467 (± 246.765)		
Week 67 (n=17,15)	-127.824 (± 192.148)	29.667 (± 269.918)		
Week 69 (n=16,16)	-113.625 (± 197.270)	36.563 (± 303.550)		
Week 71 (n=13,15)	-101.692 (± 320.348)	4.067 (± 307.924)		
Week 73 (n=14,16)	-174.500 (± 177.153)	7.063 (± 245.723)		
Week 75 (n=14,15)	-157.429 (± 184.525)	7.067 (± 285.183)		
Week 77 (n=14,15)	-142.857 (± 199.169)	-24.867 (± 291.754)		
Week 79 (n=13,16)	-98.077 (± 271.632)	-20.063 (± 265.761)		
Week 81 (n=13,15)	-127.846 (± 233.663)	7.200 (± 219.952)		
Week 83 (n=13,11)	-59.000 (± 346.917)	8.818 (± 250.068)		
Week 85 (n=13,15)	-72.000 (± 350.021)	28.400 (± 282.626)		
Week 87 (n=13,13)	-101.385 (± 285.590)	83.385 (± 288.731)		
Week 89 (n=12,12)	-78.667 (± 351.059)	10.833 (± 323.647)		

Week 91 (n=9,13)	-143.000 (± 273.540)	0.846 (± 288.451)		
Week 93 (n=10,11)	-133.500 (± 254.332)	10.818 (± 268.308)		
Week 95 (n=11,13)	-59.364 (± 368.708)	18.231 (± 241.354)		
Week 97 (n=11,10)	-53.364 (± 343.820)	-38.500 (± 188.403)		
Week 99 (n=11,12)	-80.909 (± 312.405)	-12.917 (± 183.844)		
Week 101 (n=11,11)	-90.273 (± 293.680)	-17.182 (± 249.134)		
Week 103 (n=11,13)	-50.273 (± 331.072)	5.692 (± 211.233)		
Week 105 (n=11,12)	-96.455 (± 276.907)	-34.250 (± 147.738)		
Week 107 (n=11,13)	-28.091 (± 354.244)	20.769 (± 222.772)		
Week 109 (n=11,11)	-50.727 (± 335.078)	-2.000 (± 243.243)		
Week 111 (n=10,12)	-83.000 (± 303.258)	-5.583 (± 219.850)		
Week 113 (n=10,12)	-80.700 (± 319.283)	0.667 (± 294.904)		
Week 115 (n=10,10)	-109.500 (± 256.395)	44.700 (± 295.946)		
Week 117 (n=9,10)	-140.444 (± 280.944)	12.700 (± 254.786)		
Week 119 (n=9,10)	-149.556 (± 237.771)	-26.500 (± 274.168)		
Week 121 (n=9,8)	-195.778 (± 225.978)	-42.375 (± 211.840)		
Week 123 (n=9,9)	-185.000 (± 231.489)	22.222 (± 278.037)		
Week 125 (n=7,7)	-99.429 (± 285.513)	-85.143 (± 265.374)		
Week 127 (n=7,8)	-154.714 (± 231.922)	-28.875 (± 312.483)		
Week 129 (n=7,7)	-136.429 (± 234.954)	-18.571 (± 354.584)		
Week 131 (n=6,6)	-120.833 (± 300.454)	-2.000 (± 270.245)		
Week 133 (n=5,4)	-179.000 (± 298.811)	-47.500 (± 367.639)		
Week 135 (n=5,5)	-211.800 (± 265.438)	58.000 (± 449.233)		
Week 137 (n=4,2)	-252.500 (± 264.591)	46.500 (± 768.625)		
Week 139 (n=5,3)	-181.800 (± 284.966)	-48.667 (± 373.339)		
Week 141 (n=3,3)	-259.667 (± 362.136)	30.667 (± 372.889)		
Week 143 (n=4,2)	-160.250 (± 357.021)	-7.500 (± 21.920)		
Week 145 (n=2,2)	-340.500 (± 458.912)	290.000 (± 562.857)		
Week 147 (n=3,2)	-248.667 (± 355.136)	311.000 (± 547.301)		
Week 149 (n=1,2)	-78.000 (± 99999)	116.000 (± 175.362)		
Week 151 (n=2,1)	58.000 (± 32.527)	295.000 (± 99999)		

Week 153 (n=1,1)	7.000 (± 99999)	75.000 (± 99999)		
Week 155 (n=1,0)	-50.000 (± 99999)	9999 (± 99999)		
Week 157 (n=1,1)	-50.000 (± 99999)	369.000 (± 99999)		
Week 159 (n=1,1)	-155.000 (± 99999)	365.000 (± 99999)		
Week 161 (n=1,0)	-175.000 (± 99999)	9999 (± 99999)		
Week 163 (n=1,1)	-149.000 (± 99999)	782.000 (± 99999)		
Week 165 (n=1,0)	-155.000 (± 99999)	9999 (± 99999)		
Week 167 (n=1,0)	-162.000 (± 99999)	9999 (± 99999)		
Week 169 (n=1,0)	-180.000 (± 99999)	9999 (± 99999)		
Week 171 (n=1,0)	-167.000 (± 99999)	9999 (± 99999)		
Week 173 (n=1,0)	-171.000 (± 99999)	9999 (± 99999)		
Week 175 (n=1,0)	-121.000 (± 99999)	9999 (± 99999)		
ET/SFU Visit (n=16,17)	-2.500 (± 195.967)	-11.706 (± 206.321)		

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 of BIVV009 (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/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: blood transfusions per subject				
arithmetic mean (standard deviation)	0.4 (± 0.8)	0.3 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Part B: Mean 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 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 184). Haptoglobin values <0.2 were imputed as 0.2. 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 of BIVV009 (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 SD was not estimable since only one subject was available for analysis and "9999 & 99999" denotes no subject was available for analysis.

End point type	Secondary

End point timeframe:

Baseline (Week 0), every 2 weeks starting from Week 27 till Week 175 and at ET/SFU visit (i.e., up to Week 184)

End point values	BIVV009/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: grams per litre				
arithmetic mean (standard deviation)				
Week 27 (n=19,19)	0.219 (± 0.380)	0.082 (± 0.197)		
Week 29 (n=18,20)	0.240 (± 0.317)	0.182 (± 0.482)		
Week 31 (n=19,20)	0.183 (± 0.311)	0.256 (± 0.516)		
Week 33 (n=19,17)	0.212 (± 0.423)	0.229 (± 0.379)		
Week 35 (n=18,19)	0.207 (± 0.355)	0.151 (± 0.280)		
Week 37 (n=18,18)	0.232 (± 0.419)	0.187 (± 0.291)		
Week 39 (n=16,16)	0.213 (± 0.330)	0.165 (± 0.295)		
Week 41 (n=19,18)	0.119 (± 0.238)	0.082 (± 0.168)		
Week 43 (n=18,18)	0.100 (± 0.224)	0.161 (± 0.234)		
Week 45 (n=18,20)	0.114 (± 0.205)	0.189 (± 0.275)		

Week 47 (n=15,20)	0.135 (± 0.243)	0.255 (± 0.416)		
Week 49 (n=16,18)	0.139 (± 0.205)	0.172 (± 0.345)		
Week 51 (n=15,17)	0.083 (± 0.197)	0.207 (± 0.369)		
Week 53 (n=16,19)	0.045 (± 0.137)	0.122 (± 0.296)		
Week 55 (n=17,18)	0.149 (± 0.251)	0.179 (± 0.343)		
Week 57 (n=16,17)	0.158 (± 0.234)	0.158 (± 0.362)		
Week 59 (n=17,17)	0.132 (± 0.229)	0.131 (± 0.306)		
Week 61 (n=17,18)	0.153 (± 0.286)	0.184 (± 0.350)		
Week 63 (n=17,17)	0.202 (± 0.265)	0.177 (± 0.357)		
Week 65 (n=16,16)	0.101 (± 0.232)	0.198 (± 0.384)		
Week 67 (n=17,16)	0.178 (± 0.241)	0.162 (± 0.363)		
Week 69 (n=16,17)	0.168 (± 0.255)	0.169 (± 0.348)		
Week 71 (n=14,15)	0.220 (± 0.288)	0.236 (± 0.388)		
Week 73 (n=14,16)	0.261 (± 0.335)	0.174 (± 0.348)		
Week 75 (n=15,16)	0.275 (± 0.321)	0.197 (± 0.362)		
Week 77 (n=14,16)	0.249 (± 0.374)	0.232 (± 0.398)		
Week 79 (n=14,16)	0.299 (± 0.419)	0.290 (± 0.464)		
Week 81 (n=13,16)	0.438 (± 0.463)	0.207 (± 0.421)		
Week 83 (n=14,13)	0.297 (± 0.379)	0.233 (± 0.394)		
Week 85 (n=13,15)	0.374 (± 0.374)	0.266 (± 0.426)		
Week 87 (n=12,13)	0.334 (± 0.409)	0.344 (± 0.471)		
Week 89 (n=12,13)	0.348 (± 0.482)	0.198 (± 0.351)		
Week 91 (n=11,12)	0.313 (± 0.449)	0.279 (± 0.449)		
Week 93 (n=11,12)	0.262 (± 0.383)	0.178 (± 0.373)		
Week 95 (n=11,13)	0.263 (± 0.495)	0.198 (± 0.414)		
Week 97 (n=11,12)	0.245 (± 0.306)	0.210 (± 0.407)		
Week 99 (n=11,13)	0.266 (± 0.351)	0.213 (± 0.370)		
Week 101 (n=11,12)	0.289 (± 0.289)	0.207 (± 0.417)		
Week 103 (n=11,13)	0.219 (± 0.291)	0.212 (± 0.389)		
Week 105 (n=11,12)	0.216 (± 0.291)	0.174 (± 0.399)		
Week 107 (n=11,13)	0.182 (± 0.273)	0.245 (± 0.459)		

Week 109 (n=10,11)	0.207 (± 0.311)	0.254 (± 0.507)		
Week 111 (n=11,12)	0.282 (± 0.556)	0.263 (± 0.459)		
Week 113 (n=11,12)	0.248 (± 0.366)	0.335 (± 0.614)		
Week 115 (n=10,11)	0.324 (± 0.413)	0.165 (± 0.432)		
Week 117 (n=9,10)	0.450 (± 0.492)	0.181 (± 0.489)		
Week 119 (n=9,10)	0.348 (± 0.400)	0.187 (± 0.404)		
Week 121 (n=9,8)	0.459 (± 0.414)	0.174 (± 0.479)		
Week 123 (n=9,9)	0.350 (± 0.375)	0.192 (± 0.512)		
Week 125 (n=8,7)	0.303 (± 0.425)	0.114 (± 0.298)		
Week 127 (n=7,8)	0.309 (± 0.401)	0.220 (± 0.420)		
Week 129 (n=7,7)	0.393 (± 0.506)	0.191 (± 0.506)		
Week 131 (n=6,5)	0.480 (± 0.529)	0.222 (± 0.430)		
Week 133 (n=5,4)	0.342 (± 0.469)	0.125 (± 0.155)		
Week 135 (n=5,5)	0.454 (± 0.643)	0.280 (± 0.425)		
Week 137 (n=4,3)	0.545 (± 0.631)	0.070 (± 0.121)		
Week 139 (n=5,3)	0.494 (± 0.676)	0.293 (± 0.508)		
Week 141 (n=3,2)	0.667 (± 0.583)	0.025 (± 0.035)		
Week 143 (n=4,3)	0.513 (± 0.604)	0.270 (± 0.292)		
Week 145 (n=2,3)	0.580 (± 0.820)	0.130 (± 0.141)		
Week 147 (n=3,2)	0.400 (± 0.592)	0.195 (± 0.276)		
Week 149 (n=1,2)	0.000 (± 99999)	0.000 (± 0.000)		
Week 151 (n=2,1)	0.000 (± 0.000)	0.000 (± 99999)		
Week 153 (n=1,1)	0.000 (± 99999)	0.000 (± 99999)		
Week 155 (n=1,1)	0.000 (± 99999)	0.000 (± 99999)		
Week 157 (n=1,1)	0.000 (± 99999)	0.000 (± 99999)		
Week 159 (n=1,1)	0.000 (± 99999)	0.000 (± 99999)		
Week 161 (n=1,1)	0.180 (± 99999)	0.000 (± 99999)		
Week 163 (n=1,1)	0.000 (± 99999)	0.000 (± 99999)		
Week 165 (n=1,0)	0.000 (± 99999)	9999 (± 99999)		
Week 167 (n=1,0)	0.000 (± 99999)	9999 (± 99999)		
Week 169 (n=1,0)	0.000 (± 99999)	99999 (± 99999)		

Week 171 (n=1,0)	0.000 (± 99999)	9999 (± 99999)		
Week 173 (n=1,0)	0.000 (± 99999)	9999 (± 99999)		
Week 175 (n=1,0)	0.000 (± 99999)	9999 (± 99999)		
ET/SFU Visit (n=19,18)	0.055 (± 0.200)	0.181 (± 0.426)		

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 of BIVV009 (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/BIVV009	Placebo/BIVV009		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: visits				
number (not applicable)				
Non-study healthcare resource utilisation visits	13	12		
Hospitalisation	3	1		
Visit to a hospital emergency room	1	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A:first dose (Day 0) up to Week 25; Part B 6.5 g cohort:first dose (Week 26) up to 149 weeks of treatment+9 weeks of follow-up (up to Week 184); Part B, 7.5 g cohort:first dose (Week 26) up to 137 weeks of treatment+9 weeks follow up (up to Week 172)

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 and without a recent history of blood transfusion during the last 6 months prior to enrollment 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 and without a recent history of blood transfusion during the last 6 months prior to enrollment 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 A: Placebo

Reporting group description:

Subjects with primary CAD and without a recent history of blood transfusion during the last 6 months prior to enrollment in this study, received an IV infusion of placebo matched to BIVV009 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) were eligible to be enrolled in Part B where they were treated for up to an additional 149 weeks. Subjects who received placebo in Part A received BIVV009 6.5 g on Week 26, Week 27 and every 2 weeks thereafter; subjects who received BIVV009 6.5 g in Part A received placebo on Week 26, BIVV009 6.5 g on Week 27 and every 2 weeks thereafter for up to an additional 149 weeks.

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) were eligible to be enrolled in Part B where they were treated for up to an additional 137 weeks. Subjects who received placebo in Part A received BIVV009 7.5 g on Week 26, Week 27 and every 2 weeks thereafter; subjects who received BIVV009 7.5 g in Part A received placebo on Week 26, BIVV009 7.5 g on Week 27 and every 2 weeks thereafter for up to an additional 137 weeks.

Serious adverse events	Part A: BIVV009 6.5 g	Part A: BIVV009 7.5 g	Part A: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	1 / 5 (20.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events			
Investigations			
Blood Immunoglobulin M Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous Cell Carcinoma Of Lung			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Injury, poisoning and procedural complications			
Hip Fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Muscle Strain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Congenital, familial and genetic disorders			
Polycystic Liver Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Raynaud's Phenomenon			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (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

Nervous system disorders			
Cerebral Venous Sinus Thrombosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Musculoskeletal and connective tissue disorders			
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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
Infections and infestations			
Febrile Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (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			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (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

Serious adverse events	Part B: BIVV009 6.5 g	Part B: BIVV009 7.5 g	

Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 32 (18.75%)	1 / 7 (14.29%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Investigations			
Blood Immunoglobulin M Increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous Cell Carcinoma Of Lung			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Hip Fracture			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Strain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Polycystic Liver Disease			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Raynaud's Phenomenon			

subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral Venous Sinus Thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Febrile Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			

subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	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 A: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	5 / 5 (100.00%)	3 / 20 (15.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Melanocytic Naevus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Cyanosis			
subjects affected / exposed	4 / 17 (23.53%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	10	0	0
Extremity Necrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	4 / 17 (23.53%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	7	1	0
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Orthostatic Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Poor Venous Access			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Raynaud's Phenomenon			
subjects affected / exposed	3 / 17 (17.65%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	4	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Catheter Site Dryness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest Discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
General Physical Health Deterioration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza Like Illness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Injection Site Erythema			

subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injection Site Pruritus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vaccination Site Erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vaccination Site Pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Vaccination Site Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Breast Calcifications			

subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Breast Cyst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cervical Dysplasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	2 / 5 (40.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Depressed Mood			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Product issues			
Device Kink			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Investigations			

Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood Immunoglobulin M Increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Blood Pressure Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood Urine Present			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Transaminases Increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
White Blood Cell Count Decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Face Injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Fibula Fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Infusion Related Reaction			

subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Skin Laceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Tooth Fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vaccination Complication			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 17 (23.53%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	7	1	0
Memory Impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Parkinsonism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Phantom Limb Syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 5 (40.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Blood Loss Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haemolysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Visual Acuity Reduced			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			

subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Angular Cheilitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Colitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Dental Caries			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	4	0
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Faeces Discoloured			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Odynophagia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Paraesthesia Oral			

subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Tongue Ulceration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Biliary Colic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dry Skin			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Night Sweats			

subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Rash			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Skin Discolouration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Skin Lesion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Toxic Skin Eruption			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Renal Cyst			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 5 (20.00%)	1 / 20 (5.00%)
occurrences (all)	2	1	1
Back Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Bone Swelling			

subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Neck Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain In Jaw			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Anal Abscess			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes Zoster			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Mastoiditis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	2 / 5 (40.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Oral Candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	3 / 17 (17.65%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Skin Candida			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Staphylococcal Skin Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Tooth Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulval Abscess			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Diabetes Mellitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Iron Deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part B: BIVV009 6.5 g	Part B: BIVV009 7.5 g	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 32 (87.50%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Melanocytic Naevus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Cyanosis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 7 (28.57%)	
occurrences (all)	2	3	
Extremity Necrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flushing			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Haematoma			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	5 / 32 (15.63%)	2 / 7 (28.57%)	
occurrences (all)	7	3	
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Orthostatic Hypotension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Poor Venous Access			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Raynaud's Phenomenon			
subjects affected / exposed	3 / 32 (9.38%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 32 (12.50%)	2 / 7 (28.57%)	
occurrences (all)	6	2	
Catheter Site Dryness			

subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Chest Discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Chest Pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	7 / 32 (21.88%)	5 / 7 (71.43%)	
occurrences (all)	7	10	
General Physical Health Deterioration			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Influenza Like Illness			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Injection Site Erythema			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Injection Site Pruritus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Oedema Peripheral			
subjects affected / exposed	2 / 32 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Pyrexia			

subjects affected / exposed	5 / 32 (15.63%)	1 / 7 (14.29%)	
occurrences (all)	6	1	
Vaccination Site Erythema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vaccination Site Pain			
subjects affected / exposed	2 / 32 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Vaccination Site Rash			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Breast Calcifications			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Breast Cyst			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Cervical Dysplasia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	2 / 32 (6.25%)	3 / 7 (42.86%)	
occurrences (all)	2	4	
Epistaxis			

subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal Pain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Depressed Mood			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	4 / 32 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	8	0	
Product issues			
Device Kink			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	2	
Blood Immunoglobulin M Increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood Pressure Increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Blood Urine Present			

subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Transaminases Increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Face Injury			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	4 / 32 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	5	3	
Fibula Fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infusion Related Reaction			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin Laceration			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Sunburn			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tooth Fracture			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Vaccination Complication			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Wound			

subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 32 (3.13%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Tachycardia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 32 (9.38%)	2 / 7 (28.57%)	
occurrences (all)	3	2	
Headache			
subjects affected / exposed	4 / 32 (12.50%)	2 / 7 (28.57%)	
occurrences (all)	9	5	
Memory Impairment			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Parkinsonism			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Phantom Limb Syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 32 (28.13%)	2 / 7 (28.57%)	
occurrences (all)	11	3	
Blood Loss Anaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haemolysis			

subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Iron Deficiency Anaemia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Leukocytosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Visual Acuity Reduced			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 32 (9.38%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Abdominal Pain Upper			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Angular Cheilitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Colitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Dental Caries			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Diarrhoea			

subjects affected / exposed	6 / 32 (18.75%)	1 / 7 (14.29%)	
occurrences (all)	13	1	
Dyspepsia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Faeces Discoloured			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Glossodynia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	3 / 32 (9.38%)	2 / 7 (28.57%)	
occurrences (all)	3	2	
Odynophagia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Paraesthesia Oral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tongue Ulceration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Biliary Colic			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Cholelithiasis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dry Skin			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Erythema			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Night Sweats			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin Discolouration			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin Lesion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Toxic Skin Eruption			

subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haemoglobinuria			
subjects affected / exposed	3 / 32 (9.38%)	2 / 7 (28.57%)	
occurrences (all)	3	2	
Renal Cyst			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 32 (18.75%)	2 / 7 (28.57%)	
occurrences (all)	7	2	
Back Pain			
subjects affected / exposed	2 / 32 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Bone Swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Muscle Spasms			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Myalgia			

subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Neck Pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Pain In Extremity			
subjects affected / exposed	2 / 32 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Pain In Jaw			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Anal Abscess			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 7 (28.57%)	
occurrences (all)	2	2	
Diverticulitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis			
subjects affected / exposed	3 / 32 (9.38%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Herpes Zoster			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Mastoiditis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	5 / 32 (15.63%)	2 / 7 (28.57%)	
occurrences (all)	9	3	

Oral Candidiasis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Oral Herpes			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory Tract Infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Sinusitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin Candida			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Staphylococcal Skin Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tooth Infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 32 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	5	2	
Urinary Tract Infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Vulval Abscess			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Diabetes Mellitus			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Iron Deficiency			
subjects affected / exposed	1 / 32 (3.13%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2017	Following changes were done: Incorporated a change in responsibility and obligations of the study sponsor; deleted exploratory efficacy end-point PGIS; changed timing of 12 lead electrocardiogram assessments.
21 March 2018	Following Changes were made: Consolidated all of changes in Amendments 1.1 to 1.6; added Phase 3 to title; updated background and study rationale; specified Part B length of study was 1 year and not approximately 1 year; End of Study/EOT visits were changed from 6 weeks to 9 weeks post last dose; number of subjects was changed from 40 subjects to approximately 40 subjects; added that subjects who received transfusion during Part A would be eligible for Part B; Inclusion criterion 5: Updated to include subjects with Gilbert's Syndrome with bilirubin > upper limit of normal; inclusion criterion 6: added that subjects with ferritin values <lowe were not to be included and allowed concurrent treatment with iron supplementation if subject on a stable dose; Inclusion criterion 9: serogroup B meningococcus was added as a requirement; added inclusion criterion 10: subjects had to be willing to receive transfusion during study if they met study criteria for infusion; Inclusion criteria 12 and 13: post treatment birth control requirement increased from 6 to 9 weeks; Exclusion criterion 2: changed to exclude subjects with a blood transfusion within 6 months of screening or >1 transfusion within 12 months of screening; Exclusion criterion 4: Added that subjects with existing ANA could be adjudicated; Exclusion criterion 14 added: excluded subjects with hypersensitivity to sutimlimab or its components; original Appendix B (Vaccination Schedule) was removed and vaccination instructions were included within body of protocol; original Appendix C (Guidelines for Diagnosis and Treatment of Hypersensitivity Reactions and Anaphylaxis) was removed; healthcare resource utilisation survey was added to the assessments and description of the survey was added as an appendix; appendices were renumbered; For consistency across protocols, hemolytic "flare" was changed to hemolytic breakthrough; beginning on Day 0, urine pregnancy testing was changed to serum or urine pregnancy testing.
19 July 2018	Following changes were done: The study number was revised; PGIS was added per United States Food and Drug Administration request; a 25 milliliter (mL) vial (50 mg/mL) vial was added; inclusion criterion 9: added that previous vaccinations had to be documented records and serogroup B meningococcus vaccine requirement only applied where available (this was already included elsewhere in the protocol); corrected start date for the collection of pharmacokinetics and pharmacodynamics samples during Part B; sutimlimab background information of the study was revised for clarity and updated to mention Part E; added that subjects who received transfusion(s) during screening/observation period had to have their baseline visit at least 7 days after the transfusion; for subjects who had a transfusion, screening period could have been extended from 6 to 7 weeks; updated clinical experience section; the vaccination schedule from the country-specific protocol for Japan (Version 3.1) was added to the vaccination schedule for the other participating countries; windows were added for post-dose vital signs, ECGs, and PK/PD sampling time points; modified text to indicate sutimlimab would be supplied in larger volume and concentration.

15 October 2019	Following changes were done: Added home infusion in prespecified countries (US, Netherlands, Norway, France, Italy, Austria, Germany, Spain) in Part B, which was to be supported by a healthcare professional caregiver; added exploratory objective to describe the safety and subjects satisfaction with the convenience of home infusions with sutimlimab in a subset of subjects in Part B; added secondary objective to Part B to exploratory objective to evaluate immunogenicity of sutimlimab; added more time points for ADA sample collection and same objective added as an exploratory objective to Parts A and B; efficacy endpoint added to assess satisfaction with home infusion; safety endpoint added to assess AEs with home infusion; specified that predose PD back-up samples could be used to assess immunogenicity in subjects who consented to future use of sample; added time points for systemic lupus erythematosus panel sample collection during Part B. • Clarified PK/PD sampling schedules for Part B to match text description to assessment table • Corrected Appendix A to delete iron from chemistry panel • Added Appendix K which described country-specific requirements for home infusion substudy
07 July 2020	Following changes were done: Hypersensitivity or allergic reactions including anaphylaxis to IMP were added to reasons for study discontinuation; to match the statistical analysis plan, the intent-to-treat population was to be referred to as the Full Analysis Set; for home infusion substudy, removed requirements for cardiac resuscitation equipment during home infusion as the risk of emergency situations occurring during home infusions was minimized by enrolling subjects without a history of hypersensitivity reactions to IMP and assistance by personnel trained in basic life support was implemented; added that substudy is only open to subjects who have not or do not plan to receive undiluted infusions; introduced the option of infusion with undiluted solution of sutimlimab in a subset of subjects in Part B; added exploratory endpoint to describe safety of undiluted infusions in Part B; reworded primary endpoint (“responder”) definition for clarity, but definition was unchanged; clarified the order of post dose assessments so that assessments that may impact vital signs (eg, blood draws) occur after vital signs are measured.
04 November 2020	Following changes were done: “Post-infusion vital signs and” were added to the list of endpoints for the subjects receiving undiluted infusions; for the primary endpoint (responder status) analysis for Part A, Fisher’s Exact test was replaced by “Cochran-Mantel-Haenszel (CMH) test”; post infusion vital signs and” were added to the list of endpoints for the subjects receiving undiluted infusions; In Table 3, footnote “l” “added the follow text, “or for post-infusion vital signs in case of undiluted administration, after each undiluted infusion”; references to the study procedural manual were either removed or replaced by references to the applicable study manuals; references to the central laboratory were removed from the laboratory evaluation section; primary efficacy analysis method was changed from Fisher’s exact test to a stratified CMH test.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported