EU Clinical Trials Register

Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Mechanistic Insight and Dosage Optimization Study of the Efficacy and Safety of VIB4920 in Patients with Rheumatoid Arthritis (RA)

Summary

EudraCT number	2019-003697-70
Trial protocol	PL
Global end of trial date	28 December 2021

Results information

Result version number	v1 (current)
This version publication date	01 January 2023
First version publication date	01 January 2023

Trial information

Trial identification

Sponsor protocol code	VIB4920.P2.S3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04163991
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Horizon Therapeutics USA, Inc.
Sponsor organisation address	1 Horizon Way , Deerfield, IL, United States, 60015-3888
Public contact	Ilias Alevizos, PhD, DMD, Viela Bio (acquired by Horizon Therapeutics), +1 866-479-6742, clinicaltrials@horizontherapeutics.com
Scientific contact	Ilias Alevizos, PhD, DMD, Viela Bio (acquired by Horizon Therapeutics), +1 866-479-6742, clinicaltrials@horizontherapeutics.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	28 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the effect of VIB4920 on disease activity as assessed by a composite measure in subjects with adult-onset RA.
• To evaluate the safety and tolerability of VIB4920 in subjects with adult-onset RA.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Council for Harmonisation (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements, and the Sponsor's policy on Ethical Interactions. Written and/or oral information about the nature, purpose, possible risk, and benefit of the study was provided to all participants in a language understandable by the participants. Participants were also notified that they were free to discontinue from the study at any time. Written informed consent was obtained from each participant before any study procedures or assessments were performed.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	09 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 63
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	78
EEA total number of subjects	63

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)	54
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After a screening period of up to 28 days, eligible participants were randomized in a 1:1:1:1:1 ratio into 5 cohorts.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

This was a double-blind study in which VIB4920 and the saline placebo were not identical in appearance. For maintaining the blinding of the participants, investigators, site staff, Sponsor, contract research organization, and staff, a local unblinded pharmacy staff member was nominated by each site and had the responsibility of allocating, dispensing, and preparing the investigational product (IP), and covering the intravenous (IV) bags with an opaque bag to maintain the blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received IV infusion of placebo matched to VIB4920 on Days 1, 15, 29, and 57.

Arm type	Placebo
Investigational medicinal product name	0.9% saline for IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Arm title	VIB4920 3000 mg Once

Arm description:

Participants received IV infusion of VIB4920 3000 mg on Day 1 and placebo on Days 15, 29, and 57.

Arm type	Experimental
Investigational medicinal product name	VIB4920
Investigational medicinal product code	
Other name	MEDI4920, dazodalibep
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Investigational medicinal product name	0.9% saline for IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Arm title	VIB4920 1500 mg Twice

Arm description:

Participants received IV infusion of VIB4920 1500 mg on Days 1 and 57, placebo on Days 15 and 29.

Arm type	Experimental
Investigational medicinal product name	VIB4920
Investigational medicinal product code	
Other name	MEDI4920, dazodalibep
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Investigational medicinal product name	0.9% saline for IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Arm title	VIB4920 3000 mg Twice

Arm description:

Participants received IV infusion of VIB4920 3000 mg on Days 1 and 57, placebo on Days 15 and 29.

Arm type	Experimental
Investigational medicinal product name	VIB4920
Investigational medicinal product code	
Other name	MEDI4920, dazodalibep
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Investigational medicinal product name	0.9% saline for IV infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Arm title	VIB4920 1500 mg 4 Times

Arm description:

Participants received IV infusion of VIB4920 1500 mg on Days 1, 15, 29, and 57.

Arm type	Experimental
Investigational medicinal product name	VIB4920
Investigational medicinal product code	
Other name	MEDI4920, dazodalibep
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IP was infused using an IV infusion pump.

Number of subjects in period 1	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice
Started	16	16	16
Completed	15	13	11
Not completed	1	3	5
Consent withdrawn by subject	1	1	3
Adverse Event	-	-	-
Death	-	-	1
Lost to follow-up	-	1	-
Other, Not Specified	-	1	1

Number of subjects in period 1	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times
Started	15	15
Completed	12	14
Not completed	3	1
Consent withdrawn by subject	1	1
Adverse Event	1	-
Death	-	-
Lost to follow-up	-	-
Other, Not Specified	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received IV infusion of placebo matched to VIB4920 on Days 1, 15, 29, and 57.	
Reporting group title	VIB4920 3000 mg Once
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Day 1 and placebo on Days 15, 29, and 57.	
Reporting group title	VIB4920 1500 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 3000 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 1500 mg 4 Times
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1, 15, 29, and 57.	

Reporting group values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice
Number of subjects	16	16	16
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	56.3	53.2	59.0
standard deviation	± 14.0	± 10.7	± 12.2
Gender categorical			
Units: Subjects			
Female	12	14	11
Male	4	2	5
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	1
Not Hispanic or Latino	15	15	15
Race			
Units: Subjects			
Black or African American	2	0	0
White	14	16	15
Other, Not Specified	0	0	1
Disease Activity Score 28 C-reactive Protein (DAS28-CRP)			
The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity.			
Units: score on a scale			
arithmetic mean	5.443	5.473	5.945

standard deviation	± 1.066	± 0.883	± 0.736

Reporting group values	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	Total
Number of subjects	15	15	78
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	56.5	56.4	
standard deviation	± 12.2	± 15.2	-
Gender categorical			
Units: Subjects			
Female	13	12	62
Male	2	3	16
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	3
Not Hispanic or Latino	15	15	75
Race			
Units: Subjects			
Black or African American	1	1	4
White	14	14	73
Other, Not Specified	0	0	1
Disease Activity Score 28 C-reactive Protein (DAS28-CRP)			
The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity.			
Units: score on a scale			
arithmetic mean	5.452	5.761	
standard deviation	± 0.644	± 0.711	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received IV infusion of placebo matched to VIB4920 on Days 1, 15, 29, and 57.	
Reporting group title	VIB4920 3000 mg Once
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Day 1 and placebo on Days 15, 29, and 57.	
Reporting group title	VIB4920 1500 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 3000 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 1500 mg 4 Times
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1, 15, 29, and 57.	

Primary: Change From Baseline to Day 113 in DAS28-CRP

End point title	Change From Baseline to Day 113 in DAS28-CRP

End point description:

The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity. A negative change from baseline indicates improvement in disease activity. Results are from a mixed-effect model for repeated measures (MMRM) analysis with treatment, visit, visit by treatment interaction, and baseline DAS28-CRP score included in the model.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized. Participants with an assessment at given time point by group.

End point type	Primary

End point timeframe:

Day 1 (Baseline), Day 113

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	15	14
Units: score on a scale				
least squares mean (standard error)	-1.06 (± 0.26)	-1.90 (± 0.27)	-1.87 (± 0.27)	-1.87 (± 0.27)

End point values	VIB4920 1500 mg 4 Times			

Subject group type	Reporting group			
Number of subjects analysed	14			
Units: score on a scale				
least squares mean (standard error)	-1.83 (± 0.28)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Least Squares (LS) Mean difference is VIB4920 minus placebo. Differences less than 0 favor VIB4920.	
Comparison groups	Placebo v VIB4920 3000 mg Once
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0296 [1]
Method	MMRM
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.47
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[1] - Results are from MMRM analysis with treatment, visit, visit by treatment interaction, and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
LS Mean difference is VIB4920 minus placebo. Differences less than 0 favor VIB4920.	
Comparison groups	Placebo v VIB4920 1500 mg Twice
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0355 [2]
Method	MMRM
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.44
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[2] - Results are from MMRM analysis with treatment, visit, visit by treatment interaction, and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
LS Mean difference is VIB4920 minus placebo. Differences less than 0 favor VIB4920.	
Comparison groups	Placebo v VIB4920 3000 mg Twice
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0364 [3]
Method	MMRM
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.44
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[3] - Results are from MMRM analysis with treatment, visit, visit by treatment interaction, and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
LS Mean difference is VIB4920 minus placebo. Differences less than 0 favor VIB4920.	
Comparison groups	Placebo v VIB4920 1500 mg 4 Times
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0478 [4]
Method	MMRM
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.41
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[4] - Results are from MMRM analysis with treatment, visit, visit by treatment interaction, and baseline DAS28-CRP score included in the model.

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), and Treatment-Emergent Adverse Events of Special Interest (TEAESIs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), and Treatment-Emergent Adverse Events of Special

		Interest (TEAESIs)[5][6]	

End point description:

Adverse event (AE): any untoward medical occurrence associated with the use of an intervention in humans, whether or not it is considered intervention-related. Serious adverse event (SAE): AE resulting in any of the following outcomes: death; life-threatening AE; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant incapacity; congenital anomaly/birth defect; other important medical event jeopardizing the participant's well being. AEs of special interest (AESIs) include: thrombotic and embolic events; anaphylaxis and clinically significant (Common Terminology Criteria for Adverse Events [CTCAE] Grade 3 or higher) hypersensitivity reactions; severe infusion-related reactions (CTCAE Grade 3 or higher); immune complex disease; severe (CTCAE Grade 3 or higher) and/or opportunistic infections; hepatic function abnormality meeting the definition of Hy's Law; malignant neoplasm. (CTCAE Grade 3=Severe; Grade 4=Life-threatening; Grade 5=Fatal.)

End point type	Primary

End point timeframe:

From first dose of study drug through Day 309 ± 7 days

Notes:

[5] - 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: Descriptive statistics are presented per protocol.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Due to EudraCT system limitations, reporting of data for the "VIB4920 1500 mg Twice" and "VIB4920 3000 mg Once" arms was not possible. Please see the attached Word document in this endpoint for full data reporting.

End point values	Placebo	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16[7]	13[8]	14[9]	
Units: participants				
At least 1 event	10	11	11	
At least 1 study drug-related event	4	2	2	
At least 1 event of ≥ Grade 3 severity	0	0	0	
Death (Grade 5 severity)	0	0	0	
At least 1 serious event	0	0	1	
At least 1 serious and/or ≥ Grade 3 severity event	0	0	0	
At least 1 related serious event	0	0	0	
At least 1 event leading to study drug discontinue	0	0	0	
At least 1 event of special interest	0	0	0	

Notes:

[7] - Participants who received any dose of study drug, analyzed according to treatment actually received.

[8] - Participants who received any dose of study drug, analyzed according to treatment actually received.

[9] - Participants who received any dose of study drug, analyzed according to treatment actually received.

Attachments (see zip file)	Number of Participants With Treatment-Emergent Adverse

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of VIB4920: Maximum Observed Concentration (Cmax)

End point title	Pharmacokinetics (PK) of VIB4920: Maximum Observed

| | | | Concentration (Cmax)[10] |

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only performed for participants who received active study drug. In addition, due to EudraCT system limitations, reporting of data for the "VIB4920 1500 mg Twice" arm was not possible. Please see the attached Word document in this endpoint for full data reporting.

End point values	VIB4920 3000 mg Once	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16[11]	13	14	
Units: µg/mL				
arithmetic mean (standard deviation)				
Dose 1; n=16, 13, 13	877 (± 204)	860 (± 275)	421 (± 102)	
Dose 2; n=0, 13, 13	9999 (± 9999)	1050 (± 349)	564 (± 163)	
Dose 3; n=0, 0, 14	9999 (± 9999)	9999 (± 9999)	601 (± 181)	
Dose 4; n=0, 0, 14	9999 (± 9999)	9999 (± 9999)	568 (± 140)	

Notes:

[11] - 9999=not applicable (0 participants analyzed).

Attachments (see zip file)	PK of VIB4920_Maximum Observed Concentration (Cmax).docx

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Time to Cmax (Tmax)

End point title	PK of VIB4920: Time to Cmax (Tmax)[12]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only performed for participants who received active study drug. In

addition, due to EudraCT system limitations, reporting of data for the "VIB4920 1500 mg Twice" arm was not possible. Please see the attached Word document in this endpoint for full data reporting.

End point values	VIB4920 3000 mg Once	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16[13]	13[14]	14[15]	
Units: day				
median (full range (min-max))				
Dose 1; n=16, 13, 13	0.0899 (0.0868 to 0.100)	0.0875 (0.0840 to 0.0917)	0.0903 (0.0840 to 0.108)	
Dose 2; n=0, 13, 13	9999 (9999 to 9999)	0.0667 (0.0486 to 0.0882)	0.0486 (0.0437 to 0.0521)	
Dose 3; n=0, 0, 14	9999 (9999 to 9999)	9999 (9999 to 9999)	0.0472 (0.0438 to 0.0486)	
Dose 4; n=0, 0, 14	9999 (9999 to 9999)	9999 (9999 to 9999)	0.0667 (0.0486 to 0.0708)	

Notes:

[13] - 9999=not applicable (0 participants analyzed).

[14] - 9999=not applicable (0 participants analyzed).

[15] - 9999=not applicable (0 participants analyzed).

Attachments (see zip file)	PK of VIB4920_Time to Cmax (Tmax).docx

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Area Under the Concentration-Time Curve From Time 0 to the Last Quantifiable Concentration (AUClast)

End point title	PK of VIB4920: Area Under the Concentration-Time Curve From Time 0 to the Last Quantifiable Concentration (AUClast)[16]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK analyses were only performed for participants who received active study drug. In addition, due to EudraCT system limitations, reporting of data for the "VIB4920 1500 mg Twice" arm was not possible. Please see the attached Word document in this endpoint for full data reporting.

End point values	VIB4920 3000 mg Once	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16[17]	13[18]	14[19]	
Units: µg·day/mL				
arithmetic mean (standard deviation)				
Dose 1; n=16, 13, 13	7350 (± 1380)	7870 (± 2570)	2960 (± 604)	
Dose 2; n=0, 13, 13	9999 (± 9999)	10000 (± 3320)	4060 (± 1290)	
Dose 3; n=0, 0, 14	9999 (± 9999)	9999 (± 9999)	6350 (± 1840)	
Dose 4; n=0, 0, 14	9999 (± 9999)	9999 (± 9999)	5770 (± 1110)	

Notes:

[17] - 9999=not applicable (0 participants analyzed).

[18] - 9999=not applicable (0 participants analyzed).

[19] - 9999=not applicable (0 participants analyzed).

Attachments (see zip file)	PK of VIB4920_Area Under the Concentration-Time Curve From

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Area Under the Concentration-Time Curve From Time 0 to Day 56 (AUC0-56D)

End point title	PK of VIB4920: Area Under the Concentration-Time Curve From Time 0 to Day 56 (AUC0-56D)[20]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received. Participants with an assessment at given dose time points.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), Day 56

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK analyses were only performed for participants who received active study drug.

End point values	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16[21]	15[22]	13[23]	0[24]
Units: µg·day/mL				
arithmetic mean (standard deviation)				
Dose 1; n=16, 15, 13, 0	7280 (± 1370)	4280 (± 1280)	7870 (± 2570)	()
Dose 2; n=0, 14, 13, 0	9999 (± 9999)	5310 (± 2000)	9910 (± 3250)	()
Dose 3; n=0, 0, 0, 0	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	()
Dose 4; n=0, 0, 0, 0	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	()

Notes:

[21] - 9999=not applicable (0 participants analyzed).

[22] - 9999=not applicable (0 participants analyzed).

[23] - 9999=not applicable (0 participants analyzed).

[24] - Per protocol, due to the nature of the dosing and sampling for this arm, the analysis was not done.

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Total Body Clearance (CL) for Dose 1 and Total Body Clearance at Steady State (CLss) for Doses 2 to 4

End point title	PK of VIB4920: Total Body Clearance (CL) for Dose 1 and Total Body Clearance at Steady State (CLss) for Doses 2 to 4[25]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only performed for participants who received active study drug.

End point values	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[26]	15[27]	13[28]	14[29]
Units: mL/day				
arithmetic mean (standard deviation)				
Dose 1 (CL); n=15, 15, 13, 0	430 (± 91.9)	371 (± 92.5)	417 (± 144)	99999 (± 99999)
Dose 2 (CLss); n=0, 14, 13, 0	9999 (± 9999)	314 (± 104)	340 (± 140)	99999 (± 99999)
Dose 3 (CLss); n=0, 0, 0, 0	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	99999 (± 99999)
Dose 4 (CLss); n=0, 0, 0, 14	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	294 (± 49.8)

Notes:

[26] - 9999=not applicable (0 participants analyzed).

[27] - 9999=not applicable (0 participants analyzed).

[28] - 9999=not applicable (0 participants analyzed).

[29] - 99999=due to the nature of dosing/sampling for this arm, analysis was done for Dose 4 only.

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Terminal Elimination Half-Life (t1/2)

End point title	PK of VIB4920: Terminal Elimination Half-Life (t1/2)[30]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK analyses were only performed for participants who received active study drug.

End point values	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16[31]	15[32]	14[33]	14[34]
Units: day				
arithmetic mean (standard deviation)				
Dose 1; n=16, 15, 13, 0	9.27 (± 1.61)	9.06 (± 1.98)	9.02 (± 1.06)	99999 (± 99999)
Dose 2; n=0, 14, 13, 0	9999 (± 9999)	9.55 (± 1.51)	9.88 (± 1.41)	99999 (± 99999)
Dose 3; n=0, 0, 0, 0	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	99999 (± 99999)
Dose 4; n=0, 0, 0, 14	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	10.5 (± 2.06)

Notes:

[31] - 9999=not applicable (0 participants analyzed).

[32] - 9999=not applicable (0 participants analyzed).

[33] - 9999=not applicable (0 participants analyzed).

[34] - 99999=due to the nature of dosing/sampling for this arm, analysis was done for Dose 4 only.

Statistical analyses

No statistical analyses for this end point

Secondary: PK of VIB4920: Volume of Distribution at Steady State (Vss)

End point title	PK of VIB4920: Volume of Distribution at Steady State (Vss)[35]

End point description:

PK Analysis Set: Participants who received active study drug and had at least one quantifiable plasma PK observation post-first dose. Participants were analyzed according to the treatment that they actually received.

n=participants with an assessment at given dose time points by group.

End point type	Secondary

End point timeframe:

Predose (within 30 minutes prior to start of infusion), and within 10 minutes of the end of infusion on Days 1 (Dose 1), 15 ± 1 day (d; Dose 2), 29 ± 3d (Dose 3), 57 ± 3d (Dose 4), and Days 85 ± 3d, 113 ± 5d, 141 ± 5d, 169 ± 5d, 197 ± 7d, 225 ± 7d

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK analyses were only performed for participants who received active study drug.

End point values	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[36]	15[37]	13[38]	14[39]
Units: day				
arithmetic mean (standard deviation)				
Dose 1; n=15, 15, 13, 0	4350 (± 1300)	3750 (± 601)	4540 (± 1470)	99999 (± 99999)
Dose 2; n=0, 14, 13, 0	9999 (± 9999)	3490 (± 926)	3600 (± 1720)	99999 (± 99999)
Dose 3; n=0, 0, 0, 0	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	99999 (± 99999)
Dose 4; n=0, 0, 0, 14	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	3210 (± 865)

Notes:

[36] - 9999=not applicable (0 participants analyzed).

[37] - 9999=not applicable (0 participants analyzed).

[38] - 9999=not applicable (0 participants analyzed).

[39] - 99999=due to the nature of dosing/sampling for this arm, analysis was done for Dose 4 only.

Statistical analyses

No statistical analyses for this end point

Secondary: Total Soluble Cluster of Differentiation 40 Ligand (sCD40L) Plasma Concentration Over Time

End point title	Total Soluble Cluster of Differentiation 40 Ligand (sCD40L) Plasma Concentration Over Time

End point description:

Total sCD40L (free sCD40L and sCD40L bound to VIB4920) was measured in plasma samples using a modified commercially available kit.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized.

n=Participants with an assessment at given time point by group.

End point type	Secondary

End point timeframe:

Day 1 (Baseline), Days 15, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	15
Units: ng/mL				
arithmetic mean (standard deviation)				
Change at Day 15; n=16, 16, 16, 13, 14	4.6759 (± 3.6596)	30.7744 (± 7.4954)	36.0088 (± 14.4324)	28.2492 (± 10.4252)

Change at Day 29; n=16, 15, 15, 14, 14	4.8431 (± 3.3770)	67.5427 (± 16.4322)	66.7047 (± 15.3708)	68.0636 (± 28.6523)
Change at Day 57; n=16, 15, 15, 14, 14	0.8150 (± 1.6053)	64.4177 (± 16.4322)	62.5560 (± 14.4445)	63.6939 (± 25.5500)
Change at Day 85; n=15, 15, 15, 15, 14	0.4483 (± 1.1842)	53.1583 (± 20.6513)	77.5360 (± 18.7440)	57.2587 (± 20.0742)
Change at Day 113; n=15, 14, 15, 14, 14	0.3420 (± 1.3246)	21.4686 (± 19.3705)	75.4407 (± 18.2921)	53.4514 (± 26.2712)
Change at Day 141; n=15, 15, 14, 15, 14	0.2547 (± 0.9863)	1.6517 (± 3.7565)	55.4204 (± 28.9470)	53.2827 (± 31.6165)
Change at Day 169; n=14, 15, 14, 15, 13	0.3114 (± 1.1653)	0 (± 0)	21.1296 (± 27.1973)	18.3170 (± 20.2842)
Change at Day 197; n=14, 14, 14, 15, 14	0.2757 (± 1.0316)	0 (± 0)	4.4354 (± 9.9146)	2.5057 (± 4.4880)
Change at Day 225; n=14, 14, 14, 15, 14	0.2450 (± 0.9167)	3.1418 (± 11.7555)	-0.4043 (± 1.5127)	-0.0137 (± 1.1940)
Change at Day 253; n=14, 14, 13, 13, 13	0.3436 (± 1.2855)	0 (± 0)	-0.5946 (± 2.1439)	-0.5292 (± 1.9082)
Change at Day 281; n=14, 13, 10, 14, 13	-0.0343 (± 0.1283)	0 (± 0)	-0.5640 (± 1.7835)	-0.4729 (± 1.7693)
Change at Day 309; n=14, 12, 10, 12, 13	-0.5654 (± 2.1154)	0 (± 0)	-0.5720 (± 1.8088)	-0.7833 (± 2.7135)

End point values	VIB4920 1500 mg 4 Times			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ng/mL				
arithmetic mean (standard deviation)				
Change at Day 15; n=16, 16, 16, 13, 14	33.9007 (± 8.7777)			
Change at Day 29; n=16, 15, 15, 14, 14	68.1386 (± 12.1314)			
Change at Day 57; n=16, 15, 15, 14, 14	64.1329 (± 12.4842)			
Change at Day 85; n=15, 15, 15, 15, 14	69.8821 (± 19.2623)			
Change at Day 113; n=15, 14, 15, 14, 14	68.5636 (± 19.3458)			
Change at Day 141; n=15, 15, 14, 15, 14	52.3943 (± 29.4422)			
Change at Day 169; n=14, 15, 14, 15, 13	23.5727 (± 26.0510)			
Change at Day 197; n=14, 14, 14, 15, 14	4.6343 (± 5.3603)			
Change at Day 225; n=14, 14, 14, 15, 14	-0.2971 (± 0.8718)			
Change at Day 253; n=14, 14, 13, 13, 13	-0.9485 (± 2.3281)			
Change at Day 281; n=14, 13, 10, 14, 13	-0.9485 (± 2.3281)			
Change at Day 309; n=14, 12, 10, 12, 13	-0.9485 (± 2.3281)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Positive Anti-Drug Antibodies (ADA) to VIB4920

End point title	Percentage of Participants With Positive Anti-Drug Antibodies (ADA) to VIB4920[40]

End point description:

ADA positive at any time: observed at least once during the study (baseline included).
Treatment-emergent ADA: ADA positive post-baseline only or boosted pre-existing ADA during the study period.
Persistent positive: treatment-induced ADA positive at ≥ 2 post-baseline assessments (with ≥ 16 weeks between first and last positive) or positive at last post-baseline assessment.
Transient positive: treatment-induced ADA post-baseline positive but does not fulfill the criteria of persistent positive.

Safety analysis set: all participants who received any dose of study drug, analyzed according to the treatment that they actually received. Participants who received active study drug.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) to Day 309 Day 1 (Baseline) up to Day 309 (± 7 days)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: ADA analyses were only performed for participants who received active study drug. In addition, due to EudraCT system limitations, reporting of data for the "VIB4920 1500 mg Twice" and "VIB4920 3000 mg Once" arms was not possible. Please see the attached Word document in this endpoint for full data reporting.

End point values	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: percentage of participants				
number (not applicable)				
ADA positive at any time	38.5	28.6		
Baseline ADA positive	0	0		
Baseline only ADA positive	0	0		
Post-baseline ADA positive	38.5	28.6		
Treatment-emergent ADA	38.5	28.6		
Persistent positive	0	0		
Transient positive	38.5	28.6		

Attachments (see zip file)	Percentage of Participants With Positive Anti-Drug Antibodies

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Day 113 in Anti-Citrullinated Protein Antibodies (ACPAs)

End point title	Change From Baseline to Day 113 in Anti-Citrullinated Protein

	Antibodies (ACPAs)

End point description:

Excluding data after rescue. Adjusted geometric mean ratio to baseline (90% CI) results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model. Ratios less than 1 indicate a decrease.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized. Participants with an assessment at given time point by group.

End point type	Secondary

End point timeframe:

Day 1 (Baseline), Day 113

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	15	14
Units: ratio				
geometric mean (confidence interval 90%)	1.08 (0.83 to 1.42)	0.69 (0.52 to 0.91)	0.82 (0.62 to 1.07)	0.84 (0.63 to 1.11)

End point values	VIB4920 1500 mg 4 Times			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ratio				
geometric mean (confidence interval 90%)	0.62 (0.47 to 0.82)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.

Comparison groups	Placebo v VIB4920 3000 mg Once
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0584 [41]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.43
upper limit	0.94

Notes:

[41] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 1500 mg Twice
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2274 [42]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.51
upper limit	1.11

Notes:

[42] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 3000 mg Twice
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2794 [43]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.52
upper limit	1.14

Notes:

[43] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 1500 mg 4 Times

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0199 [44]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.57
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.39
upper limit	0.85

Notes:

[44] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Secondary: Change From Baseline to Day 113 in Rheumatoid Factor (RF)

End point title	Change From Baseline to Day 113 in Rheumatoid Factor (RF)

End point description:

Excluding data after rescue. Adjusted geometric mean ratio to baseline (90% CI) results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model. Ratios less than 1 indicate a decrease.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized. Participants with an assessment at given time point by group.

End point type	Secondary

End point timeframe:

Day 1 (Baseline), Day 113

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	15	14
Units: ratio				
geometric mean (confidence interval 90%)	1.20 (1.04 to 1.39)	0.77 (0.66 to 0.89)	0.74 (0.64 to 0.86)	0.72 (0.62 to 0.84)

End point values	VIB4920 1500 mg 4 Times			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ratio				
geometric mean (confidence interval 90%)	0.57 (0.49 to 0.66)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 3000 mg Once
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007 [45]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.52
upper limit	0.79

Notes:

[45] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 1500 mg Twice
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [46]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5
upper limit	0.76

Notes:

[46] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.	
Comparison groups	Placebo v VIB4920 3000 mg Twice
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [47]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.6

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.48
upper limit	0.74

Notes:

[47] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Ratio of geometric mean is for VIB4920:placebo. Ratios less than 1 indicate a decrease.

Comparison groups	Placebo v VIB4920 1500 mg 4 Times
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [48]
Method	MMRM
Parameter estimate	Ratio of geometric mean versus placebo
Point estimate	0.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.38
upper limit	0.59

Notes:

[48] - Results are from MMRM analysis on log(ratio to baseline) with treatment, visit, visit by treatment interaction, and log(baseline) included in the model.

Secondary: Percentage of Participants With Clinical Remission at Day 113

End point title	Percentage of Participants With Clinical Remission at Day 113

End point description:

Clinical remission is defined as DAS28-CRP < 2.6. The DAS28-CRP is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28-CRP range from 0 to approximately 10, where higher scores indicate more disease activity.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized. Participants with an assessment at given time point by group.

End point type	Secondary

End point timeframe:

Day 113

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	15
Units: percentage of participants				
number (not applicable)	18.8	18.8	6.3	13.3

End point values	VIB4920 1500 mg 4 Times			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage of participants				
number (not applicable)	13.3			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	

Odds ratio is VIB4920/placebo, with associated 90% CI and p-value. Odds ratios greater than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 3000 mg Once
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.775 [49]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.2
upper limit	8

Notes:

[49] - Results are from logistic regression analysis with treatment and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	

(Lower limit of 90% CI is < 0.1.) Odds ratio is VIB4920/placebo, with associated 90% CI and p-value. Odds ratios greater than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 1500 mg Twice
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6974 [50]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	5.5

Notes:

[50] - Results are from logistic regression analysis with treatment and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Odds ratio is VIB4920/placebo, with associated 90% CI and p-value. Odds ratios greater than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 3000 mg Twice
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9318 [51]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	5.7

Notes:

[51] - Results are from logistic regression analysis with treatment and baseline DAS28-CRP score included in the model.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Odds ratio is VIB4920/placebo, with associated 90% CI and p-value. Odds ratios greater than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 1500 mg 4 Times
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9108 [52]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.2
upper limit	5.1

Notes:

[52] - Results are from logistic regression analysis with treatment and baseline DAS28-CRP score included in the model.

Secondary: Time to Start of New Treatment for Rheumatoid Arthritis (Rescue Medication)

End point title	Time to Start of New Treatment for Rheumatoid Arthritis (Rescue Medication)

End point description:

Based on Kaplan-Meier method.

Full Analysis Set: all randomized participants who received any dose of study drug, analyzed according to the treatment randomized. Participants who received rescue medication.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) up to Day 309 (± 7 days)

End point values	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice	VIB4920 3000 mg Twice
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1[53]	1[54]	1[55]	3[56]
Units: days				
median (confidence interval 90%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Notes:

[53] - 99999=Not calculable due to small number of participants rescued.

[54] - 99999=Not calculable due to small number of participants rescued.

[55] - 99999=Not calculable due to small number of participants rescued.

[56] - 99999=Not calculable due to small number of participants rescued.

End point values	VIB4920 1500 mg 4 Times			
Subject group type	Reporting group			
Number of subjects analysed	1[57]			
Units: days				
median (confidence interval 90%)	99999 (196 to 99999)			

Notes:

[57] - 99999=Not calculable due to small number of participants rescued.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Hazard ratio is VIB4920/placebo. Hazard ratios less than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 3000 mg Once
Number of subjects included in analysis	2
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9805 [58]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	10.6

Notes:

[58] - Based on Cox regression method with treatment group included in the model.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Hazard ratio is VIB4920/placebo. Hazard ratios less than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 1500 mg Twice
Number of subjects included in analysis	2
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9805 [59]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	10.6

Notes:

[59] - Based on Cox regression method with treatment group included in the model.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Hazard ratio is VIB4920/placebo. Hazard ratios less than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 3000 mg Twice
Number of subjects included in analysis	4
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3407 [60]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.45
upper limit	20.09

Notes:

[60] - Based on Cox regression method with treatment group included in the model.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Hazard ratio is VIB4920/placebo. Hazard ratios less than 1 favor VIB4920.

Comparison groups	Placebo v VIB4920 1500 mg 4 Times
Number of subjects included in analysis	2
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9805 [61]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1
upper limit	10.6

Notes:

[61] - Based on Cox regression method with treatment group included in the model.

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From first dose of study drug (adverse events) through through Day 309 ± 7 days.	
Adverse event reporting additional description:	
Safety analysis set: all participants who received any dose of study drug, analyzed according to the treatment that they actually received.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received IV infusion of placebo matched to VIB4920 on Days 1, 15, 29, and 57	
Reporting group title	VIB4920 3000 mg Once
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Day 1 and placebo on Days 15, 29, and 57.	
Reporting group title	VIB4920 1500 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 3000 mg Twice
Reporting group description:	
Participants received IV infusion of VIB4920 3000 mg on Days 1 and 57, placebo on Days 15 and 29.	
Reporting group title	VIB4920 1500 mg 4 Times
Reporting group description:	
Participants received IV infusion of VIB4920 1500 mg on Days 1, 15, 29, and 57.	

Serious adverse events	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	1 / 17 (5.88%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (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			
COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	VIB4920 3000 mg Once	VIB4920 1500 mg Twice
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 16 (62.50%)	10 / 18 (55.56%)	11 / 17 (64.71%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Haemorrhoid operation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus inflammation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders

Insomnia

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Investigations

Alanine aminotransferase increased

subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	2 / 17 (11.76%)
occurrences (all)	0	1	2

Aspartate aminotransferase increased

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2

Blood glucose abnormal

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Blood pressure increased

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Body temperature increased

subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

Heart sounds abnormal

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Hepatic enzyme increased

subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

Respiratory rate increased

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

SARS-CoV-2 antibody test positive

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Injury, poisoning and procedural complications

Chest injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Post vaccination syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Synovial rupture			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Ventricular extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Parkinsonian rest tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Lymphopenia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	4
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Eye disorders			
Cataract			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Reflux gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Pruritus			

subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Rosacea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders
  Haematuria

subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Leukocyturia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

Musculoskeletal and connective tissue disorders
  Arthralgia

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Osteoporosis postmenopausal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Rheumatoid arthritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	3 / 17 (17.65%)
occurrences (all)	1	0	3
Sacroiliac joint dysfunction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

  Spinal osteoarthritis

subjects affected / exposed	0 / 16 (0.00%)	2 / 18 (11.11%)	2 / 17 (11.76%)
occurrences (all)	0	2	2
Tenosynovitis stenosans			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Infections and infestations

Bronchitis

subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	1	0

COVID-19

subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	3 / 17 (17.65%)
occurrences (all)	1	1	3

Cystitis

subjects affected / exposed	2 / 16 (12.50%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0

Laryngitis

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Nasal herpes

subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

Nasopharyngitis

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Oral candidiasis

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Oral herpes

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Pharyngitis

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Pneumonia

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	2 / 16 (12.50%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	5	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Impaired fasting glucose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	VIB4920 3000 mg Twice	VIB4920 1500 mg 4 Times	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	10 / 14 (71.43%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Haemorrhoid operation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Paranasal sinus inflammation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Blood glucose abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Heart sounds abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Respiratory rate increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
SARS-CoV-2 antibody test positive			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Chest injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Muscle strain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Post vaccination syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Synovial rupture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Ventricular extrasystoles			

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Nervous system disorders

Dizziness

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Headache

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Parkinsonian rest tremor

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Syncope

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Blood and lymphatic system disorders

Anaemia

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Lymphopenia

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Neutropenia

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Thrombocytopenia

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Ear and labyrinth disorders

Vertigo

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Eye disorders

Cataract

subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Gastrointestinal disorders

Diarrhoea		
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Hiatus hernia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Reflux gastritis		
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)
occurrences (all)	1	0
Skin and subcutaneous tissue disorders		
Alopecia		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Pruritus		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Rosacea		
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Renal and urinary disorders		
Haematuria		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Leukocyturia		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Musculoskeletal and connective tissue disorders		
Arthralgia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Back pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	3 / 13 (23.08%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Osteoporosis postmenopausal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Rheumatoid arthritis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 14 (7.14%)	
occurrences (all)	4	1	
Sacroiliac joint dysfunction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Tenosynovitis stenosans			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	3 / 14 (21.43%)	
occurrences (all)	0	3	
Cystitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Laryngitis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Nasal herpes
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Nasopharyngitis
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)
occurrences (all)	1	2

Oral candidiasis
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)
occurrences (all)	1	0

Oral herpes
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Pharyngitis
subjects affected / exposed	2 / 13 (15.38%)	1 / 14 (7.14%)
occurrences (all)	3	1

Pneumonia
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)
occurrences (all)	1	0

Upper respiratory tract infection
subjects affected / exposed	3 / 13 (23.08%)	0 / 14 (0.00%)
occurrences (all)	3	0

Urinary tract infection
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Viral upper respiratory tract infection
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Vulvovaginal mycotic infection
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1

Metabolism and nutrition disorders
Diabetes mellitus
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0

Hypercholesterolaemia		
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)
occurrences (all)	2	0
Hyperuricaemia		
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Impaired fasting glucose		
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)
occurrences (all)	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2019	- Removed RF isotypes from list of screening assessments. RF isotypes will be assessed during the study, but not at screening. - Removed antinuclear antibodies (ANA) from list of assessments. ANA will not be assessed during the study. - Removed anti-citrullinated protein autoantibodies (ACPA) from the autoantibody panel planned for the study assessments. ACPA will still be assessed at screening. "ACPA will be assessed with a fit-for-purpose quantitative assay (in development)." - Removed IgE from list of plasma immunoglobulins that will be assessed. - Removed "Flow cytometry (T regulatory panel" from list of study assessments and procedures.
26 June 2020	- Inserted lead Investigator's name and address and clinical trial registry identifiers. - Removed the reference to Vectra DA testing in the exploratory endpoints and replaced it with "other biomarkers"; removed Vectra DA testing and replaced it with a blood sample for other biomarkers; removed the reference related to Vectra DA testing. - In Dose Preparation section, added a sentence about the required filter. - In Exclusion criterion 18, added text to require investigators to: 1) Consider the risks associated with SARS-CoV-2 circulation when assessing the suitability of a participant for enrollment, including both the participant's epidemiologic risk and health-related risks. 2) Ensure that the participant has a documented negative SARS-CoV-2 viral test within 2 weeks prior to randomization. - Added potential risks of VIB4920 as they relate to COVID-19 or to COVID-19 vaccine response and individual participant risk factors for SARS-CoV-2 infection and for severe COVID-19 disease; added relevant references. - Added text addressing the benefit-risk of conducting this study during the potential circulation of SARS-CoV-2 and steps taken to minimize risk. - In Screening Assessments and Procedures, added a requirement for participant to have a documented negative SAR-CoV-2 viral test within 14 days of randomization. - Provided description of testing for SARS-CoV-2.
30 September 2020	- The circumstance under which a participant can be enrolled if methotrexate (MTX) intolerant was expanded to clarify that this includes if MTX is contraindicated. - Blood tests at screening that exclude from enrollment were changed from a prothrombin time (PT) or partial thromboplastin time (PTT) > upper limoit of normal (ULN) to > 1.2 × ULN. - Under "Repeat of screening laboratory tests", guidance is provided to allow for some tests to be repeated within the initial screening period to assess for eligibility. - Dose Preparation: the timing between vial puncture to start of IV bag administration may not exceed 4 hours at room temperature or 24 hours at 2°C to 8°C. - The process for reporting of AESIs was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported