Clinical trial results:
A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Proof of Concept Study to Evaluate the Efficacy and Safety of VIB4920 in subjects with Sjögren's Syndrome (SS)

Summary

EudraCT number	2019-002713-19
Trial protocol	GB PL HU IT
Global end of trial date	10 March 2023

Results information

Result version number	v1 (current)
This version publication date	23 March 2024
First version publication date	23 March 2024

Trial information

Trial identification

Sponsor protocol code	VIB4920.P2.S2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04129164
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 128905

Notes:

Sponsors

Sponsor organisation name	Horizon Therapeutics USA, Inc.
Sponsor organisation address	1 Horizon Way, Deerfield, United States, 60015-3888
Public contact	Medical director, Horizon Therapeutics USA, Inc., clinicaltrials@horizontherapeutics.com
Scientific contact	Medical director, Horizon Therapeutics USA, Inc., clinicaltrials@horizontherapeutics.com
Sponsor organisation name	Horizon Therapeutics USA, Inc.
Sponsor organisation address	1 Horizon Way , Deerfield, United States, 60015-3888
Public contact	Medical director, Horizon Therapeutics USA, Inc., clinicaltrials@horizontherapeutics.com
Scientific contact	Medical director, Horizon Therapeutics USA, Inc., 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	10 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Population #1:
To evaluate the clinical efficacy of multiple doses of VIB4920 (Dazodalibep) in glandular and extraglandular manifestations of SS patients with moderate to high systemic disease activity.

Population #2:
To evaluate the clinical efficacy of multiple doses of VIB4920 in the key subjective complaints of SS (dryness, fatigue, pain).

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	14 November 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: 50
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Peru: 25
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	United States: 49
Country: Number of subjects enrolled	Mexico: 23

Worldwide total number of subjects	183
EEA total number of subjects	67

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)	162
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Population #1 will be composed of subjects with moderate to severe systemic disease activity defined by ESSDAI ≥ 5. Population #2 will be composed of subjects with mild systemic disease activity defined by ESSDAI score < 5 but with moderate to severe subjective symptoms defined by ESSPRI score ≥ 5 and residual stimulated salivary flow.

Pre-assignment

Screening details:

Sjogren syndrome subjects meeting the 2016 ACR/EULAR classification criteria and the inclusion/exclusion criteria were enrolled in this study. Randomization were stratified by ESSDAI score at screening (< 10 points vs ≥ 10 points) for Population 1 and by ESSPRI score at screening (< 7.5 points vs ≥ 7.5 points) for Population 2.

Period 1

Period 1 title	Stage 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Population 1

Arm description:

Subjects with moderate to severe systemic disease activity received placebo by intravenous (IV) infusion, once every two weeks (Q2W) for three doses and then once every four weeks (Q4W) for 4 additional doses.

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:

Placebo was administered by intravenous infusion following dilution in normal saline.

Arm title	Dazodalibep Population 1

Arm description:

Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Arm type	Experimental
Investigational medicinal product name	Dazodalibep
Investigational medicinal product code	
Other name	VIB4920
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dazodalibep 1500 mg was administered by intravenous infusion following dilution in normal saline.

Arm title	Placebo Population 2

Arm description:

Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

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:

Placebo was administered by intravenous infusion.

Arm title	Dazodalibep Population 2

Arm description:

Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Arm type	Active comparator
Investigational medicinal product name	VIB4920
Investigational medicinal product code	
Other name	Dazodalibep
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dazodalibep 1500 mg was administered by intravenous infusion following dilution in normal saline.

Number of subjects in period 1	Placebo Population 1	Dazodalibep Population 1	Placebo Population 2
Started	38	36	55
Completed	37	34	52
Not completed	1	2	3
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	-	-	2

Number of subjects in period 1	Dazodalibep Population 2
Started	54
Completed	50
Not completed	4
Adverse event, serious fatal	-
Consent withdrawn by subject	4
Adverse event, non-fatal	-

Period 2

Period 2 title	Stage 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to dazodalibep Population 1

Arm description:

Subjects with moderate to severe systemic disease activity who received placebo in stage 1, received dazodalibep 1500 mg by IV infusion, Q4W for five doses.

Arm type	Experimental
Investigational medicinal product name	Dazodalibep
Investigational medicinal product code	
Other name	VIB4920
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dazodalibep 1500 mg was administered by intravenous infusion following dilution in normal saline.

Arm title	Dazodalibep to Placebo Population 1

Arm description:

Subjects with moderate to severe systemic disease activity who received dazodalibep in stage 1, received placebo, Q4W for five doses.

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:

Placebo was administered by intravenous infusion following dilution in normal saline.

Arm title	Placebo to dazodalibep Population 2

Arm description:

Subjects with low systemic disease activity who received placebo in stage 1, received dazodalibep 1500 mg by IV infusion, Q4W for five doses in stage 2.

Arm type	Experimental
Investigational medicinal product name	Dazodalibep
Investigational medicinal product code	
Other name	VIB4920
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dazodalibep 1500 mg was administered by intravenous infusion following dilution in normal saline.

Arm title	Dazodalibep to placebo Population 2

Arm description:

Subjects with low systemic disease activity who received dazodalibep in stage 1, received placebo by IV infusion, Q4W for five doses in stage 2.

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:

Placebo was administered by intravenous infusion following dilution in normal saline.

Number of subjects in period 2	Placebo to dazodalibep Population 1	Dazodalibep to Placebo Population 1	Placebo to dazodalibep Population 2
Started	37	34	52
Completed	35	32	47
Not completed	2	2	5
Consent withdrawn by subject	2	1	3
Miscellaneous	-	-	2
Pregnancy	-	-	-
Lost to follow-up	-	1	-

Number of subjects in period 2	Dazodalibep to placebo Population 2
Started	50
Completed	47
Not completed	3
Consent withdrawn by subject	2
Miscellaneous	-
Pregnancy	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity received placebo by intravenous (IV) infusion, once every two weeks (Q2W) for three doses and then once every four weeks (Q4W) for 4 additional doses.	
Reporting group title	Dazodalibep Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	
Reporting group title	Placebo Population 2
Reporting group description:	
Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	
Reporting group title	Dazodalibep Population 2
Reporting group description:	
Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	

Reporting group values	Placebo Population 1	Dazodalibep Population 1	Placebo Population 2
Number of subjects	38	36	55
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	48.8	51.7	49.0
standard deviation	± 12.1	± 9.6	± 12.6
Gender categorical Units: Subjects			
Female	38	35	50
Male	0	1	5
Race Units: Subjects			
American Indian or Alaska Native	1	4	11
Asian	0	2	5
Black or African American	1	3	3
White	34	26	31
Other	2	1	5

Ethnicity Units: Subjects			
Hispanic or Latino	8	8	23
Not Hispanic or Latino	30	28	32
ESSDAI total score			
ESSDAI grades disease activity in 12 domains (cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathic, and biological). The weights of each domain were obtained by multiple regression modeling, using the Physician's Global Assessment of Activity as gold standard. Each domain is weighted from 1 (Biologic domain) to 6 (Muscular domain) and has 3 or 4 levels of activity per domain, ranging from 0 (no activity) to 3 (high activity). The theoretical range of values for the ESSDAI is 0 to 123			
Units: Score on a scale			
arithmetic mean	10.1	11.4	2.5
standard deviation	± 4.1	± 4.5	± 1.6
ESSPRI total score			
ESSPRI is a self-evaluation tool that was developed in a multicenter international cohort of 230 patients. The ESSPRI uses a 0 to 10 numerical analog scale (ranging from 0 [no symptoms] to 10 [maximal imaginable severity]), one for the assessment of each of the 3 domains: dryness, fatigue, and pain (articular and/or muscular). The weights of the domains are identical, and the mean of the scores of the 3 domains represents the final score. The recall period was stated in each question as "the last 2 weeks." The instrument was completed in approximately 1 minute.			
Units: Score on a scale			
arithmetic mean	6.6	6.6	6.8
standard deviation	± 1.8	± 1.6	± 1.2

Reporting group values	Dazodalibep Population 2	Total	
Number of subjects	54	183	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	50.9		
standard deviation	± 11.7	-	
Gender categorical Units: Subjects			
Female	53	176	
Male	1	7	
Race Units: Subjects			
American Indian or Alaska Native	9	25	
Asian	11	18	
Black or African American	4	11	
White	23	114	
Other	7	15	

Ethnicity Units: Subjects			
Hispanic or Latino	22	61	
Not Hispanic or Latino	32	122	
ESSDAI total score			
ESSDAI grades disease activity in 12 domains (cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathic, and biological). The weights of each domain were obtained by multiple regression modeling, using the Physician's Global Assessment of Activity as gold standard. Each domain is weighted from 1 (Biologic domain) to 6 (Muscular domain) and has 3 or 4 levels of activity per domain, ranging from 0 (no activity) to 3 (high activity). The theoretical range of values for the ESSDAI is 0 to 123			
Units: Score on a scale			
arithmetic mean	3.1		
standard deviation	± 1.8	-	
ESSPRI total score			
ESSPRI is a self-evaluation tool that was developed in a multicenter international cohort of 230 patients. The ESSPRI uses a 0 to 10 numerical analog scale (ranging from 0 [no symptoms] to 10 [maximal imaginable severity]), one for the assessment of each of the 3 domains: dryness, fatigue, and pain (articular and/or muscular). The weights of the domains are identical, and the mean of the scores of the 3 domains represents the final score. The recall period was stated in each question as "the last 2 weeks." The instrument was completed in approximately 1 minute.			
Units: Score on a scale			
arithmetic mean	7.1		
standard deviation	± 1.6	-	

End points

End points reporting groups

Reporting group title	Placebo Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity received placebo by intravenous (IV) infusion, once every two weeks (Q2W) for three doses and then once every four weeks (Q4W) for 4 additional doses.	
Reporting group title	Dazodalibep Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	
Reporting group title	Placebo Population 2
Reporting group description:	
Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	
Reporting group title	Dazodalibep Population 2
Reporting group description:	
Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.	
Reporting group title	Placebo to dazodalibep Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity who received placebo in stage 1, received dazodalibep 1500 mg by IV infusion, Q4W for five doses.	
Reporting group title	Dazodalibep to Placebo Population 1
Reporting group description:	
Subjects with moderate to severe systemic disease activity who received dazodalibep in stage 1, received placebo, Q4W for five doses.	
Reporting group title	Placebo to dazodalibep Population 2
Reporting group description:	
Subjects with low systemic disease activity who received placebo in stage 1, received dazodalibep 1500 mg by IV infusion, Q4W for five doses in stage 2.	
Reporting group title	Dazodalibep to placebo Population 2
Reporting group description:	
Subjects with low systemic disease activity who received dazodalibep in stage 1, received placebo by IV infusion, Q4W for five doses in stage 2.	
Subject analysis set title	Placebo - Dazodalibep 1500mg Population 1 - PK Set
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects with moderate to severe systemic disease activity received placebo by intravenous (IV) infusion, once every two weeks (Q2W) for three doses and then once every four weeks (Q4W) for 4 additional doses during stage 1 and received dazodalibep 1500 mg by IV infusion, Q4W for five doses during stage 2.	
Subject analysis set title	Dazodalibep 1500mg - Placebo Population 1 - PK Set
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses during stage 1 and received placebo, Q4W for five doses during stage 2.	
Subject analysis set title	Placebo - Dazodalibep 1500mg Population 2 - PK Set
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses during stage 1 and received dazodalibep 1500 mg by IV infusion, Q4W for five doses in stage 2.	

Subject analysis set title	Dazodalibep 1500mg - Placebo Population 2 - PK Set
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses during stage 1 and received placebo by IV infusion, Q4W for five doses in stage 2.

Subject analysis set title	Placebo to Dazodalibep 1500mg - Population 1 - VIB4920 Set
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects with moderate to severe systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses in stage 1 and dazodalibep 1500 mg in stage 2 by IV infusion, Q4W for five doses.

Subject analysis set title	Dazodalibep 1500mg to Placebo - Population 1 - VIB4920 Set
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses in stage 1 and placebo in stage 2 by IV infusion, Q4W for five doses.

Subject analysis set title	Placebo to Dazodalibep 1500 mg - Population 2 - VIB4920 Set
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses in stage 1 and dazodalibep 1500 mg by IV infusion, Q4W for five doses in stage 2.

Subject analysis set title	Dazodalibep 1500mg to Placebo - Population 2 - VIB4920 Set
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses in stage 1 and placebo by IV infusion, Q4W for five doses in stage 2.

Primary: Change From Baseline in EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) - Population 1

End point title	Change From Baseline in EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) - Population 1[1]

End point description:

The ESSDAI is a systemic disease activity index that includes organ-by-organ definitions of disease activity. The ESSDAI grades disease activity in 12 domains (cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathic, and biological). The weights of each domain were obtained by multiple regression modeling, using the Physician's Global Assessment of Activity as gold standard. Each domain is weighted from 1 (Biologic domain) to 6 (Muscular domain) and has 3 or 4 levels of activity per domain, ranging from 0 (no activity) to 3 (high activity). The theoretical range of values for the ESSDAI is 0 to 123, with the final score being calculated as follows:

Final Score = Sum of all 12 domain scores
Domain score = Activity level × Domain weight

Analysis Population: The full analysis set (FAS) includes all randomized subjects who received any dose of investigational product.

End point type	Primary

End point timeframe:

Baseline, day 169

Notes:

[1] - 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: This endpoint is planned for only population 1 as primary endpoint

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: Score on a scale				
least squares mean (standard error)	-4.1 (± 0.6)	-6.3 (± 0.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0167 [3]
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-2.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.6
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.9

Notes:

[2] - Mixed-effect model for repeated measures (MMRM)

[3] - MMRM analysis with treatment, visit, visit by treatment interaction, and baseline ESSDAI score included in the model. LSMean difference is VIB4920-placebo, with associated 90% confidence interval and p-value. Differences less than 0 favor dazodalibep

Primary: Change From Baseline in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) - Population 2

End point title	Change From Baseline in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) - Population 2[4]

End point description:

ESSPRI is a self-evaluation tool that was developed in a multicenter international cohort of 230 patients. The ESSPRI uses a 0 to 10 numerical analog scale (ranging from 0 [no symptoms] to 10 [maximal imaginable severity]), one for the assessment of each of the 3 domains: dryness, fatigue, and pain (articular and/or muscular). The weights of the domains are identical, and the mean of the scores of the 3 domains represents the final score. The recall period was stated in each question as "the last 2 weeks." The instrument was completed in approximately 1 minute.

Analysis Population: FAS population with available data at specified time point.

End point type	Primary

End point timeframe:

Baseline, day 169

Notes:

[4] - 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: This endpoint is planned for only population 2 as primary endpoint

End point values	Placebo Population 2	Dazodalibep Population 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	51		
Units: Score on a scale				
least squares mean (standard error)	-0.53 (± 0.23)	-1.80 (± 0.23)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 2 v Placebo Population 2
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0002
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-1.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.82
upper limit	-0.73
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[5] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization factor, and the baseline ESSPRI score included in the model. LSMean difference is Dazodalibep-placebo, with associated 90% confidence interval & p-value. Differences less than 0 favor dazodalibep

Secondary: Change From Baseline in ESSPRI - Population 1

End point title	Change From Baseline in ESSPRI - Population 1[6]

End point description:

ESSPRI is a self-evaluation tool that was developed in a multicenter international cohort of 230 patients. The ESSPRI uses a 0 to 10 numerical analog scale (ranging from 0 [no symptoms] to 10 [maximal imaginable severity]), one for the assessment of each of the 3 domains: dryness, fatigue, and pain (articular and/or muscular). The weights of the domains are identical, and the mean of the scores of the 3 domains represents the final score. The recall period was stated in each question as "the last 2 weeks." The instrument was completed in approximately 1 minute.

Analysis Population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[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: This endpoint is planned for only population 1 as secondary endpoint

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: Score on a scale				
least squares mean (standard error)	-1.12 (± 0.29)	-1.80 (± 0.31)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.111 [7]
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-0.68
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.39
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[7] - MMRM analysis with treatment, visit, visit by treatment interaction, and baseline ESSDAI score included in the model. LSMean difference is VIB4920-placebo, with associated 90% confidence interval & p-value. Differences less than 0 favor dazodalibep.

Secondary: Percentage of Subjects Achieving ESSDAI[3] and ESSDAI[4] Response - Population 1

End point title	Percentage of Subjects Achieving ESSDAI[3] and ESSDAI[4] Response - Population 1[8]

End point description:

ESSDAI is a systemic disease activity index that includes organ-by-organ definitions of disease activity. ESSDAI grades disease activity in 12 domains (cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathic, and biological). Weights of each domain were obtained by multiple regression modeling, using Physician's Global Assessment of Activity as gold standard. Each domain is weighted from 1 (Biologic domain) to 6 (Muscular domain) and has 3 or 4 levels of activity per domain, ranging from 0 (no activity) to 3 (high activity). Theoretical range of values for ESSDAI is 0 to 123. Final score being calculated as follows:
Final Score = Sum of all 12 domain scores
Domain score = Activity level × Domain weight

ESSDAI[3] and ESSDAI[4] response: Decrease of at least 3 and 4 points respectively from baseline in the ESSDAI.

FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Day 169

Notes:

[8] - 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: This endpoint is planned for only population 1 as secondary endpoint

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	36		
Units: Percentage of participants				
number (confidence interval 90%)				
ESSDAI[3]	61.2 (47.2 to 73.6)	72.3 (58.2 to 83.0)		
ESSDAI[4]	50.9 (36.9 to 64.8)	67.2 (52.4 to 79.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: ESSDAI[3]	
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3283 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	3.8

Notes:

[9] - Logistic regression analysis with treatment and baseline ESSDAI score included in the model. Odds ratio is VIB4920/placebo, with associated 90% confidence interval and p-value. Odds ratios greater than 1 favor dazodalibep.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: ESSDAI[4]	
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1823 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	4.6

Notes:

[10] - Logistic regression analysis with treatment and baseline ESSDAI score included in the model. Odds ratio is VIB4920/placebo, with associated 90% confidence interval and p-value. Odds ratios greater than 1 favor dazodalibep.

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue score - Population 1

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue score - Population 1[11]

End point description:

The FACIT-Fatigue is a 13-item questionnaire, subject-completed, used to assess the impact of fatigue. Its recall period is 7 days. The responses range from 0 (Not at all) to 4 (Very Much). To calculate the total score, the negatively stated items are reversed by subtracting the response from "4". Final scores are the sum of the responses and range from 0 to 52. Higher scores indicate better QoL. It takes 5-10 minutes to complete.

Analysis population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[11] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: Score on a scale				
least squares mean (standard error)	5.8 (± 1.6)	8.1 (± 1.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.3028
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	2.3

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.4
upper limit	6.1
Variability estimate	Standard error of the mean
Dispersion value	2.3

Notes:

[12] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline FACIT score included in the model. LSMean difference is VIB4920-placebo, with associated 90% confidence interval and p-value. Differences greater than 0 favor dazodalibep.

Secondary: Change from baseline in Ocular Surface Disease Index (OSDI) - Population 1

End point title	Change from baseline in Ocular Surface Disease Index (OSDI) - Population 1[13]

End point description:

OSDI is a valid and reliable instrument for assessing effect on vision-related function and dry eye disease severity (normal, mild, moderate, and severe). Its recall period is 1 week. It is composed of 12 questions that the physician asks the subject and circles the number that best represents each question. The responses for each question range from 0 (None of the time) to 4 (All of the time). The OSDI score is calculated as (sum of scores for questions answered)/(number of questions answered)×25, which ranges from 0 to 100 with higher scores signifying greater disability. The assessment can be completed in 5 minutes.

Analysis population FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[13] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	31		
Units: Score on a scale				
least squares mean (standard error)	-14.02 (± 3.06)	-16.00 (± 3.22)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.6583
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	0.6583

Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.38
upper limit	5.44
Variability estimate	Standard error of the mean
Dispersion value	4.44

Notes:

[14] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline OSDI score included in the model. LSMean difference is VIB4920-placebo, with associated 90% CI and p-value. Differences less than 0 favor dazodalibep.

Secondary: Change from Baseline in PGIS Scale - Population 1

End point title	Change from Baseline in PGIS Scale - Population 1[15]

End point description:

The PGIS is a single item designed to capture the subject's perception of overall symptom severity over the past week on a 5-point categorical response scale (none, mild, moderate, severe, or very severe).

Analysis population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[15] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 1	Dazodalibep Population 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: Score on a scale				
least squares mean (standard error)	-0.5 (± 0.1)	-0.6 (± 0.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 1 v Placebo Population 1
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.3629
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.4
upper limit	0.1

Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[16] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline PGIS score included in the model. LSMean difference is VIB4920-placebo, with associated 90% CI and p-value. Differences less than 0 favor dazodalibep.

Secondary: Percentage of Subjects Achieving ESSPRI response - Population 2

End point title	Percentage of Subjects Achieving ESSPRI response - Population 2[17]

End point description:

ESSPRI is a self-evaluation tool that was developed in a multicenter international cohort of 230 patients. The ESSPRI uses a 0 to 10 numerical analog scale (ranging from 0 [no symptoms] to 10 [maximal imaginable severity]), one for the assessment of each of the 3 domains: dryness, fatigue, and pain (articular and/or muscular). The weights of the domains are identical, and the mean of the scores of the 3 domains represents the final score. The recall period was stated in each question as "the last 2 weeks." The instrument was completed in approximately 1 minute.

ESSPRI response, defined as ≥ 1 point or 15% reduction from baseline in ESSPRI score at Day 169 without premature discontinuation from the study and without receiving rescue therapy.

Analysis population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Day 169

Notes:

[17] - 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: This endpoint is planned for population 2 as secondary endpoint

End point values	Placebo Population 2	Dazodalibep Population 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: Percentage of participants				
number (confidence interval 90%)	33.2 (23.6 to 44.4)	66.4 (54.9 to 76.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 2 v Placebo Population 2
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.0008
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4

Confidence interval	
level	90 %
sides	2-sided
lower limit	2
upper limit	7.8

Notes:

[18] - logistic regression analysis with treatment and baseline ESSPRI score included in the model. Odds ratio is Dazodalibep/placebo, with associated 90% confidence interval and p-value. Odds ratios greater than 1 favor dazodalibep.

Secondary: Change From Baseline in FACIT-Fatigue Score - Population 2

End point title	Change From Baseline in FACIT-Fatigue Score - Population 2[19]

End point description:

The FACIT-Fatigue is a 13-item questionnaire, subject-completed, used to assess the impact of fatigue. Its recall period is 7 days. The responses range from 0 (Not at all) to 4 (Very Much). To calculate the total score, the negatively stated items are reversed by subtracting the response from "4". Final scores are the sum of the responses and range from 0 to 52. Higher scores indicate better QoL. It takes 5-10 minutes to complete.

Analysis population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[19] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 2	Dazodalibep Population 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Score on a scale				
least squares mean (standard error)	2.8 (± 1.4)	8.1 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 2 v Placebo Population 2
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.0095
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	5.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	2
upper limit	8.7

Variability estimate	Standard error of the mean
Dispersion value	2

Notes:

[20] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline FACIT score included in the model. LSMean difference is Dazodalibep-placebo, with associated 90% confidence interval and p-value. Differences greater than 0 favor dazodalibep.

Secondary: Change From Baseline in OSDI - Population 2

End point title	Change From Baseline in OSDI - Population 2[21]

End point description:

OSDI is a valid and reliable instrument for assessing effect on vision-related function and dry eye disease severity (normal, mild, moderate, and severe). Its recall period is 1 week. It is composed of 12 questions that the physician asks the subject and circles the number that best represents each question. The responses for each question range from 0 (None of the time) to 4 (All of the time). The OSDI score is calculated as (sum of scores for questions answered)/(number of questions answered)×25, which ranges from 0 to 100 with higher scores signifying greater disability. The assessment can be completed in 5 minutes.

Analysis population FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[21] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 2	Dazodalibep Population 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	51		
Units: Score on a scale				
least squares mean (standard error)	-8.52 (± 2.94)	-13.95 (± 2.95)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 2 v Placebo Population 2
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.1936
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-5.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.31
upper limit	1.46
Variability estimate	Standard error of the mean
Dispersion value	4.15

Notes:

[22] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline OSDI score included in the model. LSMean difference is Dazodalibep-placebo, with associated 90% confidence interval and p-value. Differences less than 0 favor dazodalibep.

Secondary: Change From Baseline in PGIS - Population 2

End point title	Change From Baseline in PGIS - Population 2[23]

End point description:

The PGIS is a single item designed to capture the subject's perception of overall symptom severity over the past week on a 5-point categorical response scale (none, mild, moderate, severe, or very severe).

Analysis population: FAS population with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, day 169

Notes:

[23] - 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: This endpoint is planned for population 1 and 2 as separate secondary endpoints

End point values	Placebo Population 2	Dazodalibep Population 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Score on a scale				
least squares mean (standard error)	-0.4 (± 0.1)	-0.6 (± 0.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dazodalibep Population 2 v Placebo Population 2
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.1781
Method	MMRM
Parameter estimate	LSMean difference
Point estimate	-0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.5
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[24] - MMRM analysis with treatment, visit, visit by treatment interaction, randomization stratification factor and baseline PGIS score included in the model. LSMean difference is Dazodalibep-placebo, with associated 90% confidence interval and p-value. Differences less than 0 favor Dazodalibep.

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) - Population 1 and 2

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) - Population 1 and 2

End point description:

An adverse event is any untoward medical occurrence associated with the use of an intervention in humans whether or not it is considered intervention-related. If an adverse event onset is on or after the first dose of IP administration, the AE was considered as a TEAE. Otherwise, the AE will be considered as a non-treatment emergent AE.

Analysis population: The safety analysis set included all subjects who received any dose of IP. Subjects were analyzed according to the treatment that they actually received.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of the study (Up to 365 days)

End point values	Placebo Population 1	Dazodalibep Population 1	Placebo Population 2	Dazodalibep Population 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	36	55	54
Units: Participants	23	28	38	37

End point values	Placebo to dazodalibep Population 1	Dazodalibep to Placebo Population 1	Placebo to dazodalibep Population 2	Dazodalibep to placebo Population 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	34	52	49
Units: Participants	28	25	34	32

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Dazodalibep - Population 1 and 2

End point title	Serum Concentrations of Dazodalibep - Population 1 and 2

End point description:

Plasma concentrations of dazodalibep were reported.

Analysis Population: The pharmacokinetic analysis set included all subjects who received IP and had at least one quantifiable serum PK observation post-first dose.

End point type	Secondary

End point timeframe:

Day 1 predose, day 1 post-dose, day 15, day 29, day 57, day 85, day 113, day 141 predose, day 141 postdose, day 169 predose, day 169 postdose, day 197, day 225, day 253, day 281, day 309, day 365

End point values	Placebo - Dazodalibep 1500mg Population 1 - PK Set	Dazodalibep 1500mg - Placebo Population 1 - PK Set	Placebo - Dazodalibep 1500mg Population 2 - PK Set	Dazodalibep 1500mg - Placebo Population 2 - PK Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37[25]	36[26]	52[27]	54[28]
Units: Milliragm per liter				
arithmetic mean (standard deviation)				
Day 1, predose	99999 (± 99999)	0.002 (± 0.013)	99999 (± 99999)	0.002 (± 0.013)
Day 1, Post dose	99999 (± 99999)	470.370 (± 111.047)	99999 (± 99999)	496.984 (± 182.915)
Day 15	99999 (± 99999)	97.058 (± 26.480)	99999 (± 99999)	111.636 (± 56.244)
Day 29	99999 (± 99999)	128.228 (± 31.805)	99999 (± 99999)	141.365 (± 100.163)
Day 57	99999 (± 99999)	62.363 (± 25.562)	99999 (± 99999)	80.093 (± 64.358)
Day 85	99999 (± 99999)	53.716 (± 21.300)	99999 (± 99999)	68.812 (± 60.349)
Day 113	99999 (± 99999)	25.796 (± 29.229)	99999 (± 99999)	66.778 (± 59.558)
Day 141, Predose	99999 (± 99999)	49.318 (± 27.952)	99999 (± 99999)	80.912 (± 125.684)
Day 141, Postdose	0.577 (± 99999)	525.702 (± 155.286)	25.004 (± 99999)	532.216 (± 241.670)
Day 169, predose	99999 (± 99999)	50.390 (± 18.717)	99999 (± 99999)	54.031 (± 30.161)
Day 169, postdose	469.366 (± 92.413)	65.459 (± 113.805)	572.071 (± 200.235)	57.018 (± 31.592)
Day 197	39.535 (± 16.655)	10.808 (± 9.982)	39.399 (± 15.325)	14.958 (± 28.728)
Day 225	46.885 (± 21.633)	1.903 (± 1.594)	73.173 (± 194.836)	1.979 (± 1.624)
Day 253	45.069 (± 23.143)	0.360 (± 0.343)	63.950 (± 77.006)	0.427 (± 0.485)
Day 281	46.368 (± 23.349)	0.086 (± 0.160)	54.050 (± 50.595)	0.139 (± 0.340)
Day 309	52.409 (± 23.754)	0.008 (± 0.026)	44.732 (± 24.888)	0.018 (± 0.044)
Day 365	2.446 (± 2.536)	0 (± 0)	1.531 (± 1.017)	0.003 (± 0.014)

Notes:

[25] - n = 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 36, 34, 37, 36, 36, 33, 21

99999 = Not applicable

[26] - n = 36, 33, 35, 35, 34, 36, 31, 35, 33, 34, 34, 34, 32, 33, 33, 31, 22

99999 = Not applicable

[27] - n = 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 51, 52, 51, 49, 49, 49, 46

99999 = Not Applicable

[28] -
n = 54, 52, 51, 52, 51, 51, 50, 48, 47, 51, 44, 48, 49, 49, 46, 46, 45

99999 = Not Applicable

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-Drug Antibodies (ADA) - Population 1 and 2

End point title	Number of Subjects With Positive Anti-Drug Antibodies (ADA) - Population 1 and 2

End point description:

Number of subjects with positive ADA were reported.

Analysis population: Any VIB4920 analysis set.

End point type	Secondary

End point timeframe:

From first dose of study drug until end of the study (up to 365 days)

End point values	Placebo to Dazodalibep 1500mg - Population 1 - VIB4920 Set	Dazodalibep 1500mg to Placebo - Population 1 - VIB4920 Set	Placebo to Dazodalibep 1500 mg - Population 2 - VIB4920 Set	Dazodalibep 1500mg to Placebo - Population 2 - VIB4920 Set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	36	52	54
Units: Participants	1	6	6	12

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose until end of the study (up to 365 days)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo Population 1 - Stage 1

Reporting group description:

Subjects with moderate to severe systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Reporting group title	Dazodalibep 1500 mg Population 1 -Stage 1

Reporting group description:

Subjects with moderate to severe systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Reporting group title	Placebo to Dazodalibep 1500 mg Population 1 - Stage 2

Reporting group description:

Subjects with moderate to severe systemic disease activity who received placebo had received dazodalibep 1500 mg by IV infusion, Q4W for five doses.

Reporting group title	Dazodalibep 1500 mg to Placebo Population 1 - Stage 2

Reporting group description:

Subjects with moderate to severe systemic disease activity who received dazodalibep in stage 1 had received placebo, Q4W for five doses.

Reporting group title	Placebo Population 2 - Stage 1

Reporting group description:

Subjects with low systemic disease activity received placebo by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Reporting group title	Dazodalibep 1500 mg - Population 2 - Stage 1

Reporting group description:

Subjects with low systemic disease activity received dazodalibep 1500 mg by IV infusion, Q2W for three doses and then Q4W for 4 additional doses.

Reporting group title	Placebo to Dazodalibep 1500 mg Population 2 - Stage 2

Reporting group description:

Subjects with low systemic disease activity who received placebo in stage 1 had received dazodalibep 1500 mg by IV infusion, Q4W for five doses in stage 2.

Reporting group title	Dazodalibep 1500 mg to Placebo Population 2 - Stage 2

Reporting group description:

Subjects with low systemic disease activity who received dazodalibep in stage 1 had received placebo by IV infusion, Q4W for five doses in stage 2.

Serious adverse events	Placebo Population 1 - Stage 1	Dazodalibep 1500 mg Population 1 - Stage 1	Placebo to Dazodalibep 1500 mg Population 1 - Stage 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	1 / 37 (2.70%)
number of deaths (all causes)	0	1	0

number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gammopathy			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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			
Multiple injuries			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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			
Cholecystitis chronic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 37 (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
Pneumonia influenzal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
Post-acute COVID-19 syndrome			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (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	Dazodalibep 1500 mg to Placebo Population 1 - Stage 2	Placebo Population 2 - Stage 1	Dazodalibep 1500 mg - Population 2 - Stage 1
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 34 (8.82%)	1 / 55 (1.82%)	3 / 54 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gammopathy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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			
Multiple injuries			
subjects affected / exposed	1 / 34 (2.94%)	0 / 55 (0.00%)	0 / 54 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 55 (0.00%)	0 / 54 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
General disorders and administration site conditions			
Death			

subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 55 (1.82%)	0 / 54 (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
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 55 (0.00%)	0 / 54 (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
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-acute COVID-19 syndrome			

subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (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	Placebo to Dazodalibep 1500 mg Population 2 - Stage 2	Dazodalibep 1500 mg to Placebo Population 2 - Stage 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 52 (1.92%)	2 / 49 (4.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gammopathy			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 52 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Atrial flutter			
subjects affected / exposed	1 / 52 (1.92%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (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			
Neutropenia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			

subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-acute COVID-19 syndrome			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (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 / 52 (0.00%)	1 / 49 (2.04%)	
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	Placebo Population 1 - Stage 1	Dazodalibep 1500 mg Population 1 - Stage 1	Placebo to Dazodalibep 1500 mg Population 1 - Stage 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 38 (26.32%)	11 / 36 (30.56%)	17 / 37 (45.95%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 38 (2.63%)	3 / 36 (8.33%)	0 / 37 (0.00%)
occurrences (all)	1	5	0
Headache			
subjects affected / exposed	5 / 38 (13.16%)	4 / 36 (11.11%)	4 / 37 (10.81%)
occurrences (all)	8	5	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 38 (7.89%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	4	2	0
Diarrhoea			

subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	4
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 38 (0.00%)	4 / 36 (11.11%)	6 / 37 (16.22%)
occurrences (all)	0	4	6
Upper respiratory tract infection			
subjects affected / exposed	2 / 38 (5.26%)	3 / 36 (8.33%)	5 / 37 (13.51%)
occurrences (all)	3	3	6
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	4
Nasopharyngitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dazodalibep 1500 mg to Placebo Population 1 - Stage 2	Placebo Population 2 - Stage 1	Dazodalibep 1500 mg - Population 2 - Stage 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 34 (52.94%)	13 / 55 (23.64%)	15 / 54 (27.78%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 34 (5.88%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 55 (3.64%)	4 / 54 (7.41%)
occurrences (all)	0	2	4
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 34 (8.82%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 34 (17.65%)	7 / 55 (12.73%)	8 / 54 (14.81%)
occurrences (all)	6	7	8
Upper respiratory tract infection			
subjects affected / exposed	5 / 34 (14.71%)	4 / 55 (7.27%)	2 / 54 (3.70%)
occurrences (all)	7	5	2
Urinary tract infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	5 / 55 (9.09%)	5 / 54 (9.26%)
occurrences (all)	0	5	5

Non-serious adverse events	Placebo to Dazodalibep 1500 mg Population 2 - Stage 2	Dazodalibep 1500 mg to Placebo Population 2 - Stage 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 52 (17.31%)	10 / 49 (20.41%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 52 (17.31%)	5 / 49 (10.20%)	
occurrences (all)	10	5	
Upper respiratory tract infection			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	2 / 52 (3.85%)	6 / 49 (12.24%)	
occurrences (all)	2	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2020	Text addressing COVID-19 risk, and steps to minimize COVID-19 risk was added. This includes the requirement for a negative SARS-CoV-2 test within 2 weeks prior to randomization. SARS-CoV-2 testing added to screening procedures. Text providing additional details regarding appropriate contraception methods that must be adhered to in order to meet eligibility criteria was added. The phrase "(the minimum age for adult participants can be higher than 18 years in countries with different regulations)" was added. Text clarifying additional exclusion criteria relating to infections (bacterial/viral/other), including COVID-19 risk was added. The screening procedure "Exploratory biomarker sample (serum)" added. Number of visits when an autoantibody panel needs to be conducted has been revised. The term "cryoglobulins" was deleted from "C3, C4, serum free light chains, cryoglobulins, serum and urine immunofixation" procedure. Exploratory Flow Cytometry (T-reg panel)" procedure deleted from schedule of study assessments. Inserted requirement for additional urine pregnancy test(s) at Visit 15 and EDV. The procedures "Autoantibody panel" and "Cryoglobulins" deleted. IgE was removed from the list of plasma immunoglobulins to be assessed. Assessment of T regulatory cells removed from exploratory flow cytometry. Text inserted explaining Investigator discretion to give "medications that are considered necessary for the safety and well-being of subjects". New section stating, "The initiation or increase in dose of the restricted medications in Section 7.4.2 are also considered as rescue medications for Population #1" was inserted. New section stating, "The initiation or increase in dose of the restricted medications in Section7.4.4 are also considered as rescue medications for Population #2" was inserted.
07 October 2022	Text clarifying the MR team will remain blinded to the treatment assignment for individual subjects until the completion of the study. Text clarifying any communication of unblinded results will be documented in an unblinding memo. Population-based treatment group level results may be released after completion of primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported