Clinical trial results:
A Phase 2, Open-Label Study of INCB050465 in Participants With Autoimmune Hemolytic Anemia

Summary

EudraCT number	2017-003652-22
Trial protocol	FR AT IT
Global end of trial date	02 April 2024

Results information

Result version number	v1 (current)
This version publication date	03 January 2025
First version publication date	03 January 2025

Trial information

Trial identification

Sponsor protocol code	INCB 50465-206

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.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	02 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of parsaclisib administered orally to participants with autoimmune hemolytic anemia (AIHA) who had decreased hemoglobin and evidence of ongoing hemolysis that required treatment intervention.

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Conference on Harmonisation Good Clinical Practice consolidated guidelines (E6) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	25
EEA total number of subjects	21

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)	14
From 65 to 84 years	10
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in 25 participants enrolled in 8 sites in Austria, France, Italy, and the United States.

Period 1

Period 1 title	12-Week Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib 1 mg QD

Arm description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg tablets taken orally

Arm title	Parsaclisib 2.5 mg QD

Arm description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg tablets taken orally

Number of subjects in period 1	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD
Started	10	15
Completed	9	13
Not completed	1	2
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	1

Period 2

Period 2 title	Treatment Extension Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib 1 mg QD

Arm description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg tablets taken orally

Arm title	Parsaclisib 2.5 mg QD

Arm description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Arm type	Experimental

Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg tablets taken orally

Number of subjects in period 2[1]	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD
Started	7	11
Completed	0	0
Not completed	7	11
Adverse event, serious fatal	-	1
Physician decision	1	1
Adverse event, non-fatal	4	1
Transitioned to Rollover Study	1	4
Lack of efficacy	1	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants completing the 12-week Treatment Period opted to enter the Treatment Extension Period.

Baseline characteristics

Reporting groups	
Reporting group title	Parsaclisib 1 mg QD

Reporting group description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group title	Parsaclisib 2.5 mg QD

Reporting group description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD	Total
Number of subjects	10	15	25
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	8	14
From 65-84 years	4	6	10
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	63.5	60.3	
standard deviation	± 9.63	± 20.74	-
Sex: Female, Male Units: participants			
Female	6	8	14
Male	4	7	11
Race, Customized Units: Subjects			
White/Caucasian	9	14	23
Black/African-American	1	0	1
Captured as "Other"	0	1	1

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	9	14	23
Unknown or Not Reported	0	1	1
Hemoglobin Units: grams per deciliter (g/dL)			
arithmetic mean	9.1	8.7	
standard deviation	± 0.80	± 0.85	-

End points

End points reporting groups

Reporting group title	Parsaclisib 1 mg QD

Reporting group description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group title	Parsaclisib 2.5 mg QD

Reporting group description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group title	Parsaclisib 1 mg QD

Reporting group description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group title	Parsaclisib 2.5 mg QD

Reporting group description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Subject analysis set title	Cohort 1: parsaclisib 1 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received oral parsaclisib 1 mg QD for 12 weeks and did not qualify for a dose increase to 2.5 mg QD starting at Week 6 (they did not continue to require transfusions or they attained a meaningful clinical response [at least a stabilization of a ≥ 2 g/dL increase in hemoglobin from Baseline to Week 6]) were analyzed for pharmacokinetics (PK).

Subject analysis set title	Cohort 1: parsaclisib 2.5 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who initially received oral parsaclisib 1 mg QD, but had their dose increased, with sponsor preapproval, to 2.5 mg QD starting at Week 6 (up to Week 12) because they continued to require transfusions or did not attain a meaningful clinical response (at least a stabilization of a ≥ 2 g/dL increase in hemoglobin from Baseline to Week 6) were analyzed for PK.

Subject analysis set title	Cohort 2: parsaclisib 2.5 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received oral parsaclisib 2.5 mg QD for 12 weeks were analyzed for PK.

Primary: Percentage of participants attaining a complete response at any visit from Week 6 to Week 12

End point title	Percentage of participants attaining a complete response at any visit from Week 6 to Week 12[1]

End point description:

A complete response was defined as hemoglobin >12 grams per deciliter (g/dL) not attributed to a transfusion effect and the normalization of hemolytic markers. No transfusion effect was defined as > 1 week since the last transfusion. Analysis was conducted in members of the Full Analysis Set, defined as all participants who enrolled in the study who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Week 6 to Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not conducted for this endpoint.

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[2]	15[3]		
Units: percentage of participants				
number (not applicable)	20.0	40.0		

Notes:

[2] - Full Analysis Set

[3] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants attaining a partial response at any visit from Week 6 to Week 12

End point title	Percentage of participants attaining a partial response at any visit from Week 6 to Week 12[4]

End point description:

A partial response was defined as hemoglobin 10-12 g/dL or at least a 2 g/dL increase from Baseline not attributed to a transfusion effect and the normalization of hemolytic markers. No transfusion effect was defined as > 1 week since the last transfusion.

End point type	Primary

End point timeframe:

Week 6 to Week 12

Notes:

[4] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[5]	15[6]		
Units: percentage of participants				
number (not applicable)	60.0	66.7		

Notes:

[5] - Full Analysis Set

[6] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE)[7]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related, that occurred after a participant provided informed consent. Abnormal laboratory values or test results occurring after informed consent constituted AEs only if they induced clinical signs or symptoms, were considered clinically meaningful, required therapy, or required changes in the study drug. Anemia and transfusions should not have been reported as AEs unless they represented a clinically meaningful decrease from Baseline in hemoglobin. A TEAE was defined as any AE either reported for the first time or the worsening of a pre-existing event after the first dose of study drug.

End point type	Primary

End point timeframe:

up to 1638 days

Notes:

[7] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[8]	15[9]		
Units: participants	10	15		

Notes:

[8] - Full Analysis Set

[9] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants attaining a complete response during post-Baseline visits

End point title	Percentage of participants attaining a complete response during post-Baseline visits

End point description:

A complete response was defined as hemoglobin >12 g/dL) not attributed to a transfusion effect and the normalization of hemolytic markers. No transfusion effect was defined as > 1 week since the last transfusion.

End point type	Secondary

End point timeframe:

up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[10]	15[11]		
Units: percentage of participants				
number (not applicable)				
Week 1, n=10, 15	0.0	6.7		
Week 2, n=10, 15	10.0	6.7		
Week 4, n=9, 14	22.2	21.4		
Week 6, n=9, 14	22.2	28.6		
Week 8, n=9, 13	22.2	23.1		
Week 10, n=9, 13	22.2	23.1		
Week 12, n=9, 14	22.2	42.9		
Follow-up Month 1, n=2, 3	0.0	0.0		
Follow-up Month 2, n=2, 2	0.0	0.0		
Follow-up Month 3, n=2, 2	0.0	0.0		
Extension End of Treatment, n=6, 10	50.0	50.0		

Notes:

[10] - Full Analysis Set. Only participants with available data were analyzed.

[11] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants attaining a partial response during post-Baseline visits

End point title	Percentage of participants attaining a partial response during post-Baseline visits

End point description:

A partial response was defined as hemoglobin 10-12 g/dL or at least a 2 g/dL increase from Baseline not attributed to a transfusion effect and the normalization of hemolytic markers. No transfusion effect was defined as > 1 week since the last transfusion.

End point type	Secondary

End point timeframe:

up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[12]	15[13]		
Units: percentage of participants				
number (not applicable)				
Week 1, n=10, 15	50.0	53.3		
Week 2, n=10, 15	50.0	66.7		

Week 4, n=9, 14	44.4	64.3		
Week 6, n=9, 14	44.4	50.0		
Week 8, n=9, 13	55.6	61.5		
Week 10, n=9, 13	55.6	61.5		
Week 12, n=9, 14	55.6	64.3		
Follow-up Month 1, n=2, 3	50.0	0.0		
Follow-up Month 2, n=2, 2	0.0	0.0		
Follow-up Month 3, n=2, 2	0.0	50.0		
Extension End of Treatment, n=6, 10	83.3	50.0		

Notes:

[12] - Full Analysis Set. Only participants with available data were analyzed.

[13] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants attaining a ≥ 2 g/dL increase in hemoglobin from Baseline

End point title	Percentage of participants attaining a ≥ 2 g/dL increase in hemoglobin from Baseline
End point description: Hemoglobin levels were assessed throughout the study.	
End point type	Secondary
End point timeframe: up to 1638 days	

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[14]	15[15]		
Units: percentage of participants				
number (not applicable)				
Week 1, n=10, 15	0.0	26.7		
Week 2, n=10, 15	10.0	46.7		
Week 4, n=9, 14	22.2	42.9		
Week 6, n=9, 14	22.2	35.7		
Week 8, n=9, 13	33.3	38.5		
Week 10, n=9, 13	22.2	46.2		
Week 12, n=9, 14	33.3	50.0		
Follow-up Month 1, n=2, 3	0.0	0.0		
Follow-up Month 2, n=2, 2	0.0	0.0		
Follow-up Month 3, n=2, 2	0.0	0.0		
Extension End of Treatment, n=6, 10	66.7	50.0		

Notes:

[14] - Full Analysis Set. Only participants with available data were analyzed.

[15] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin

End point title	Change from Baseline in hemoglobin

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[16]	15[17]		
Units: grams per deciliter (g/dL)				
arithmetic mean (standard deviation)				
Baseline, n=10, 15	9.1 (± 0.80)	8.7 (± 0.85)		
CFB at Week 1, n=10, 15	0.9 (± 0.84)	1.2 (± 1.30)		
CFB at Week 2, n=10, 15	0.6 (± 0.96)	1.5 (± 1.75)		
CFB at Week 4, n=9, 14	0.9 (± 1.06)	1.6 (± 1.79)		
CFB at Week 6, n=9, 14	1.2 (± 0.80)	1.7 (± 1.96)		
CFB at Week 8, n=9, 13	1.2 (± 1.14)	2.0 (± 2.07)		
CFB at Week 10, n=9, 13	1.3 (± 1.14)	2.1 (± 2.22)		
CFB at Week 12, n=9, 14	1.3 (± 1.46)	2.5 (± 2.67)		
CFB at Follow-up Month 1. n=2. 3	0.1 (± 1.06)	-0.4 (± 0.72)		
CFB at Follow-up Month 2, n=2, 2	-0.1 (± 0.28)	-0.2 (± 0.28)		
CFB at Follow-up Month 3, n=2, 2	0.5 (± 0.92)	0.2 (± 1.63)		
CFB at Extension End of Treatment, n=6, 10	2.8 (± 2.70)	2.6 (± 2.73)		

Notes:

[16] - Full Analysis Set. Only participants with available data were analyzed.

[17] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in hemoglobin

End point title	Percentage change from Baseline in hemoglobin

End point description:

Percentage change from Baseline was calculated as: ([post-Baseline value minus the Baseline value] / Baseline value) x 100.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[18]	15[19]		
Units: percent change				
arithmetic mean (standard deviation)				
Week 1, n=10, 15	10.1 (± 9.23)	14.4 (± 16.31)		
Week 2, n=10, 15	6.0 (± 10.26)	18.5 (± 20.71)		
Week 4, n=9, 14	9.9 (± 10.83)	19.2 (± 20.65)		
Week 6, n=9, 14	13.3 (± 8.35)	19.5 (± 22.35)		
Week 8, n=9, 13	12.7 (± 12.16)	23.4 (± 24.57)		
Week 10, n=9, 13	14.1 (± 11.54)	25.1 (± 26.30)		
Week 12, n=9, 14	13.9 (± 15.72)	30.2 (± 33.95)		
Follow-up Month 1, n=2, 3	0.0 (± 12.26)	-4.1 (± 7.92)		
Follow-up Month 2, n=2, 2	-1.0 (± 3.18)	-2.0 (± 2.89)		
Follow-up Month 3, n=2, 2	5.7 (± 11.14)	2.0 (± 17.32)		
Extension End of Treatment, n=6, 10	31.6 (± 33.86)	30.9 (± 33.52)		

Notes:

[18] - Full Analysis Set. Only participants with available data were analyzed.

[19] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants requiring transfusions

End point title	Percentage of participants requiring transfusions

End point description:

A participant was defined to have required a transfusion if his or her last transfusion was within 7 days of the visit date.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[20]	15[21]		
Units: percentage of participants				
number (not applicable)				
Week 1, n=10, 15	0.0	6.7		
Week 2, n=10, 15	0.0	0.0		
Week 4, n=9, 14	22.2	0.0		
Week 6, n=9, 14	0.0	0.0		
Week 8, n=9, 13	0.0	15.4		
Week 10, n=9, 13	0.0	7.7		
Week 12, n=9, 14	0.0	0.0		
Follow-up Month 1, n=2, 3	0.0	0.0		
Follow-up Month 2, n=2, 2	0.0	0.0		
Follow-up Month 3, n=2, 2	0.0	0.0		

Extension End of Treatment, n=6, 10	0.0	0.0		

Notes:

[20] - Full Analysis Set. Only participants with available data were analyzed.

[21] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieved normalization of hemoglobin, haptoglobin, lactate dehydrogenase (LDH), reticulocyte count, total bilirubin, direct bilirubin, and indirect bilirubin

End point title	Percentage of participants who achieved normalization of hemoglobin, haptoglobin, lactate dehydrogenase (LDH), reticulocyte count, total bilirubin, direct bilirubin, and indirect bilirubin

End point description:

Normalization was determined by the Investigator based on normal ranges for the clinical reference laboratory. 8888=No participants were analyzed at this time point.

End point type	Secondary

End point timeframe:

up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[22]	15[23]		
Units: percentage of participants				
number (not applicable)				
Hemoglobin, Week 1, n=10, 15	0.0	6.7		
Hemoglobin, Week 2, n=10, 15	0.0	6.7		
Hemoglobin, Week 4, n=9, 14	0.0	14.3		
Hemoglobin, Week 6, n=9, 14	0.0	21.4		
Hemoglobin, Week 8, n=9, 13	0.0	15.4		
Hemoglobin, Week 10, n=9, 13	0.0	15.4		
Hemoglobin, Week 12, n=9, 14	11.1	35.7		
Hemoglobin, Follow-up Month 1, n=2, 3	0.0	0.0		
Hemoglobin, Follow-up Month 2, n=2, 2	0.0	0.0		
Hemoglobin, Follow-up Month 3, n=2, 2	0.0	0.0		
Haptoglobin, Week 1, n=8, 9	12.5	22.2		
Haptoglobin, Week 2, n=6, 11	0.0	18.2		
Haptoglobin, Week 4, n=7, 13	14.3	15.4		
Haptoglobin, Week 6, n=7, 13	14.3	23.1		
Haptoglobin, Week 8, n=7, 9	0.0	11.1		
Haptoglobin, Week 10, n=8, 7	12.5	14.3		
Haptoglobin, Week 12, n=7, 12	14.3	25.0		
Haptoglobin, Follow-up Month 2, n=1, 0	0.0	0.0		
LDH, Week 1, n=8, 10	12.5	10.0		
LDH, Week 2, n=9, 12	11.1	16.7		

LDH, Week 4, n=8, 14	12.5	21.4		
LDH, Week 6, n=7, 14	14.3	14.3		
LDH, Week 8, n=8, 11	25.0	9.1		
LDH, Week 10, n=9, 11	33.3	9.1		
LDH, Week 12, n=8, 13	25.0	15.4		
LDH, Follow-up Month 2, n=1, 0	0.0	8888		
Reticulocytes, Week 1, n=10, 14	20.0	14.3		
Reticulocytes, Week 2, n=7, 15	28.6	20.0		
Reticulocytes, Week 4, n=8, 14	25.0	28.6		
Reticulocytes, Week 6, n=9, 14	22.2	28.6		
Reticulocytes, Week 8, n=8, 12	25.0	25.0		
Reticulocytes, Week 10, n=6, 12	33.3	25.0		
Reticulocytes, Week 12, n=8, 13	37.5	23.1		
Reticulocytes, Follow-up Month 1, n=2, 3	50.0	0.0		
Reticulocytes, Follow-up Month 2, n=2, 2	50.0	0.0		
Reticulocytes, Follow-up Month 3, n=2, 1	50.0	8888		
Total bilirubin, Week 1, n=10, 15	30.0	40.0		
Total bilirubin, Week 2, n=10, 15	20.0	40.0		
Total bilirubin, Week 4, n=9, 14	33.3	42.9		
Total bilirubin, Week 6, n=9, 14	33.3	42.9		
Total bilirubin, Week 8, n=9, 12	44.4	50.0		
Total bilirubin, Week 10, n=9, 11	44.4	36.4		
Total bilirubin, Week 12, n=9, 14	44.4	50.0		
Total bilirubin, Follow-up Month 2, n=1, 0	100.0	8888		
Direct bilirubin, Week 1, n=6, 8	0.0	25.0		
Direct bilirubin, Week 2, n=8, 9	12.5	22.2		
Direct bilirubin, Week 4, n=6, 8	0.0	12.5		
Direct bilirubin, Week 6, n=6, 8	0.0	25.0		
Direct bilirubin, Week 8, n=5, 5	0.0	20.0		
Direct bilirubin, Week 10, n=5, 7	0.0	14.3		
Direct bilirubin, Week 12, n=5, 7	0.0	28.6		
Indirect bilirubin, Week 1, n=6, 8	0.0	12.5		
Indirect bilirubin, Week 2, n=8, 9	0.0	0.0		
Indirect bilirubin, Week 4, n=6, 8	0.0	0.0		
Indirect bilirubin, Week 6, n=6, 8	0.0	0.0		
Indirect bilirubin, Week 8, n=5, 5	0.0	0.0		
Indirect bilirubin, Week 10, n=5, 7	0.0	0.0		
Indirect bilirubin, Week 12, n=5, 7	0.0	0.0		

Notes:

[22] - Full Analysis Set. Only participants with available data were analyzed.

[23] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants requiring a prednisone dose change (increase or decrease)

End point title	Percentage of participants requiring a prednisone dose change (increase or decrease)

End point description:

Prednisone use was monitored throughout the study.

End point type	Secondary

End point timeframe:

up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[24]	15[25]		
Units: percentage of participants				
number (not applicable)				
Week 1, increased	0.0	6.7		
Week 1, decreased	20.0	6.7		
Week 2, increased	0.0	0.0		
Week 2, decreased	20.0	13.3		
Week 4, increased	0.0	0.0		
Week 4, decreased	10.0	6.7		
Week 6, increased	0.0	0.0		
Week 6, decreased	10.0	6.7		
Week 8, increased	0.0	0.0		
Week 8, decreased	10.0	6.7		
Week 10, increased	0.0	0.0		
Week 10, decreased	10.0	6.7		
Week 12, increased	0.0	0.0		
Week 12, decreased	10.0	20.0		
Extension End of Treatment, increased	10.0	6.7		
Extension End of Treatment, decreased	10.0	6.7		

Notes:

[24] - Full Analysis Set

[25] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) subscale scores

End point title	Change from Baseline in the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) subscale scores

End point description:

The FACIT-F subscale is a 13-item instrument designed to assess fatigue/tiredness and its impact on daily activities and functioning in a number of chronic diseases. Participants were asked to respond to 13 statements that people with the illness have said are important on the following scale: 0, not at all; 1, a little bit; 2, somewhat; 3, quite a bit; 4, very much. Participants were asked to indicate the response as it applied to the last 7 days. The total fatigue subscale score ranges from 0 to 52; a higher score indicates more severe impact on daily activities and functioning. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[26]	15[27]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=10, 15	32.6 (± 12.80)	30.1 (± 13.88)		
CFB at Week 6, n=9, 14	6.7 (± 12.44)	8.2 (± 9.28)		
CFB at Week 12, n=9, 14	6.2 (± 16.08)	5.4 (± 15.49)		
CFB at Follow-up Month 1, n=2, 3	2.0 (± 2.83)	2.3 (± 10.69)		
CFB at Follow-up Month 2, n=2, 2	1.5 (± 7.78)	7.0 (± 15.56)		
CFB at Follow-up Month 3, n=2, 2	-2.0 (± 21.21)	13.0 (± 14.14)		

Notes:

[26] - Full Analysis Set. Only participants with available data were analyzed.

[27] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Cmax of parsaclisib

End point title	Mean Cmax of parsaclisib

End point description:

Cmax was defined as the maximum observed concentration. Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose. Analysis was conducted in members of the Pharmacokinetic (PK)/Pharmacodynamic (PD) Evaluable Population, comprised of all participants who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK or biomarker assessment.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[28]	6[29]	15[30]	
Units: nanomoles per Liter (nmol/L)				
geometric mean (geometric coefficient of variation)				
Week 2	94.9 (± 33.5)	8888 (± 8888)	191 (± 56.2)	
Week 8	107 (± 17.8)	219 (± 45.2)	199 (± 39.7)	

Notes:

[28] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[29] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[30] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

Statistical analysis title	Cmax
Statistical analysis description: Week 2	
Comparison groups	Cohort 1: parsaclisib 1 mg QD v Cohort 2: parsaclisib 2.5 mg QD
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2815
Method	ANOVA

Secondary: Mean tmax of parsaclisib

End point title	Mean tmax of parsaclisib
End point description: tmax was defined as the time to the maximum concentration. Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. -8888, 8888=No participants were analyzed at this time point at this dose.	
End point type	Secondary
End point timeframe: predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8	

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[31]	6[32]	15[33]	
Units: hours				
median (full range (min-max))				
Week 2	1.00 (0.00 to 2.07)	8888 (-8888 to 8888)	1.00 (0.00 to 3.33)	
Week 8	1.00 (1.00 to 1.05)	1.04 (0.917 to 2.00)	1.02 (0.833 to 4.00)	

Notes:

[31] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[32] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[33] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

Statistical analysis title	tmax
Statistical analysis description: Week 2	
Comparison groups	Cohort 1: parsaclisib 1 mg QD v Cohort 2: parsaclisib 2.5 mg QD

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2921
Method	Kruskal-wallis

Secondary: Mean AUC0-4 of parsaclisib

End point title	Mean AUC0-4 of parsaclisib

End point description:

AUC0-4 was defined as the area under the concentration-time curve from time = 0 to 4 hours postdose. Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[34]	6[35]	15[36]	
Units: hours*nmol/L				
geometric mean (geometric coefficient of variation)				
Week 2	260 (± 24.0)	8888 (± 8888)	542 (± 46.7)	
Week 8	287 (± 5.73)	631 (± 41.9)	524 (± 50.8)	

Notes:

[34] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[35] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[36] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

Statistical analysis title	AUC0-4

Statistical analysis description:

Week 2

Comparison groups	Cohort 1: parsaclisib 1 mg QD v Cohort 2: parsaclisib 2.5 mg QD
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2676
Method	ANOVA

Secondary: Mean Cmin of parsaclisib

End point title	Mean Cmin of parsaclisib

End point description:

Cmin was defined as the minimum observed concentration over the dose interval. Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[37]	6[38]	15[39]	
Units: nmol/L				
geometric mean (geometric coefficient of variation)				
Week 2	20.0 (± 88.7)	8888 (± 8888)	32.3 (± 55.4)	
Week 8	14.2 (± 80.9)	39.4 (± 26.1)	25.5 (± 91.4)	

Notes:

[37] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[38] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[39] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

Statistical analysis title	Cmin

Statistical analysis description:

Week 2

Comparison groups	Cohort 1: parsaclisib 1 mg QD v Cohort 2: parsaclisib 2.5 mg QD
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1267
Method	ANOVA

Secondary: Mean Clast of parsaclisib

End point title	Mean Clast of parsaclisib

End point description:

Clast was defined as the last measurable concentration (above the quantification limit). Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[40]	6[41]	15[42]	
Units: nmol/L				
geometric mean (geometric coefficient of variation)				
Week 2	59.6 (± 21.3)	8888 (± 8888)	128 (± 53.3)	
Week 8	62.4 (± 7.31)	134 (± 54.2)	138 (± 42.3)	

Notes:

[40] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[41] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[42] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean AUC0-t of parsaclisib

End point title	Mean AUC0-t of parsaclisib

End point description:

AUC0-t was defined as the area under the concentration-time curve from time = 0 to the last measureable concentration at time = t. Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[43]	6[44]	15[45]	
Units: hours*nmol/L				
geometric mean (geometric coefficient of variation)				
Week 2	260 (± 24.0)	8888 (± 8888)	553 (± 41.3)	
Week 8	287 (± 5.73)	633 (± 42.4)	524 (± 50.8)	

Notes:

[43] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[44] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[45] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in reticulocyte count

End point title	Change from Baseline in reticulocyte count

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=The

standard deviation cannot be calculated for a single participant. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[46]	15[47]		
Units: 10^9 cells per Liter (10^9 cells/L)				
arithmetic mean (standard deviation)				
Baseline in the Treatment Period (TP), n=10, 14	240.7460 (± 110.0788)	268.1429 (± 128.3266)		
CFB at Week 1 of the TP, n=10, 13	-6.8244 (± 75.4853)	-37.9910 (± 90.4026)		
CFB at Week 2 of the TP, n=7, 14	-17.2571 (± 87.7742)	-55.4934 (± 88.8296)		
CFB at Week 4 of the TP, n=8, 13	-24.8375 (± 52.5381)	-67.8155 (± 86.6172)		
CFB at Week 6 of the TP, n=9, 13	-45.4739 (± 61.9611)	-46.3599 (± 106.7383)		
CFB at Week 8 of the TP, n=8, 11	-43.0819 (± 87.7012)	-74.8763 (± 97.2582)		
CFB at Week 10 of the TP, n=6, 11	-24.3667 (± 55.3112)	-50.4759 (± 104.4132)		
CFB at Week 12 of the TP, n=8, 12	-27.1250 (± 63.3308)	-80.7566 (± 112.2789)		
CFB at Follow-up Month 1 of the TP, n=2, 3	0.0000 (± 26.1630)	2.6297 (± 16.8763)		
CFB Follow-up Month 2 of the TP, n=2, 2	-18.2000 (± 17.6777)	-16.4500 (± 23.2638)		
CFB at Follow-up Month 3 of the TP, n=2, 1	-31.1500 (± 11.2430)	-131.900 (± 9999)		
Baseline of the Extension Period (EP), n=7, 10	233.3086 (± 121.4996)	243.9526 (± 104.4420)		
CFB at EP End of Treatment, n=5, 9	184.4096 (± 102.9469)	191.7013 (± 131.3629)		

Notes:

[46] - Full Analysis Set. Only participants with available data were analyzed.

[47] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Tlast of parsaclisib

End point title	Mean Tlast of parsaclisib

End point description:

Tlast was defined as the time of the last measurable concentration (above the quantification limit). Participants in Cohort 1 were not eligible to receive parsaclisib 2.5 mg at Week 2. 8888=No participants were analyzed at this time point at this dose.

End point type	Secondary

End point timeframe:

predose at Weeks 1 and 12; predose and 1, 2, and 4 hours postdose at Weeks 2 and 8

End point values	Cohort 1: parsaclisib 1 mg QD	Cohort 1: parsaclisib 2.5 mg QD	Cohort 2: parsaclisib 2.5 mg QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9[48]	6[49]	15[50]	
Units: hours				
geometric mean (geometric coefficient of variation)				
Week 2	3.85 (± 4.77)	8888 (± 8888)	3.98 (± 9.67)	
Week 8	3.83 (± 5.84)	3.92 (± 3.71)	3.84 (± 6.56)	

Notes:

[48] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[49] - PK/PD Evaluable Population. Only participants with available data were analyzed.

[50] - PK/PD Evaluable Population. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cold hemagglutinin levels

End point title	Change from Baseline in cold hemagglutinin levels
End point description:	
Change from Baseline was calculated as the post-Baseline value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline; Week 12	

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[51]	6[52]		
Units: titer				
arithmetic mean (standard deviation)				
Baseline	3200 (± 2715.29)	11206.67 (± 10309.03)		
Change from Baseline at Week 12	-1760 (± 1131.371)	960 (± 1357.645)		

Notes:

[51] - Full Analysis Set. Only participants with available data were analyzed.

[52] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cardiolipin immunoglobulin G (IgG) antibody and cardiolipin immunoglobulin M (IgM) antibody

End point title	Change from Baseline in cardiolipin immunoglobulin G (IgG)

	antibody and cardiolipin immunoglobulin M (IgM) antibody

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=No participants were analyzed at this time point.

End point type	Secondary

End point timeframe:

Baseline; Week 12

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[53]	12[54]		
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)				
IgG at Baseline, n=9, 12	0.0 (± 0.00)	5.8 (± 20.21)		
Change from Baseline in IgG at Week 12, n=0, 0	9999 (± 9999)	9999 (± 9999)		
IgM at Baseline, n=9, 12	0.0 (± 0.0)	1.7 (± 3.24)		
Change from Baseline in IgM at Week 12, n=0, 0	9999 (± 9999)	9999 (± 9999)		

Notes:

[53] - Full Analysis Set. Only participants with available data were analyzed.

[54] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in haptoglobin, total bilirubin, direct bilirubin, and indirect bilirubin

End point title	Change from Baseline in haptoglobin, total bilirubin, direct bilirubin, and indirect bilirubin

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=The standard deviation cannot be calculated for a single participant. 8888=No participants were analyzed at this time point. CFB=Change from Baseline. FU=Follow-up. Bili=Bilirubin.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[55]	15[56]		
Units: micromoles (µmol)/L				
arithmetic mean (standard deviation)				
Haptoglobin, Baseline of the TP, n=10, 14	0.00 (± 0.000)	0.81 (± 3.020)		
Haptoglobin, CFB at Week 1 of the TP, n=8, 9	0.65 (± 1.838)	1.20 (± 1.879)		

Haptoglobin, CFB at Week 2 of the TP, n=6, 11	0.00 (± 0.000)	0.90 (± 1.640)		
Haptoglobin, CFB at Week 4 of the TP, n=7, 13	0.73 (± 1.928)	0.75 (± 2.066)		
Haptoglobin, CFB at Week 6 of the TP, n=7, 13	1.09 (± 2.873)	2.48 (± 5.069)		
Haptoglobin, CFB at Week 8 of the TP, n=7, 9	0.00 (± 0.000)	1.36 (± 3.293)		
Haptoglobin, CFB at Week 10 of the TP, n=8, 7	1.55 (± 3.579)	1.04 (± 2.759)		
Haptoglobin, CFB at Week 12 of the TP, n=7, 12	0.73 (± 1.928)	1.34 (± 2.654)		
Haptoglobin, CFB at FU Month 2 of the TP, n=1, 0	0.00 (± 9999)	8888 (± 8888)		
Haptoglobin, Baseline of the EP, n=7, 11	0.0000 (± 0.0000)	0.0000 (± 0.0000)		
Haptoglobin, CFB at Extension EOT, n=5, 7	2.9200 (± 5.4906)	4.0000 (± 5.2386)		
Indirect bili, Baseline of the TP, n=6, 14	32.7 (± 13.29)	36.1 (± 22.77)		
Indirect bili, CFB at Week 1 of the TP, n=5, 8	-6.2 (± 7.66)	-11.9 (± 18.73)		
Indirect bili, CFB at Week 2 of the TP, n=6, 9	-2.3 (± 4.59)	-11.6 (± 17.67)		
Indirect bili, CFB at Week 4 of the TP, n=5, 8	-7.6 (± 9.63)	-11.1 (± 21.63)		
Indirect bili, CFB at Week 6 of the TP, n=5, 8	-11.0 (± 14.20)	-13.6 (± 22.39)		
Indirect bili, CFB at Week 8 of the TP, n=4, 5	-3.5 (± 15.63)	-16.8 (± 34.58)		
Indirect bili, CFB at Week 10 of the TP, n=4, 7	-6.5 (± 9.95)	-14.7 (± 25.44)		
Indirect bili, CFB at Week 12 of the TP, n=4, 7	-2.5 (± 13.03)	-17.0 (± 24.39)		
Indirect bili, Baseline of the EP, n=4, 10	35.2500 (± 15.7348)	33.4000 (± 24.5185)		
Indirect bili, CFB at Extension EOT, n=1, 3	-34.3610 (± 9999)	-0.7057 (± 8.3763)		
Total bili, Baseline of the TP, n=10, 15	34.7 (± 19.58)	54.3 (± 51.65)		
Total bili, CFB at Week 1 of the TP, n=10, 15	-2.8 (± 14.65)	-18.3 (± 34.92)		
Total bili, CFB at Week 2 of the TP, n=10, 15	1.7 (± 11.94)	-18.7 (± 34.92)		
Total bili, CFB at Week 4 of the TP, n=9, 14	-2.2 (± 16.53)	-19.5 (± 35.14)		
Total bili, CFB at Week 6 of the TP, n=9, 14	-3.6 (± 22.82)	-21.6 (± 31.27)		
Total bili, CFB at Week 8 of the TP, n=9, 12	-0.9 (± 17.24)	-22.3 (± 41.89)		
Total bili, CFB at Week 10 of the TP, n=9, 11	-2.7 (± 17.59)	-23.6 (± 29.83)		
Total bili, CFB at Week 12 of the TP, n=9, 14	-2.0 (± 14.86)	-21.3 (± 24.03)		
Total bili, CFB at FU Month 2 of the TP, n=1, 0	2.0 (± 9999)	8888 (± 8888)		
Total bili, CFB at FU Month 2 of the TP, n=7, 11	34.7143 (± 22.2165)	40.0000 (± 27.6586)		
Total bili, CFB at Extension EOT, n=6, 9	-11.7758 (± 31.5724)	-10.6219 (± 24.1217)		
Direct bili, Baseline of the TP, n=6, 14	14.7 (± 2.16)	22.9 (± 39.88)		
Direct bili, CFB at Week 1 of the TP, n=5, 8	-1.6 (± 4.72)	-12.1 (± 33.14)		

Direct bili, CFB at Week 2 of the TP, n=6, 9	-0.5 (± 1.97)	-12.0 (± 33.84)		
Direct bili, CFB at Week 4 of the TP, n=5, 8	-1.2 (± 4.27)	-14.1 (± 38.46)		
Direct bili, CFB at Week 6 of the TP, n=5, 8	-1.2 (± 5.89)	-14.5 (± 35.89)		
Direct bili, CFB at Week 8 of the TP, n=4, 5	0.0 (± 4.24)	-22.0 (± 49.79)		
Direct bili, CFB at Week 10 of the TP, n=4, 7	-0.3 (± 2.99)	-13.7 (± 32.36)		
Direct bili, CFB at Week 12 of the TP, n=4, 7	1.0 (± 4.76)	-12.4 (± 28.98)		
Direct bili, Baseline of the EP, n=4, 10	14.2500 (± 2.6300)	11.70000 (± 2.9458)		
Direct bili, CFB at Extension EOT, n=2, 7	-7.1322 (± 3.4977)	0.1213 (± 6.2545)		

Notes:

[55] - Full Analysis Set. Only participants with available data were analyzed.

[56] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lactate dehydrogenase (LDH)

End point title	Change from Baseline in lactate dehydrogenase (LDH)

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=The standard deviation cannot be calculated for a single participant. 8888=No participants were analyzed at this time point. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[57]	15[58]		
Units: Units (U)/L				
arithmetic mean (standard deviation)				
Baseline of the TP, n=10, 14	328.9 (± 78.34)	469.0 (± 208.96)		
CFB at Week 1 of the TP, n=8, 10	11.8 (± 70.89)	-85.1 (± 128.31)		
CFB at Week 2 of the TP, n=9, 11	32.2 (± 167.98)	-82.8 (± 129.32)		
CFB at Week 4 of the TP, n=8, 13	65.8 (± 190.35)	-61.8 (± 152.80)		
CFB at Week 6 of the TP, n=7, 13	23.9 (± 133.94)	-71.4 (± 137.51)		
CFB at Week 8 of the TP, n=8, 10	59.4 (± 144.20)	-66.8 (± 144.36)		
CFB at Week 10 of the TP, n=9, 10	36.6 (± 118.68)	-73.5 (± 153.74)		

CFB at Week 12 of the TP, n=8, 13	33.8 (± 117.39)	-66.8 (± 137.28)		
CFB at Follow-up Month 2 of the TP, n=1, 0	44.0 (± 9999)	8888 (± 8888)		
Baseline of the EP, n=7, 10	316.9 (± 86.74)	439.8 (± 178.39)		
CFB at Extension End of Treatment, n=5, 8	0.0 (± 173.26)	105.0 (± 444.64)		

Notes:

[57] - Full Analysis Set. Only participants with available data were analyzed.

[58] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CH50

End point title	Change from Baseline in CH50

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=The standard deviation cannot be calculated for a single participant. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[59]	15[60]		
Units: microgram equivalents per Liter (µgEq/L)				
arithmetic mean (standard deviation)				
Baseline of the TP, n=9, 14	84.3 (± 53.91)	69.5 (± 53.53)		
CFB at Week 12 of the TP, n=8, 13	5.4 (± 21.66)	17.2 (± 31.74)		
Baseline of the EP, n=6, 10	91.5 (± 52.20)	67.6 (± 56.61)		
CFB at Extension End of Treatment, n=1, 1	27.0 (± 9999)	12.0 (± 9999)		

Notes:

[59] - Full Analysis Set. Only participants with available data were analyzed.

[60] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Complement C3 and Complement C4

End point title	Change from Baseline in Complement C3 and Complement C4

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. 9999=The standard deviation cannot be calculated for a single participant. 8888=No participants were analyzed at this time point. CFB=Change from Baseline.

End point type	Secondary

End point timeframe:

Baseline; up to 1638 days

End point values	Parsaclisib 1 mg QD	Parsaclisib 2.5 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[61]	15[62]		
Units: grams per Liter (g/L)				
arithmetic mean (standard deviation)				
Complement C3, Baseline of the TP, n=8, 14	0.96 (± 0.288)	0.91 (± 0.183)		
Complement C3, CFB at Week 2 of the TP, n=1, 0	0.20 (± 9999)	8888 (± 8888)		
Complement C3, CFB at Week 6 of the TP, n=1, 0	0.20 (± 9999)	8888 (± 8888)		
Complement C3, CFB at Week 12 of the TP, n=7, 13	0.04 (± 0.098)	0.12 (± 0.199)		
Complement C3, Baseline of the EP, n=5, 10	0.9400 (± 0.1949)	0.9400 (± 0.1897)		
Complement C3, CFB at EOT in the EP, n=1, 1	0.1000 (± 9999)	0.1400 (± 9999)		
Complement C4, Baseline of the TP, n=8, 14	0.1736 (± 0.0974)	0.1242 (± 0.1046)		
Complement C4, CFB at Week 2 of the TP, n=1, 0	0.0410 (± 9999)	8888 (± 8888)		
Complement C4, CFB at Week 6 of the TP, n=1, 0	0.0330 (± 9999)	8888 (± 8888)		
Complement C4, CFB at Week 12 of the TP, n=7, 13	0.0136 (± 0.0283)	0.0274 (± 0.0366)		
Complement C4, Baseline of the EP, n=5, 10	0.1628 (± 0.0407)	0.1160 (± 0.0842)		
Complement C4, CFB at Extension EOT, n=1, 1	0.0170 (± 9999)	0.1100 (± 9999)		

Notes:

[61] - Full Analysis Set. Only participants with available data were analyzed.

[62] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 1638 days

Adverse event reporting additional description:

As dose increases and decreases, based on clinical benefit and tolerability issues, respectively, were allowed during the course of the study for participants randomized to receive both 1 mg and 2.5 mg, AEs are reported per the treatment participants were randomized to rather than the dose level that was administered at the time the AE occurred.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Parsaclisib 2.5 mg QD

Reporting group description:

Participants received oral parsaclisib 2.5 mg QD for 12 weeks. If there were any tolerability issues in individual participants, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period could have entered into an Extension Period, during which they, with sponsor approval, continued to receive parsaclisib 2.5 mg QD until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. Following the last dose of parsaclisib, in either the Treatment Period (for participants not entering the Extension Period) or the Extension Period, participants were eligible for a 12-week (3-month) follow-up period.

Reporting group title	Parsaclisib 1 mg QD

Reporting group description:

Participants received oral parsaclisib once daily (QD) for 12 weeks at an initial dose of parsaclisib 1 milligram (mg). At Week 6, participants who continued to require transfusions or did not attain at least a stabilization of a ≥ 2 grams per deciliter (g/dL) increase in hemoglobin from Baseline to Week 6 may have had their dose increased to parsaclisib 2.5 mg QD until Week 12. If there were tolerability issues, the dose could have been decreased to 1 mg. Participants who continued to receive clinical benefit after the 12-week Treatment Period (TP) could have entered into an Extension Period (EP), during which they continued to receive parsaclisib 1 mg or 2.5 mg QD until the drug was available through another clinical study, was commercially available, or the sponsor stopped the study or study drug development. Following the last dose of parsaclisib, in either the TP (for participants not entering the EP) or the EP, participants were eligible for a 12-week (3-month) follow-up period.

Serious adverse events	Parsaclisib 2.5 mg QD	Parsaclisib 1 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	6 / 10 (60.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes insipidus			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Amoebic dysentery			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterococcal infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection reactivation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter colitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical mycobacterial infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	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	Parsaclisib 2.5 mg QD	Parsaclisib 1 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	10 / 10 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypertension			

subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	2	
Chest discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	4 / 15 (26.67%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Injection site pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	6 / 15 (40.00%)	4 / 10 (40.00%)	
occurrences (all)	6	7	
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 15 (6.67%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	1 / 10 (10.00%)	
occurrences (all)	2	2	
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tachypnoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pneumonitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Delirium			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Disorientation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

Insomnia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Complement factor C4 decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Breath sounds abnormal			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Blood potassium decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Lipids increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Urine protein/creatinine ratio increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Total complement activity decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
SARS-CoV-2 test positive			

subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Cardiac discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Mitral valve incompetence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Headache			
subjects affected / exposed	2 / 15 (13.33%)	3 / 10 (30.00%)	
occurrences (all)	4	4	
Tremor			

subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Autoimmune haemolytic anaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eosinophilia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Haemolysis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 10 (20.00%)	
occurrences (all)	2	4	
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Macular oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vitreous haemorrhage			

subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	5 / 15 (33.33%)	4 / 10 (40.00%)	
occurrences (all)	5	5	
Dry mouth			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Crohn's disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eosinophilic colitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Ileus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

Nausea			
subjects affected / exposed	1 / 15 (6.67%)	3 / 10 (30.00%)	
occurrences (all)	1	4	
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Jaundice			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Drug eruption			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Lichen planus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Palmoplantar keratoderma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psoriasis			

subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Purpura			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 15 (20.00%)	2 / 10 (20.00%)	
occurrences (all)	5	3	
Rash erythematous			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Rash macular			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			
subjects affected / exposed	0 / 15 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	3	
Skin ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Urinary tract obstruction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Bone pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Haemarthrosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	3 / 15 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Osteoporosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Plantar fasciitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infections and infestations			
Bacteraemia			

subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Cystitis				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Cytomegalovirus infection reactivation				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Conjunctivitis				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
COVID-19				
subjects affected / exposed	3 / 15 (20.00%)	0 / 10 (0.00%)		
occurrences (all)	6	0		
Fungal infection				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Gastroenteritis				
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Gastroenteritis viral				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Influenza				
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Oral candidiasis				
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)		
occurrences (all)	1	1		
Oropharyngeal candidiasis				
subjects affected / exposed	0 / 15 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Upper respiratory tract infection				
subjects affected / exposed	1 / 15 (6.67%)	1 / 10 (10.00%)		
occurrences (all)	1	2		

Pneumonia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fluid overload			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fluid retention			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Hyperuricaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Hypomagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2018	The primary purpose of this amendment was to limit the autoimmune hemolytic anemia (AIHA) population to participants who had disease progression after treatment with standard therapies and to add a stopping rule for futility.
20 June 2018	The primary purpose of this amendment was to clarify that the AIHA population enrolled in this study did not include treatment-naive participants and to provide further information on sample size determination.
01 February 2019	The primary purpose of this amendment was to add an extension period for participants who were receiving clinical benefit from the study treatment and to provide guidance for hematology panel collection.
31 October 2019	The primary purpose of this amendment was to increase the number of participants in Cohort 2 (from 10 to approximately 15) and change the proportion of cold agglutinin disease (CAD) and warm AIHA patients. These changes were based on the recommendations from the internal Safety Review Committee meeting.
02 November 2020	The primary purpose of this amendment was to allow participants in the open-label extension period to continue to receive treatment until the drug was available through another clinical study, or was commercially available, or the sponsor stopped the study or the study drug development. In addition, due to the impact of the COVID-19 pandemic on study enrollment, and the rare occurrence of patients with CAD, Cohort 2 changed the enrollment of CAD AIHA to approximately 5 CAD AIHA participants.
07 September 2022	The primary purpose of this amendment was to describe risks associated with COVID-19.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported