Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Parsaclisib in Participants with Primary Warm Autoimmune Hemolytic Anemia (PATHWAY)

Summary

EudraCT number	2021-002844-66
Trial protocol	DE AT IT ES NL HU FR
Global end of trial date	29 April 2024

Results information

Result version number	v1
This version publication date	25 October 2024
First version publication date	25 October 2024

Trial information

Trial identification

Sponsor protocol code	INCB 50465-309

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	29 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of parsaclisib compared with placebo in participants with Primary Warm Autoimmune Hemolytic Anemia (wAIHA).

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki (Brazil 2013) and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations, including WMO (Medical Research Involving Human Participants Act) and Clinical Trials Regulation (European Union) No. 536/2014, in which the study was being conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 2022
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	Austria: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	13
EEA total number of subjects	10

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)	7
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was designed to evaluate parsaclisib 2.5 mg QD compared with placebo over a 24-week double-blind treatment period followed by a 24-week open-label treatment period with parsaclisib. Participants could then continue to receive parsaclisib in a long-term extension period.

Period 1

Period 1 title	24-week Double-blind Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib

Arm description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

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 QD

Arm title	Placebo followed by parsaclisib

Arm description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

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

Dosage and administration details:

2.5 mg QD

Number of subjects in period 1	Parsaclisib	Placebo followed by parsaclisib
Started	7	6
Completed	4	4
Not completed	3	2
Physician decision	1	-
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Study Terminated by Sponsor	1	1

Period 2

Period 2 title	24-week Open-label Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib

Arm description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

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 QD

Arm title	Placebo followed by parsaclisib

Arm description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

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 QD

Number of subjects in period 2	Parsaclisib	Placebo followed by parsaclisib
Started	4	4
Completed	2	2
Not completed	2	2
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	2

Period 3

Period 3 title	Long-term Extension Period (~2 years)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib

Arm description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

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 QD

Arm title	Placebo followed by parsaclisib

Arm description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

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 QD

Number of subjects in period 3	Parsaclisib	Placebo followed by parsaclisib
Started	2	2
Completed	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Parsaclisib
Reporting group description:	
Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.	
Reporting group title	Placebo followed by parsaclisib
Reporting group description:	
Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.	

Reporting group values	Parsaclisib	Placebo followed by parsaclisib	Total
Number of subjects	7	6	13
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)	3	4	7
From 65-84 years	4	2	6
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	62.3	57.8	
standard deviation	± 14.28	± 15.54	-
Sex: Female, Male Units: participants			
Female	4	6	10
Male	3	0	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	7	4	11
Unknown or Not Reported	0	1	1
Race/Ethnicity, Customized Units: Subjects			
White/Caucasian	6	4	10
Asian	1	1	2
Missing	0	1	1

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period.

Reporting group values	Placebo		
Number of subjects	6		
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)	4		
From 65-84 years	2		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male Units: participants			
Female			
Male			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
Race/Ethnicity, Customized Units: Subjects			
White/Caucasian			
Asian			
Missing			

End points

End points reporting groups

Reporting group title	Parsaclisib

Reporting group description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

Reporting group title	Placebo followed by parsaclisib

Reporting group description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

Reporting group title	Parsaclisib

Reporting group description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

Reporting group title	Placebo followed by parsaclisib

Reporting group description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

Reporting group title	Parsaclisib

Reporting group description:

Participants received parsaclisib 2.5 milligrams (mg) once daily (QD) for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for an additional 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

Reporting group title	Placebo followed by parsaclisib

Reporting group description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period. Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment had the option of continuing into an open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD, and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years. Participants may have received parsaclisib before reaching Week 24.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received matching placebo QD for 24 weeks during the double-blind treatment period.

Primary: Percentage of participants attaining a durable hemoglobin response

End point title	Percentage of participants attaining a durable hemoglobin response[1]

End point description:

A durable hemoglobin response was defined as hemoglobin ≥10 grams per deciliter (g/dL) with an

increase from Baseline of ≥2 g/dL not attributed to rescue therapy at ≥3 of the 4 available visits at Week 12 and/or later during the 24-week double-blind treatment period. Analysis was conducted in members of the Safety Analysis Set, comprised of all randomized participants who received at least 1 dose of study drug. Treatment groups were determined according to the actual treatment the participant received on Day 1 regardless of assigned study treatment.

End point type	Primary

End point timeframe:

up to Week 24

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	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[2]	4[3]		
Units: percentage of participants				
number (not applicable)	33.3	25.0		

Notes:

[2] - Safety Analysis Set. Only participants with available data were analyzed.

[3] - Safety Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a ≥3-point increase from Baseline in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) score at Week 24

End point title	Percentage of participants with a ≥3-point increase from Baseline in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) score at Week 24

End point description:

The FACIT-F scale was developed to assess anemia-related fatigue. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days. A clinically meaningful change in the FACIT-F score was defined as ≥3-point increase from Baseline. Item scores range from 0 (“not at all”) to 4 (“very much”), and the total score ranges from 0 to 52; lower scores indicate greater fatigue. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[4]	4[5]		
Units: percentage of participants				
number (not applicable)	66.7	50.0		

Notes:

[4] - Safety Analysis Set. Only participants with available data were analyzed.

[5] - Safety Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a 50 meter increase from Baseline to Week 24 in a 6-minute walk test (6MWT)

End point title	Percentage of participants with a 50 meter increase from Baseline to Week 24 in a 6-minute walk test (6MWT)

End point description:

The 6MWT is used to evaluate submaximal exercise capacity. It is a self-paced measurement of the distance that a participant can quickly walk on a flat, hard surface in a period of 6 minutes. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: percentage of participants				
number (not applicable)				

Notes:

[6] - Data analysis was not performed for this outcome measure.

[7] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in the FACIT-F score at each post-Baseline visit

End point title	Percentage change from Baseline in the FACIT-F score at each post-Baseline visit

End point description:

The FACIT-F scale was developed to assess anemia-related fatigue. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days. A clinically meaningful change in the FACIT-F score was defined as ≥3-point increase from Baseline. Item scores range from 0 (“not at all”) to 4 (“very much”), and the total score ranges from 0 to 52; lower scores indicate greater fatigue. Percentage change from Baseline was calculated as ([the post-Baseline value minus the Baseline value]/Baseline value) x 100. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Day 1; Weeks 8, 12, 16, 20, 24, 28, 32, 40, 48, 56, and every 16 weeks post-Week 56

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - Data analysis was not performed for this outcome measure.

[9] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the FACIT-F score at each post-Baseline visit

End point title	Change from Baseline in the FACIT-F score at each post-Baseline visit

End point description:

The FACIT-F scale was developed to assess anemia-related fatigue. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days. A clinically meaningful change in the FACIT-F score was defined as ≥3-point increase from Baseline. Item scores range from 0 (“not at all”) to 4 (“very much”), and the total score ranges from 0 to 52; lower scores indicate greater fatigue. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Day 1; Weeks 8, 12, 16, 20, 24, 28, 32, 40, 48, 56, and every 16 weeks post-Week 56

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[10] - Data analysis was not performed for this outcome measure.

[11] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin at each post-Baseline visit

End point title	Change from Baseline in hemoglobin at each post-Baseline visit

End point description:

Change from Baseline was calculated as the post-Baseline value minus the Baseline value. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Day 1; Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, and every 8 weeks post-Week 56

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: grams per liter				
arithmetic mean (standard deviation)	()	()		

Notes:

[12] - Data analysis was not performed for this outcome measure.

[13] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in hemoglobin at each post-Baseline visit

End point title	Percentage change from Baseline in hemoglobin at each post-Baseline visit

End point description:

Percentage change from Baseline was calculated as ([the post-Baseline value minus the Baseline value]/Baseline value) x 100. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Day 1; Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, and every 8 weeks post-Week 56

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

[14] - Data analysis was not performed for this outcome measure.

[15] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily corticosteroid dose at Week 24

End point title	Change from Baseline in daily corticosteroid dose at Week 24

End point description:

A new or increased dose of corticosteroids (prednisone or equivalent) from the Day 1 dose was permitted as rescue treatment. Rescue medication was to be considered if the absolute hemoglobin level continued to decline, there was a > 1 g/dL decrease in hemoglobin from the prior assessment, or the participant developed new or worsening symptoms of wAIHA. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: milligrams				
arithmetic mean (standard deviation)	()	()		

Notes:

[16] - Data analysis was not performed for this outcome measure.

[17] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who received transfusions from Week 6 to Week 24 and from Week 24 to Week 48

End point title	Percentage of participants who received transfusions from Week 6 to Week 24 and from Week 24 to Week 48

End point description:

Transfusion was permitted as a rescue treatment. Rescue medication was to be considered if the absolute hemoglobin level continued to decline, there was a > 1 g/dL decrease in hemoglobin from the prior assessment, or the participant developed new or worsening symptoms of warm autoimmune hemolytic anemia (wAIHA). As pre-specified in the Statistical Analysis Plan, with limited participants

enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Week 6 to Week 24; Week 24 to Week 48

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: percentage of participants				
number (not applicable)				

Notes:

[18] - Data analysis was not performed for this outcome measure.

[19] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

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

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

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 it was considered drug-related. An AE could therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study drug. TEAEs were defined as AEs reported for the first time or the worsening of pre-existing events after the first dose of study drug.

End point type	Secondary

End point timeframe:

up to 446 days

End point values	Parsaclisib	Placebo followed by parsaclisib	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7[20]	4[21]	6[22]	
Units: participants	7	4	4	

Notes:

[20] - Safety Analysis Set

[21] - Safety Analysis Set

[22] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in daily corticosteroid dose at Week 24

End point title	Percentage change from Baseline in daily corticosteroid dose at Week 24

End point description:

A new or increased dose of corticosteroids (prednisone or equivalent) from the Day 1 dose was permitted as rescue treatment. Rescue medication was to be considered if the absolute hemoglobin level continued to decline, there was a > 1 g/dL decrease in hemoglobin from the prior assessment, or the participant developed new or worsening symptoms of wAIHA. Percentage change from Baseline was calculated as ([the post-Baseline value minus the Baseline value]/Baseline value) x 100. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[23]	0[24]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

[23] - Data analysis was not performed for this outcome measure.

[24] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who required rescue therapy at any visit from Week 6 through Week 24, and from Week 24 to Week 48

End point title	Percentage of participants who required rescue therapy at any visit from Week 6 through Week 24, and from Week 24 to Week 48

End point description:

Rescue medication was to be considered if the absolute hemoglobin level continued to decline, there was a > 1 g/dL decrease in hemoglobin from the prior assessment, or the participant developed new or worsening symptoms of wAIHA. As pre-specified in the Statistical Analysis Plan, with limited participants enrolled in each treatment group, as well as the option for early transition to open-label parsaclisib, the statistical analyses, as related to efficacy and defined by the Protocol, are not applicable. Thus, data analysis was not performed for this outcome measure.

End point type	Secondary

End point timeframe:

Week 6 to Week 24; Week 24 to Week 48

End point values	Parsaclisib	Placebo followed by parsaclisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	0[26]		
Units: percentage of participants				
number (not applicable)				

Notes:

[25] - Data analysis was not performed for this outcome measure.

[26] - Data analysis was not performed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any ≥Grade 3 TEAE

End point title	Number of participants with any ≥Grade 3 TEAE

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug-related. TEAEs were defined as AEs reported for the first time or the worsening of pre-existing events after the first dose of study drug. The severity of AEs were assessed using Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 Grades 1 through 5. Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated. Grade 2: moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living. Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4: life-threatening consequences; urgent treatment indicated. Grade 5: fatal.

End point type	Secondary

End point timeframe:

up to 446 days

End point values	Parsaclisib	Placebo followed by parsaclisib	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7[27]	4[28]	6[29]	
Units: participants	6	3	1	

Notes:

[27] - Safety Analysis Set

[28] - Safety Analysis Set

[29] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 446 days

Adverse event reporting additional description:

For safety analysis, participants who transitioned from treatment with placebo to treatment with parsaclisib 2.5 milligrams (mg) once daily (QD) in the the open-label treatment period and the long-term extension period have been counted both in the placebo arm and the parsaclisib arm.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Parsaclisib

Reporting group description:

Participants who completed the double-blind treatment period, tolerated study treatment, and, in the investigator's opinion, benefited from treatment continued into the open-label treatment period for 24 weeks of parsaclisib 2.5 mg QD and then the long-term extension period to receive parsaclisib 2.5 mg QD for up to 2 years.

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo once daily (QD) for 24 weeks during the double-blind treatment period.

Serious adverse events	Parsaclisib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 11 (54.55%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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			
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Parsaclisib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	4 / 6 (66.67%)	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	3	
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Oedema			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Catarrh			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Blood potassium decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Neutrophil count decreased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Constipation			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Abdominal pain lower			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Faeces soft			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Choluria			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Micturition disorder			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Iron overload			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2022	The primary purpose of the amendment was to incorporate feedback from advisory board members, which included the addition of a long-term extension for continued access to parscalisib, and to include prior Protocol Administrative Changes. This amendment also included the changes from local adaptations for Germany and France.
10 May 2023	The primary purpose of the amendment was to reduce or eliminate protocol-required procedures and visits due to closure of study enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported