



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 pascalisib 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 pascalisib. Participants could then continue to receive pascalisib 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	Pascalisib

Arm description:

Participants received pascalisib 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 pascalisib 2.5 mg QD, and then the long-term extension period to receive pascalisib 2.5 mg QD for up to 2 years.

Arm type	Experimental
Investigational medicinal product name	pascalisib
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 pascalisib
------------------	--------------------------------

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 pascalisib 2.5 mg QD, and then the long-term extension period to receive pascalisib 2.5 mg QD for up to 2 years. Participants may have received pascalisib 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 pascalisib, 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	Pascalisib	Placebo followed by pascalisib		
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: 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 pascalisib, 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: scores on a scale				
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: 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 $([\text{the post-Baseline value minus the Baseline value}]/\text{Baseline value}) \times 100$. 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 ^[10]	0 ^[11]		
Units: percent change				
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 $([\text{the post-Baseline value minus the Baseline value}]/\text{Baseline value}) \times 100$. 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 parsacalisib, 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	Parsacalisib	Placebo followed by parsacalisib		
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: 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 $(\text{[the post-Baseline value minus the Baseline value]}/\text{Baseline value}) \times 100$. 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 parsacalisib, 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	Parsacalisib	Placebo followed by parsacalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[20]	0 ^[21]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

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

[21] - 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 ^[22]	4 ^[23]	6 ^[24]	
Units: participants	7	4	4	

Notes:

[22] - Safety Analysis Set

[23] - Safety Analysis Set

[24] - Safety Analysis Set

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

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

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