# 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<br>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<br>Units: years | | | |
| arithmetic mean | 62.3 | 57.8 | |
| standard deviation | ± 14.28 | ± 15.54 | - |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 4 | 6 | 10 |
| Male | 3 | 0 | 3 |
| Ethnicity (NIH/OMB)<br>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<br>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<br>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<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Sex: Female, Male<br>Units: participants | | | |
| Female | | | |
| Male | | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| Unknown or Not Reported | | | |
| Race/Ethnicity, Customized<br>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