



Clinical trial results:

An open-label, multi-center, phase 2 basket study to assess efficacy, safety and pharmacokinetics of iptacopan (LNP023) in participants with autoimmune benign hematological disorders

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-002039-40 |
| Trial protocol | DE IT ES |
| Global end of trial date | 17 May 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 20 March 2025 |
| First version publication date | 20 March 2025 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | CLNP023L12201 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05086744 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Novartis campus, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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 | 17 May 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 May 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were:

- Cohort 1 (ITP): To assess the ability of iptacopan to induce a clinically meaningful increase in platelet count in participants with primary ITP
- Cohort 2 (CAD): To assess the ability of iptacopan to induce a clinically meaningful increase in hemoglobin levels in participants with primary CAD

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 21 December 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | Korea, Republic of: 3 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | United States: 1 |
| Worldwide total number of subjects | 19 |
| EEA total number of subjects | 11 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 12 |
| From 65 to 84 years | 7 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in 8 investigative sites in 6 countries.

Pre-assignment

Screening details:

The screening period began once patients had signed the study informed consent. Screening evaluations had to be completed within 8 weeks prior to the first dose of study treatment. The treatment period started on Day 1 of Part A.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Part A |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 (ITP) |

Arm description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Iptacopan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Iptacopan 200 mg given orally twice daily (b.i.d.)

| | |
|------------------|----------------|
| Arm title | Cohort 2 (CAD) |
|------------------|----------------|

Arm description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Iptacopan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Iptacopan 200 mg given orally twice daily (b.i.d.)

| Number of subjects in period 1 | Cohort 1 (ITP) | Cohort 2 (CAD) |
|--------------------------------|----------------|------------------|
| Started | 9 | 10 |
| PD analysis set | 8 | 10 |
| ITP - sC5b-9 low | 5 | 0 ^[1] |
| ITP - sC5b-9 high | 4 | 0 ^[2] |
| Completed | 4 | 9 |
| Not completed | 5 | 1 |
| Adverse Event | - | 1 |
| Subject decision | 1 | - |
| Protocol deviation | 1 | - |
| Lack of efficacy | 3 | - |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The stratification groups "ITP - sC5b-9 low" and "ITP - sC5b-9 low" are only applicable to Cohort 1.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The stratification groups "ITP - sC5b-9 low" and "ITP - sC5b-9 low" are only applicable to Cohort 1.

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Part B |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 (ITP) |

Arm description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Iptacopan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Iptacopan 200 mg given orally twice daily (b.i.d.)

| | |
|------------------|----------------|
| Arm title | Cohort 2 (CAD) |
|------------------|----------------|

Arm description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD)

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------|
| Investigational medicinal product name | Iptacopan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Iptacopan 200 mg given orally twice daily (b.i.d.)

| Number of subjects in period 2^[3] | Cohort 1 (ITP) | Cohort 2 (CAD) |
|---|----------------|----------------|
| Started | 1 | 8 |
| ITP - sC5b-9 high | 1 | 0 |
| ITP - sC5b-9 low | 0 | 0 |
| Completed | 0 | 0 |
| Not completed | 1 | 8 |
| Adverse event, non-fatal | - | 1 |
| Study terminated by sponsor | 1 | 6 |
| Lack of efficacy | - | 1 |

Notes:

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

Justification: Only responders and non-responders who had signs of clinical benefit according to the investigator's assessment could continue treatment with iptacopan in Part B.

Baseline characteristics

Reporting groups

| | |
|--|----------------|
| Reporting group title | Cohort 1 (ITP) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP) | |
| Reporting group title | Cohort 2 (CAD) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD) | |

| Reporting group values | Cohort 1 (ITP) | Cohort 2 (CAD) | Total |
|---|----------------|----------------|-------|
| Number of subjects | 9 | 10 | 19 |
| Age Categorical | | | |
| Units: Participants | | | |
| 18 - <65 years | 7 | 5 | 12 |
| 65 - <85 years | 2 | 5 | 7 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 44.2 | 66.7 | |
| standard deviation | ± 20.77 | ± 10.01 | - |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 5 | 10 | 15 |
| Male | 4 | 0 | 4 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Asian | 3 | 0 | 3 |
| White | 6 | 10 | 16 |
| Platelets | | | |
| Platelet count in blood at baseline for participants in Cohort 1. This is not applicable to Cohort 2. Due to EudraCT system limitations, data fields in the table cannot be empty or contain letters (e.g. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'. | | | |
| Units: platelets*10 ⁹ /liter | | | |
| arithmetic mean | 14.6 | 999 | |
| standard deviation | ± 10.53 | ± 999 | - |
| Hemoglobin | | | |
| Hemoglobin in blood at baseline for participants in Cohort 2. This is not applicable to Cohort 1. Due to EudraCT system limitations, data fields in the table cannot be empty or contain letters (e.g. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'. | | | |
| Units: gram/liter | | | |
| arithmetic mean | 999 | 86.7 | |
| standard deviation | ± 999 | ± 9.06 | - |

End points

End points reporting groups

| | |
|---|------------------------------|
| Reporting group title | Cohort 1 (ITP) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP) | |
| Reporting group title | Cohort 2 (CAD) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD) | |
| Reporting group title | Cohort 1 (ITP) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP) | |
| Reporting group title | Cohort 2 (CAD) |
| Reporting group description: Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD) | |
| Subject analysis set title | Cohort 1 (ITP) - sC5b-9 high |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Iptacopan 200 mg b.i.d. in participants with primary ITP and high complement activation (i.e., high sC5b-9 levels) | |
| Subject analysis set title | Cohort 1 (ITP) - sC5b-9 low |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Iptacopan 200 mg b.i.d. in participants with primary ITP and low complement activation (i.e., low sC5b-9 levels) | |

Primary: Cohort 1 (ITP): Number of participants with a clinically meaningful response

| | |
|--|--|
| End point title | Cohort 1 (ITP): Number of participants with a clinically meaningful response ^{[1][2]} |
| End point description: A study participant with ITP was considered a responder if all the below criteria were met: 1. Platelet count of ≥ 50 k/ μ L sustained for at least 2 consecutive weeks during the main, 12-week treatment part 2. Absence of rescue therapy or prohibited medications to treat ITP 3. Lack of treatment discontinuation | |
| End point type | Primary |
| End point timeframe: Up to 12 weeks (Part A) | |

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: No statistical analyses were planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 1 only.

| End point values | Cohort 1 (ITP) | Cohort 1 (ITP) - sC5b-9 high | Cohort 1 (ITP) - sC5b-9 low | |
|-----------------------------|-----------------|------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8 | 3 | 5 | |
| Units: participants | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 2 (CAD): Number of participants with a clinically meaningful response

| | |
|-----------------|--|
| End point title | Cohort 2 (CAD): Number of participants with a clinically meaningful response ^[3] ^[4] |
|-----------------|--|

End point description:

A study participant with CAD was considered a responder if all the below criteria were met:

1. Hemoglobin level increase of ≥ 1.5 g/dL above baseline sustained for at least 2 consecutive weeks during the main, 12-week treatment part
2. Absence of rescue therapy or prohibited medications to treat CAD
3. Lack of treatment discontinuation

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[3] - 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: No statistical analyses were planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: participants | 5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 (ITP): Time to first platelet count ≥ 50 k/ μ L

| | |
|-----------------|--|
| End point title | Cohort 1 (ITP): Time to first platelet count ≥ 50 k/ μ L ^[5] |
|-----------------|--|

End point description:

The first time that a participant had a platelet count ≥ 50 k/ μ L after first dose of study treatment. Time to the first response was assessed for responders only.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 12 weeks (Part A)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is applicable to Cohort 1 only.

| End point values | Cohort 1 (ITP) | Cohort 1 (ITP) - sC5b-9 high | Cohort 1 (ITP) - sC5b-9 low | |
|-------------------------------|------------------|---------------------------------|--------------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | 0 ^[8] | |
| Units: days | | | | |
| median (full range (min-max)) | (to) | (to) | (to) | |

Notes:

[6] - There were no responders

[7] - There were no responders

[8] - There were no responders

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Time to first hemoglobin level ≥ 1.5 g/dL above baseline

| | |
|-----------------|--|
| End point title | Cohort 2 (CAD): Time to first hemoglobin level ≥ 1.5 g/dL above baseline ^[9] |
|-----------------|--|

End point description:

The first time that a participant had a hemoglobin level ≥ 1.5 g/dL above baseline after first dose of study treatment. Time to the first response was assessed for responders only.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|-------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 29.0 (23 to 63) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 (ITP): Duration of time during which platelet count remains ≥ 50 k/ μ L without the use of rescue therapy

| | |
|-----------------|---|
| End point title | Cohort 1 (ITP): Duration of time during which platelet count remains ≥ 50 k/ μ L without the use of rescue therapy ^[10] |
|-----------------|---|

End point description:

The duration of response corresponds to the duration of time during which a participant's platelet count remains ≥ 50 k/ μ L without the use of rescue therapy. The duration of response was considered as cumulative if there were non-continuous periods of response. Duration of response was analyzed for

responders only.

| | |
|-------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to 12 weeks (Part A) | |

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 1 only.

| End point values | Cohort 1 (ITP) | Cohort 1 (ITP) - sC5b-9 high | Cohort 1 (ITP) - sC5b-9 low | |
|-------------------------------|-------------------|---------------------------------|--------------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | 0 ^[13] | |
| Units: days | | | | |
| median (full range (min-max)) | (to) | (to) | (to) | |

Notes:

[11] - There were no responders

[12] - There were no responders

[13] - There were no responders

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Duration of time during which hemoglobin level remains ≥ 1.5 g/dL above baseline without the use of rescue therapy

| | |
|-----------------|---|
| End point title | Cohort 2 (CAD): Duration of time during which hemoglobin level remains ≥ 1.5 g/dL above baseline without the use of rescue therapy ^[14] |
|-----------------|---|

End point description:

The duration of response corresponds to the duration of time during which a participant's hemoglobin level remained ≥ 1.5 g/dL above baseline without the use of rescue therapy. The duration of response was considered as cumulative if there were non-continuous periods of response. Duration of response was analyzed for responders only.

| | |
|-----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, up to 12 weeks (Part A) | |

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|-------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 56.0 (28 to 63) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 (ITP): Magnitude of platelet count increase from baseline

| | |
|-----------------|--|
| End point title | Cohort 1 (ITP): Magnitude of platelet count increase from baseline ^[15] |
|-----------------|--|

End point description:

The magnitude of increase in platelet count compared to baseline was derived for each participant at each visit and time point. Best response across all visits is presented (highest value).

The following categories were used: absolute platelet counts increase <50, ≥50 and <100, ≥100 and <150, and ≥150 k/uL.

This endpoint is only applicable to participants without rescue therapy in the treatment period.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 1 only.

| End point values | Cohort 1 (ITP) | Cohort 1 (ITP) - sC5b-9 high | Cohort 1 (ITP) - sC5b-9 low | |
|--|-----------------|---------------------------------|--------------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 | 1 | 2 | |
| Units: participants | | | | |
| Absolute platelet count increase <50 k/uL | 3 | 1 | 2 | |
| Absolute platelet count increase ≥50 & <100 k/uL | 0 | 0 | 0 | |
| Absolute platelet count increase ≥100 & <150 k/uL | 0 | 0 | 0 | |
| Absolute platelet count increase ≥150 k/uL | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Magnitude of hemoglobin increase from baseline

| | |
|-----------------|--|
| End point title | Cohort 2 (CAD): Magnitude of hemoglobin increase from baseline ^[16] |
|-----------------|--|

End point description:

The magnitude of increase in hemoglobin level compared to baseline was derived for each participant at each visit and time point. Best response across all visits is presented (highest value).

The following categories were used: Hb increase from baseline by <1, ≥1 and <1.5, ≥1.5 and <2, and ≥2 g/dL.

This endpoint is only applicable to participants without rescue therapy in the treatment period.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: participants | | | | |
| Hb increase by <1.0 g/dL | 2 | | | |
| Hb increase by ≥1.0 g/dL and <1.5 g/dL | 1 | | | |
| Hb increase by ≥1.5 g/dL and <2 g/dL | 2 | | | |
| Hb increase by ≥2 g/dL | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 (ITP): Need for rescue therapy during Part A

| | |
|-----------------|---|
| End point title | Cohort 1 (ITP): Need for rescue therapy during Part A ^[17] |
|-----------------|---|

End point description:

Rescue therapy was defined as any therapy with ITP indication that started on or after Day 1. Rescue therapy, if indicated, could be initiated at the Investigator's discretion. From Day 1 onwards, if rescue therapy was needed before response criteria were met, the participant was treated as a non-responder. Conversely, use of rescue therapy after the primary endpoint was met, would not impact the response status with respect to that endpoint. For ITP, rescue therapy generally consisted of corticosteroids, intravenous immunoglobulins or anti-Rho(D) immunoglobulin and may have been indicated in case of worsening thrombocytopenia and/or signs or symptoms of bleeding.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 12 weeks (Part A)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 1 only.

| End point values | Cohort 1 (ITP) | Cohort 1 (ITP) - sC5b-9 high | Cohort 1 (ITP) - sC5b-9 low | |
|-----------------------------|-----------------|---------------------------------|--------------------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8 | 3 | 5 | |
| Units: participants | | | | |
| No | 3 | 1 | 2 | |
| Yes | 5 | 2 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Need for rescue therapy during Part A

| | |
|-----------------|---|
| End point title | Cohort 2 (CAD): Need for rescue therapy during Part A ^[18] |
|-----------------|---|

End point description:

Rescue therapy was defined as any therapy with CAD indication that started on or after Day 1. Rescue therapy, if indicated, could be initiated at the Investigator's discretion. From Day 1 onwards, if rescue therapy was needed before response criteria were met, the participant was treated as a non-responder. Conversely, use of rescue therapy after the primary endpoint was met, would not impact the response status with respect to that endpoint.

For CAD, rescue therapy generally consisted of plasmapheresis, intravenous immunoglobulins (IVIG) and/or red blood cell transfusions and may have been indicated in case of worsening anemia and/or critical hemolysis.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 12 weeks (Part A)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Cohort 2 (CAD) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: participants | | | | |
| No | 9 | | | |
| Yes | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Change from baseline in lactate dehydrogenase (LDH)

| | |
|-----------------|---|
| End point title | Cohort 2 (CAD): Change from baseline in lactate dehydrogenase (LDH) ^[19] |
|-----------------|---|

End point description:

LDH was measured in serum samples to assess the effect of treatment with iptacopan on relevant disease biomarkers.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | Cohort 2 (CAD) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Units/liter (U/L) | | | | |
| arithmetic mean (standard deviation) | -277.83 (± 88.966) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Change from baseline in total bilirubin

| | |
|-----------------|---|
| End point title | Cohort 2 (CAD): Change from baseline in total bilirubin ^[20] |
|-----------------|---|

End point description:

Total bilirubin was measured in serum samples to assess the effect of treatment with iptacopan on relevant disease biomarkers.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: micromole/liter (µmol/L) | | | | |
| arithmetic mean (standard deviation) | -15.63 (± 12.979) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Change from baseline in reticulocyte count

| | |
|-----------------|--|
| End point title | Cohort 2 (CAD): Change from baseline in reticulocyte count ^[21] |
|-----------------|--|

End point description:

Reticulocyte count was measured in blood samples to assess the effect of treatment with iptacopan on relevant disease biomarkers.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|---|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: reticulocytes * 10 ⁹ /liter | | | | |
| arithmetic mean (standard deviation) | -37.45 (± 17.205) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2 (CAD): Change from baseline in haptoglobin

| | |
|-----------------|---|
| End point title | Cohort 2 (CAD): Change from baseline in haptoglobin ^[22] |
|-----------------|---|

End point description:

Haptoglobin was measured in serum or plasma samples to assess the effect of treatment with iptacopan on relevant disease biomarkers.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, up to 12 weeks (Part A)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is applicable to Cohort 2 only.

| End point values | Cohort 2 (CAD) | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: gram/liter (g/L) | | | | |
| arithmetic mean (standard deviation) | 0.12 (± 0.236) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Number of participants with AEs and SAEs during the on-treatment period in Part A and B

| | |
|-----------------|---|
| End point title | Cohort 1 and 2: Number of participants with AEs and SAEs during the on-treatment period in Part A and B |
|-----------------|---|

End point description:

Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (SAEs), including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. For CTCAE v5.0, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.

The on-treatment period is defined from the day of first administration of study drug up to 7 days after the last administration of study drug.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose of study treatment to 7 days after last dose, up to approximately 43 weeks (Cohort 1) and 103 weeks (Cohort 2)

| End point values | Cohort 1 (ITP) | Cohort 2 (CAD) | | |
|------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 10 | | |
| Units: participants | | | | |
| AEs | 7 | 9 | | |
| Treatment-related AEs | 2 | 3 | | |
| Severe AEs | 1 | 0 | | |
| Treatment-related severe AEs | 1 | 0 | | |
| SAEs | 0 | 1 | | |
| Treatment-related SAEs | 0 | 0 | | |
| Fatal SAEs | 0 | 0 | | |
| Treatment-related fatal SAEs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Maximum observed plasma concentration (C_{max}) of iptacopan

| | |
|-----------------|--|
| End point title | Cohort 1 and 2: Maximum observed plasma concentration (C _{max}) of iptacopan |
|-----------------|--|

End point description:

Pharmacokinetic (PK) parameters were calculated based on iptacopan plasma concentrations by using non-compartmental methods. C_{max} is defined as the maximum (peak) observed concentration following a dose.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose, 0.5, 2, 4 and 6 hours after iptacopan administration on Day 15 and Day 57 of Part A

| End point values | Cohort 1 (ITP) | Cohort 2 (CAD) | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 15 (n=7,8) | 3190.0 (± 465.00) | 4800.0 (± 838.00) | | |
| Day 57 (n=3,9) | 2940.0 (± 1020.00) | 4420.0 (± 1300.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Time to maximum observed plasma concentration (Tmax) of iptacopan

| | |
|---|---|
| End point title | Cohort 1 and 2: Time to maximum observed plasma concentration (Tmax) of iptacopan |
| End point description: PK parameters were calculated based on iptacopan plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters. | |
| End point type | Secondary |
| End point timeframe: Pre-dose, 0.5, 2, 4 and 6 hours after iptacopan administration on Day 15 and Day 57 of Part A | |

| End point values | Cohort 1 (ITP) | Cohort 2 (CAD) | | |
|-------------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Day 15 (n=7,8) | 2 (0.75 to 5.15) | 1 (1 to 2) | | |
| Day 57 (n=2,9) | 2 (2 to 2) | 1.97 (1 to 2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of iptacopan

| | |
|---|---|
| End point title | Cohort 1 and 2: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of iptacopan |
| End point description: PK parameters were calculated based on iptacopan plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for area under the curve (AUC) calculation. | |
| End point type | Secondary |
| End point timeframe: Pre-dose, 0.5, 2, 4 and 6 hours after iptacopan administration on Day 15 and Day 57 of Part A | |

| End point values | Cohort 1 (ITP) | Cohort 2 (CAD) | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 15 (n=7,8) | 24200.0 (± 6110.00) | 31100.0 (± 5830.00) | | |
| Day 57 (n=3,9) | 21300.0 (± 5280.00) | 28200.0 (± 6880.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Trough plasma concentration (Ctrough) of iptacopan

| | |
|------------------------|--|
| End point title | Cohort 1 and 2: Trough plasma concentration (Ctrough) of iptacopan |
| End point description: | Ctrough is defined as the concentration reached immediately before the next dose is administered. All drug concentrations below the lower limit of quantification were treated as zero for the calculation of PK parameters. |
| End point type | Secondary |
| End point timeframe: | Pre-dose on Day 15, 29 and 57 of Part A |

| End point values | Cohort 1 (ITP) | Cohort 2 (CAD) | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 9 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 15 (n=8,9) | 1670.0 (± 1320.00) | 1980.0 (± 1720.00) | | |
| Day 29 (n=6,7) | 1670.0 (± 927.00) | 1330.0 (± 337.00) | | |
| Day 57 (n=5,9) | 1680.0 (± 758.00) | 1410.0 (± 320.00) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment to 30 days after last dose, up to approximately 46 weeks (Cohort 1) and 106 weeks (Cohort 2)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Cohort 1 (ITP) |
|-----------------------|----------------|

Reporting group description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary immune thrombocytopenia (ITP)

| | |
|-----------------------|--------------|
| Reporting group title | All Patients |
|-----------------------|--------------|

Reporting group description:

All patients in the study

| | |
|-----------------------|----------------|
| Reporting group title | Cohort 2 (CAD) |
|-----------------------|----------------|

Reporting group description:

Iptacopan 200 mg twice daily (b.i.d.) in participants with primary cold agglutinin disease (CAD)

| Serious adverse events | Cohort 1 (ITP) | All Patients | Cohort 2 (CAD) |
|---|----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 19 (10.53%) | 1 / 10 (10.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 19 (5.26%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 19 (5.26%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|----------------|-----------------|
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Cohort 1 (ITP) | All Patients | Cohort 2 (CAD) |
|---|----------------|------------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 16 / 19 (84.21%) | 9 / 10 (90.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer recurrent | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 19 (15.79%) | 3 / 10 (30.00%) |
| occurrences (all) | 0 | 3 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 19 (10.53%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 19 (5.26%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 2 / 19 (10.53%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 19 (15.79%) | 2 / 10 (20.00%) |
| occurrences (all) | 1 | 3 | 2 |
| Psychiatric disorders | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| Depressed mood subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 19 (10.53%) 2 | 2 / 10 (20.00%) 2 |
| Investigations | | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Blood iron increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Reverse tri-iodothyronine increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Immunisation reaction subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Congenital, familial and genetic disorders | | | |
| Thyroglossal cyst subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 2 | 1 / 10 (10.00%) 2 |
| Head discomfort | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 3 | 5 / 19 (26.32%) 7 | 3 / 10 (30.00%) 4 |
| Blood and lymphatic system disorders Leukocytosis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Neutrophilia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 | 0 / 10 (0.00%) 0 |
| Vertigo positional subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 2 | 1 / 10 (10.00%) 2 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 19 (10.53%) 3 | 2 / 10 (20.00%) 3 |
| Gingival bleeding subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Haematochezia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 1 / 19 (5.26%) 2 | 0 / 10 (0.00%) 0 |
| Haemorrhoids | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 3 / 19 (15.79%) 4 | 2 / 10 (20.00%) 3 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 1 / 19 (5.26%) 2 | 0 / 10 (0.00%) 0 |
| Eczema subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 1 / 19 (5.26%) 2 | 0 / 10 (0.00%) 0 |
| Hair texture abnormal subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Petechiae subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 4 | 3 / 19 (15.79%) 4 | 0 / 10 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Renal impairment subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 19 (10.53%) 2 | 2 / 10 (20.00%) 2 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Muscle spasms | | | |

| | | | |
|-----------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 19 (10.53%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 2 | 1 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 19 (5.26%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Fungal foot infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 19 (5.26%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 19 (10.53%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 3 | 3 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 19 (5.26%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 19 (10.53%) | 1 / 10 (10.00%) |
| occurrences (all) | 2 | 3 | 1 |

| | | | |
|---|---------------------|----------------------|----------------------|
| Tooth abscess subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 19 (10.53%) 2 | 2 / 10 (20.00%) 2 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 | 1 / 10 (10.00%) 1 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 2 / 19 (10.53%) 2 | 1 / 10 (10.00%) 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 13 October 2021 | The purpose of this amendment was to address questions raised by the BfArM. Inclusion criteria were revised to clarify that ITP should be persistent or chronic and diagnosed at least 3 months prior to baseline. Exclusion criteria were revised to exclude participants with any severe concurrent co-morbidities. The protocol was also amended to implement analysis of hematology samples from CAD participants at local clinical diagnostic laboratories, due to the high risk of spontaneous red blood cell agglutination in the blood samples from these participants at room temperature. |
| 01 December 2021 | The purpose of this amendment was to address a comment received from the South Korean HA, to add South Korea-specific instruction for the ITP inclusion criteria. |
| 26 April 2022 | The purpose of this amendment was to update the eligibility criteria related to liver disease or injury. For CAD participants, the acceptable levels for AST were increased to account for potential increases due to hemolysis only. For all participants, the acceptable limit for the liver enzymes were also increased to account for the patient populations of interest, particularly for participants with cold agglutinin disease, who may be expected to have mildly elevated liver enzymes. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported