



Clinical trial results:

A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of Nipocalimab in Adult Participants with Active Systemic Lupus Erythematosus

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2020-005569-14 |
| Trial protocol | HU PL ES BG |
| Global end of trial date | 25 December 2024 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 23 January 2026 |
| First version publication date | 23 January 2026 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | 80202135SLE2001 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04882878 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen-Cilag International N.V. |
| Sponsor organisation address | Turnhoutseweg 30, Beerse, Belgium, B-2340 |
| Public contact | Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.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 | 25 December 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 December 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy and safety of nipocalimab vs placebo in participants with active systemic lupus erythematosus (SLE).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy:

Protocol permitted standard of care therapies.

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 20 August 2021 |
| 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 | Argentina: 52 |
| Country: Number of subjects enrolled | Bulgaria: 13 |
| Country: Number of subjects enrolled | Colombia: 33 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Japan: 8 |
| Country: Number of subjects enrolled | Poland: 29 |
| Country: Number of subjects enrolled | Taiwan: 9 |
| Country: Number of subjects enrolled | Ukraine: 6 |
| Country: Number of subjects enrolled | United States: 39 |
| Country: Number of subjects enrolled | South Africa: 21 |
| Worldwide total number of subjects | 228 |
| EEA total number of subjects | 60 |

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) | 225 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 228 participants were randomized and treated in the study. Out of 228, 192 participants completed the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| | |
|--|-----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received placebo matching to nipocalimab as an IV infusion q2w through Week 50.

| | |
|------------------|------------------------|
| Arm title | Nipocalimab 5 mg/kg IV |
|------------------|------------------------|

Arm description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nipocalimab |
| Investigational medicinal product code | JNJ-80202135 |
| Other name | M281 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received nipocalimab 5 mg/kg as an IV infusion q2w through Week 50.

| | |
|------------------|-------------------------|
| Arm title | Nipocalimab 15 mg/kg IV |
|------------------|-------------------------|

Arm description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nipocalimab |
| Investigational medicinal product code | JNJ-80202135 |
| Other name | M281 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received nipocalimab 15 mg/kg as an IV infusion q2w through Week 50.

| Number of subjects in period 1 | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV |
|---------------------------------------|---------|------------------------|-------------------------|
| Started | 75 | 77 | 76 |
| Completed | 60 | 65 | 67 |
| Not completed | 15 | 12 | 9 |
| Adverse event, serious fatal | - | - | 1 |
| Consent withdrawn by subject | 9 | 4 | 4 |
| Unspecified | 5 | 6 | 3 |
| Lost to follow-up | 1 | 2 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-------------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |
| Reporting group title | Nipocalimab 5 mg/kg IV |
| Reporting group description: | |
| Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |
| Reporting group title | Nipocalimab 15 mg/kg IV |
| Reporting group description: | |
| Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |

| Reporting group values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV |
|--|---------|------------------------|-------------------------|
| Number of subjects | 75 | 77 | 76 |
| Age categorical Units: Subjects | | | |
| In Utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days - 23 months) | 0 | 0 | 0 |
| Children (2 - 11 years) | 0 | 0 | 0 |
| 12 - 17 years | 0 | 0 | 0 |
| Adults (18 - 64 years) | 75 | 76 | 74 |
| From 65 - 84 years | 0 | 1 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 45.3 | 41.1 | 43.9 |
| standard deviation | ± 11.35 | ± 11.82 | ± 11.85 |
| Gender categorical Units: Subjects | | | |
| Male | 4 | 4 | 4 |
| Female | 71 | 73 | 72 |
| Reporting group values | Total | | |
| Number of subjects | 228 | | |

| | | | |
|--|-----|--|--|
| Age categorical | | | |
| Units: Subjects | | | |
| In Utero | 0 | | |
| Preterm newborn infants (gestional age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days - 23 months) | 0 | | |
| Children (2 - 11 years) | 0 | | |
| 12 - 17 years | 0 | | |
| Adults (18 - 64 years) | 225 | | |
| From 65 - 84 years | 3 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | 12 | | |
| Female | 216 | | |

End points

End points reporting groups

| | |
|--|-------------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |
| Reporting group title | Nipocalimab 5 mg/kg IV |
| Reporting group description: Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |
| Reporting group title | Nipocalimab 15 mg/kg IV |
| Reporting group description: Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58. | |

Primary: Percentage of Participants who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 Composite Response at Week 24

| | |
|---|--|
| End point title | Percentage of Participants who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 Composite Response at Week 24 |
| End point description: SRI-4 measures reduction in SLE disease activity and was composite measure that included SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) and Physician Global Assessment (PGA). SRI-4 response: ≥ 4 -point reduction from baseline (BL) in SLEDAI-2K score, no new BILAG A or >1 new BILAG B (score A: severe disease; B: moderate disease), and no worsening in PGA (PGA $<10\%$ increase from BL). Composite response: SRI-4 response in participants who did not meet treatment failure criteria. SLEDAI-2K: assesses improvement in disease activity (ranged:0-105; higher score=higher severity). BILAG: assesses disease extent, severity (A[severe]-E[no disease]). PGA: assesses worsening in participant's health, recorded on visual analogue scale (VAS) with responses for disease activity ranged 0(none)-3(severe); higher score=higher disease activity. Full analysis set (FAS): all randomized participants who received at least 1 dose (partial/complete) of any study intervention. | |
| End point type | Primary |
| End point timeframe: At Week 24 | |

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 77 | 76 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 46.7 (37.2 to 56.1) | 49.4 (39.9 to 58.9) | 53.5 (44.1 to 63.0) | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Nipocalimab 5 mg/kg IV v Placebo |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.331 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 2.1 |

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.081 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 2.9 |

Secondary: Percentage of Participants With Baseline Active Mucocutaneous Lupus Manifestations (Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI] Activity Score ≥ 6) Achieving $\geq 50\%$ Reduction in CLASI Activity Score at Week 24

| | |
|-----------------|--|
| End point title | Percentage of Participants With Baseline Active Mucocutaneous Lupus Manifestations (Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI] Activity Score ≥ 6) Achieving $\geq 50\%$ Reduction in CLASI Activity Score at Week 24 |
|-----------------|--|

End point description:

Percentage of participants with baseline active mucocutaneous lupus manifestations (CLASI activity score ≥ 6) achieving $\geq 50\%$ reduction in CLASI activity score at Week 24 was reported. CLASI assess disease activity and damage caused to skin for cutaneous lupus erythematosus patients with/without systemic involvement across 13 body areas. CLASI consisted of 2 scores; (1) Activity Score (ranged: 0-70) (2) Damage Score (ranged: 0-56). Activity was scored by the investigator based on erythema (0-3 per area), scale/hyperkeratosis (0-2 per area), mucous membrane involvement (0-1), acute hair loss (0-1) and non-scarring alopecia (0-3). Damage was scored in terms of dyspigmentation (0-2 per area), scarring (0-2 per area), scarring alopecia (3 points if present), deep scarring (1 point). Scores were calculated by addition based on the extent of symptoms. Higher scores=worse disease activity. FAS used. N (overall number of participants analyzed)=participants evaluable for this endpoint.

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

End point timeframe:

At Week 24

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 41 | 43 | 40 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 46.3 (33.5 to 59.2) | 53.2 (40.4 to 66.1) | 53.8 (40.7 to 66.9) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 3 |
|---|----------------------------------|
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.247 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 3.1 |

| Statistical analysis title | Statistical Analysis 4 |
|----------------------------|-----------------------------------|
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |

| | |
|---|----------------------|
| Number of subjects included in analysis | 81 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.09 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 4.5 |

Secondary: Percentage of Participants With Baseline Arthritis (with at Least 4 Active Joints at Baseline) Achieving Greater Than or Equal to (\geq) 50% Reduction in Active Joints at Week 24

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|-----------------|--|
| End point title | Percentage of Participants With Baseline Arthritis (with at Least 4 Active Joints at Baseline) Achieving Greater Than or Equal to (\geq) 50% Reduction in Active Joints at Week 24 |
|-----------------|--|

End point description:

The active joint was defined as a joint that was painful as reported by the participant and demonstrated tenderness and at least one additional sign of inflammation (for example [e.g.]: observed swelling such as edema or effusion) on physical examination as determined by the joint assessor. Each of 64 joints would be evaluated for symptoms of pain, tenderness and 62 joints for swelling or effusion (hips are excluded). 50% reduction in active joints: Participants with baseline arthritis who had \geq 50% reduction in active joints from baseline. FAS: all randomized participants who received at least 1 dose (partial or complete) of any study intervention. Here 'N' (overall number of participants analyzed) refers to the number of participants evaluable for this endpoint.

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

End point timeframe:

At Week 24

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 68 | 72 | 69 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 75.0 (66.4 to 83.6) | 82.0 (74.4 to 89.6) | 75.4 (66.8 to 83.9) | |

Statistical analyses

| | |
|----------------------------|----------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |

| | |
|---|----------------------|
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.122 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 3.7 |

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis 6 |
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 137 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.296 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 2.6 |

Secondary: Percentage of Participants With ≥ 4 Point Improvement From Baseline in SLE Disease Activity Index 2000 (SLEDAI-2K) at Week 24

| | |
|-----------------|--|
| End point title | Percentage of Participants With ≥ 4 Point Improvement From Baseline in SLE Disease Activity Index 2000 (SLEDAI-2K) at Week 24 |
|-----------------|--|

End point description:

SLEDAI-2K was a validated SLE activity index, based on the presence of 24 features in 9 organ systems and measures disease activity in SLE patients at the time of visit or in previous 30 days; the index was weighted according to the feature. Features were scored by assessing physician if present at the time of visit or within last 30 days, with more severe features having higher scores, and added to determine total SLEDAI-2K score, ranged: 0-105; higher scores=increased disease activity. Baseline measurement for SLEDAI-2K was defined as the closest measurement taken prior to initiation of the Week 0 study intervention administration. SLEDAI improvement was defined as a reduction from baseline in total SLEDAI-2K score. No worsening of total SLEDAI-2K from baseline was defined as a change ≤ 0 in SLEDAI-2K score and meaningful improvement was defined as a reduction in SLEDAI-2K of 4 or more. FAS used. 'N' (overall number of participants analyzed)=participants evaluable for this endpoint.

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

End point timeframe:

At Week 24

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 77 | 75 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 46.7 (37.2 to 56.1) | 49.3 (39.8 to 58.8) | 54.3 (44.7 to 63.8) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 8 |
|---|-----------------------------------|
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.069 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 3 |

| Statistical analysis title | Statistical Analysis 7 |
|---|----------------------------------|
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.338 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.2 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 2.1 |

Secondary: Percentage of Participants Achieving the British Isles Lupus Assessment

Group (BILAG) Composite Lupus Assessment (BICLA) Response at Week 24

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving the British Isles Lupus Assessment Group (BILAG) Composite Lupus Assessment (BICLA) Response at Week 24 |
|-----------------|--|

End point description:

The BILAG-based Composite Lupus Assessment (BICLA) was a composite index to assess disease activity in SLE. BICLA response defined as: (1) Reduction of all baseline (BL) BILAG-2004 A to B/C/D and BL BILAG-2004 B to C/D and no BILAG-2004 worsening in other organ systems, defined by ≥ 1 new BILAG-2004 A or ≥ 2 new BILAG-2004 B (Score A: Severely active disease; B: Moderately active disease; C: Mild stable disease; D: Inactive now but previously active; E: Never affected). (2) No worsening from BL in SLEDAI-2K: increase from BL of >0 points in SLEDAI-2K. Increase from BL corresponds to change from BL. (3) No worsening from BL in participants' lupus disease activity defined by increase ≥ 0.30 points on 3-point PGA VAS. (4) No discontinuation of study intervention or use of rescue medication beyond protocol-allowed threshold before assessment. If any of the conditions cannot be evaluated at Week 24 (due to missing values) the participant was defined as BICLA non-responder. FAS was used.

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

End point timeframe:

At Week 24

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 77 | 76 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 32.0 (23.1 to 40.9) | 39.3 (30.0 to 48.6) | 36.1 (27.0 to 45.2) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 9 |
|---|----------------------------------|
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.211 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 2.4 |

| Statistical analysis title | Statistical Analysis 10 |
|----------------------------|-----------------------------------|
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |

| | |
|---|----------------------|
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.242 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 2.3 |

Secondary: Time to First Flare Through Week 24

| | |
|---|-------------------------------------|
| End point title | Time to First Flare Through Week 24 |
| End point description: | |
| Time to first flare: Time to first occurrence of a flare. Flare was defined as at least 1 new BILAG A item score or at least 2 new BILAG B item scores meeting at least 1 of following criteria: 1) Not present at baseline, 2) The occurrence of a new/worse manifestation in a different component of an organ system that is already present, 3) at least 1 A or 2 B scores in an organ system which improves to B/C/D for at least 2 sequential study visits followed by new/worse disease activity. Here, score A: Severely active disease; B: Moderately active disease; C: Mild stable disease; D: Inactive now but previously active; E: Never affected. BILAG flare was based on adjudicated flare. FAS: all randomized participants who received at least 1 dose (partial or complete) of any study intervention. 99999 signifies that median, lower and upper limit of confidence interval could not be calculated due to low number of participants with event. | |
| End point type | Secondary |
| End point timeframe: | |
| From Week 0 up to Week 24 | |

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|----------------------------------|------------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 77 | 76 | |
| Units: Days | | | | |
| median (confidence interval 90%) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | |

Statistical analyses

| | |
|----------------------------|----------------------------------|
| Statistical analysis title | Statistical Analysis 11 |
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |

| | |
|---|-------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.459 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.33 |
| upper limit | 1.44 |

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis 12 |
| Statistical analysis description: | |
| NA | |
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.769 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 1.92 |

Secondary: Percentage of Participants who Achieved SRI-4 Composite Response at Week 52

| | |
|--|---|
| End point title | Percentage of Participants who Achieved SRI-4 Composite Response at Week 52 |
| End point description: | |
| <p>SRI-4 measures reduction in SLE disease activity and was a composite measure that included the SLEDAI-2K, BILAG and PGA. SRI-4 response was defined as ≥ 4-point reduction from baseline in SLEDAI-2K score, no new BILAG A or >1 new BILAG B, and no worsening in the PGA (PGA less than [$<$] 10% increase from baseline). Composite response was defined as SRI-4 response in participants who did not meet treatment failure criteria. SLEDAI-2K: assesses improvement in disease activity (ranged: 0 to 105; higher score = higher severity). BILAG: assesses disease extent, severity (range: A[severe] to E[no disease]). PGA: assesses worsening in participant's general health, recorded on a VAS with responses for disease activity ranging from 0 (none) to 3 (severe); higher score = higher disease activity. Modified full analysis set (mFAS) included all randomized participants, excluding those from Argentinian site W02-AR10008, who received at least 1 dose (partial or complete) of any study intervention.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 52 | |

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 74 | 74 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 39.7 (30.3 to 49.1) | 51.7 (42.1 to 61.4) | 53.6 (44.0 to 63.2) | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis 14 |
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 147 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.02 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.2 |
| upper limit | 3.9 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical Analysis 13 |
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |
| Number of subjects included in analysis | 147 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.054 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.8 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 3.3 |

Secondary: Percentage of Participants Receiving ≥ 10 milligram/day (mg/day)

Prednisone or Equivalent at Baseline who Achieved Week 6-16 Glucocorticoid (GC) Taper Goal (at Week 16 to ≤ 7.5 mg/day Prednisone or Equivalent) and Maintained that Reduction Until Week 24

| | |
|-----------------|---|
| End point title | Percentage of Participants Receiving ≥ 10 milligram/day (mg/day) Prednisone or Equivalent at Baseline who Achieved Week 6-16 Glucocorticoid (GC) Taper Goal (at Week 16 to ≤ 7.5 mg/day Prednisone or Equivalent) and Maintained that Reduction Until Week 24 |
|-----------------|---|

End point description:

Sustained (maintained) reduction was defined as achieving Week 6–16 GC taper goal (at Week 16 to less than or equal to [\leq] 7.5 mg/day prednisone or equivalent) and maintaining that reduction until Week 24. FAS included all randomized participants who received at least 1 dose (partial or complete) of any study intervention. Here 'N' (overall number of participants analyzed) refers to the number of participants evaluable for this endpoint.

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

End point timeframe:

Baseline up to Week 24

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|---------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 36 | 32 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 90%) | 69.7 (56.5 to 82.9) | 67.4 (54.2 to 80.6) | 80.8 (69.2 to 92.4) | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis 16 |
| Comparison groups | Placebo v Nipocalimab 15 mg/kg IV |
| Number of subjects included in analysis | 65 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.135 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 6.5 |

| | |
|-----------------------------------|----------------------------------|
| Statistical analysis title | Statistical Analysis 15 |
| Comparison groups | Placebo v Nipocalimab 5 mg/kg IV |

| | |
|---|----------------------|
| Number of subjects included in analysis | 69 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.718 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 1.9 |

Secondary: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) Through Week 58

| | |
|--|--|
| End point title | Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) Through Week 58 |
| End point description: | |
| An adverse event (AE) was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Serious AE was the AE resulting in any of following outcomes/deemed significant for any other reason: death; initial/prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TEAEs were defined as any AE occurring at or after the initial administration of study intervention. TEAEs included both serious and non-serious AEs. Safety analysis set included all randomized participants who received at least 1 dose (partial or complete) of any study intervention. | |
| End point type | Secondary |
| End point timeframe: | |
| From start of treatment (Week 0) up to Week 58 | |

| End point values | Placebo | Nipocalimab 5 mg/kg IV | Nipocalimab 15 mg/kg IV | |
|-----------------------------------|-----------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 77 | 76 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| TEAEs | 76.0 | 89.6 | 82.9 | |
| TESAEs | 8.0 | 7.8 | 13.2 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Week 0) up to Week 58

Adverse event reporting additional description:

Safety analysis set included all randomized participants who received at least 1 dose (partial or complete) of any study intervention.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive placebo matching to nipocalimab as an intravenous (IV) infusion every 2 weeks (q2w) from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| | |
|-----------------------|-------------------------|
| Reporting group title | Nipocalimab 15 mg/kg IV |
|-----------------------|-------------------------|

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 15 mg/kg as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| | |
|-----------------------|------------------------|
| Reporting group title | Nipocalimab 5 mg/kg IV |
|-----------------------|------------------------|

Reporting group description:

Participants with active, autoantibody-positive SLE who had an inadequate response to one or more standard-of-care treatments (immunomodulators, antimalarial drugs, and glucocorticoids) were randomized to receive nipocalimab 5 milligrams per kilogram (mg/kg) as an IV infusion q2w from Week 0 through Week 50 along with ongoing standard-of-care treatments. Participants were then followed up for safety up to Week 58.

| Serious adverse events | Placebo | Nipocalimab 15 mg/kg IV | Nipocalimab 5 mg/kg IV |
|---|----------------|-------------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 10 / 76 (13.16%) | 6 / 77 (7.79%) |
| number of deaths (all causes) | 0 | 1 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute Myocardial Infarction | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid Haemorrhage | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 0 / 76 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Ectopic Pregnancy | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 0 / 76 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis Alcoholic | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Uterine Enlargement | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Shrinking Lung Syndrome | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 0 / 76 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Foot Deformity | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic Lupus Erythematosus | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 76 (0.00%) | 2 / 77 (2.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parametritis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic Shock | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 76 (1.32%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Wound Infection | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 0 / 76 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 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 | Placebo | Nipocalimab 15 mg/kg IV | Nipocalimab 5 mg/kg IV |
|--|------------------|-------------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 75 (54.67%) | 51 / 76 (67.11%) | 53 / 77 (68.83%) |
| Injury, poisoning and procedural complications | | | |
| Limb Injury | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 0 / 76 (0.00%) | 5 / 77 (6.49%) |
| occurrences (all) | 3 | 0 | 5 |
| Vascular disorders | | | |

| | | | |
|---|--|---|--|
| Hypertension subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 5 | 4 / 76 (5.26%) 4 | 5 / 77 (6.49%) 5 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 6 / 76 (7.89%) 7 | 11 / 77 (14.29%) 11 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Oedema Peripheral subjects affected / exposed occurrences (all) | 1 / 75 (1.33%) 10 0 / 75 (0.00%) 0 | 2 / 76 (2.63%) 2 5 / 76 (6.58%) 5 | 4 / 77 (5.19%) 5 1 / 77 (1.30%) 1 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal Pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 6 / 75 (8.00%) 9 2 / 75 (2.67%) 2 4 / 75 (5.33%) 4 2 / 75 (2.67%) 3 | 4 / 76 (5.26%) 4 4 / 76 (5.26%) 5 4 / 76 (5.26%) 11 3 / 76 (3.95%) 3 | 3 / 77 (3.90%) 5 1 / 77 (1.30%) 1 8 / 77 (10.39%) 11 4 / 77 (5.19%) 4 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 75 (2.67%) 2 | 4 / 76 (5.26%) 4 | 0 / 77 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) | 2 / 75 (2.67%) 7 | 7 / 76 (9.21%) 9 | 5 / 77 (6.49%) 8 |
| Infections and infestations | | | |

| | | | |
|-----------------------------------|-----------------|------------------|------------------|
| Asymptomatic Bacteriuria | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 4 / 76 (5.26%) | 5 / 77 (6.49%) |
| occurrences (all) | 1 | 5 | 9 |
| Covid-19 | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 5 / 76 (6.58%) | 5 / 77 (6.49%) |
| occurrences (all) | 4 | 6 | 5 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 4 / 76 (5.26%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 8 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 1 / 76 (1.32%) | 4 / 77 (5.19%) |
| occurrences (all) | 5 | 1 | 4 |
| Gastroenteritis Viral | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 2 / 76 (2.63%) | 2 / 77 (2.60%) |
| occurrences (all) | 4 | 2 | 3 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 10 / 76 (13.16%) | 6 / 77 (7.79%) |
| occurrences (all) | 9 | 14 | 7 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 6 / 76 (7.89%) | 5 / 77 (6.49%) |
| occurrences (all) | 7 | 7 | 5 |
| Pharyngitis | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 3 / 76 (3.95%) | 2 / 77 (2.60%) |
| occurrences (all) | 8 | 3 | 3 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 75 (12.00%) | 10 / 76 (13.16%) | 10 / 77 (12.99%) |
| occurrences (all) | 10 | 11 | 12 |
| Influenza | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 3 / 76 (3.95%) | 6 / 77 (7.79%) |
| occurrences (all) | 3 | 3 | 7 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 27 May 2021 | The overall rationale for the amendment was to include additional safety criteria related to hyperlipidemia, hypogammaglobulinemia, anaphylaxis, and oral contraceptive use. |
| 08 July 2022 | The overall rationale for the amendment was to include details on serious adverse events (SAE) classification procedures regarding major cardiovascular events (MACE) adjudication. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported