



Clinical trial results:

An open-label, long-term safety trial of BI 655130 (SPESOLIMAB) treatment in patients with moderate to severely active ulcerative colitis who have completed previous BI 655130 trials

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2018-000334-35 |
| Trial protocol | BE AT ES GB DE NL PL NO HU IT |
| Global end of trial date | 03 May 2023 |

Results information

| | |
|--------------------------------|-------------|
| Result version number | v1 |
| This version publication date | 11 May 2024 |
| First version publication date | 11 May 2024 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 1368-0017 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03648541 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Boehringer Ingelheim, Call Centre |
| Sponsor organisation address | Binger Straße, Ingelheim am Rhein, Germany, 55216 |
| Public contact | Boehringer Ingelheim, Call Centre, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | Boehringer Ingelheim, Call Centre, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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 | 20 June 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 May 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 May 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main objectives were to evaluate the long-term safety and the long-term efficacy of spesolimab (BI 655130) in patients with moderate to severely active ulcerative colitis who completed treatment in previous trials.

Protection of trial subjects:

Only subjects that met the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 06 November 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Austria: 4 |
| Country: Number of subjects enrolled | Belgium: 5 |
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Germany: 15 |
| Country: Number of subjects enrolled | Italy: 13 |
| Country: Number of subjects enrolled | Japan: 8 |
| Country: Number of subjects enrolled | Korea, Republic of: 2 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | Russian Federation: 6 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | United States: 12 |
| Worldwide total number of subjects | 79 |
| EEA total number of subjects | 41 |

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) | 74 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

An open-label 7-year long-term extension trial in patients with moderate-to-severe ulcerative colitis who completed treatment in previous spesolimab trials 1368-0005 Part 1 and 1368-0004.

Pre-assignment

Screening details:

Only subjects that met the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Open-label study

Arms

| | |
|-----------|------------|
| Arm title | Spesolimab |
|-----------|------------|

Arm description:

Patients with moderate-to-severe ulcerative colitis who completed treatment in previous spesolimab induction trials. Patients were treated according to their previous trial outcome. Those who completed treatment in the previous trials showing a clinical response (CR) directly received maintenance treatment, consisting of 300 mg solution for injection of spesolimab administered as subcutaneous (s.c.) injection q4w for 336 weeks.

Patients who did not achieve a clinical response in the previous trials received multiple active doses of 1200 milligrams (mg) solution for infusion of spesolimab as intravenous (i.v.) infusion every 4 weeks (q4w) for 12 weeks, as re-induction treatment. If participants reached a clinical response at Week 12 of the re-induction treatment, they switched to the maintenance treatment receiving 300 mg solution of injection of spesolimab as subcutaneous (s.c.) injection q4w for up to 336 weeks.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BI 655130 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients who did not achieve a clinical response in the previous trials received multiple active doses of 1200 milligrams (mg) solution for infusion of spesolimab as intravenous (i.v.) infusion every 4 weeks (q4w) for 12 weeks, as re-induction treatment.

| | |
|--|------------------------|
| Investigational medicinal product name | BI 655130 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subconjunctival use |

Dosage and administration details:

Patients who completed treatment in the previous trials showing a clinical response and patients who reached a clinical response at Week 12 of re-induction treatment, received maintenance treatment consisting of 300 mg solution for injection of spesolimab administered as subcutaneous (s.c.) injection q4w for 336 weeks.

| Number of subjects in period 1 | Spesolimab |
|---|------------|
| Started | 79 |
| Completed | 0 |
| Not completed | 79 |
| Adverse event, serious fatal | 1 |
| Consent withdrawn by subject | 4 |
| Other reason, not listed | 4 |
| Adverse event, non-fatal | 3 |
| Did not continue due to study stop | 3 |
| No CR at week 12 of re-induction period | 35 |
| Missing | 3 |
| Lack of efficacy | 25 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|--|------------|
| Reporting group title | Spesolimab |
| Reporting group description: | |
| Patients with moderate-to-severe ulcerative colitis who completed treatment in previous spesolimab induction trials. Patients were treated according to their previous trial outcome. Those who completed treatment in the previous trials showing a clinical response (CR) directly received maintenance treatment, consisting of 300 mg solution for injection of spesolimab administered as subcutaneous (s.c.) injection q4w for 336 weeks. | |
| Patients who did not achieve a clinical response in the previous trials received multiple active doses of 1200 milligrams (mg) solution for infusion of spesolimab as intravenous (i.v.) infusion every 4 weeks (q4w) for 12 weeks, as re-induction treatment. If participants reached a clinical response at Week 12 of the re-induction treatment, they switched to the maintenance treatment receiving 300 mg solution of injection of spesolimab as subcutaneous (s.c.) injection q4w for up to 336 weeks. | |

| Reporting group values | Spesolimab | Total | |
|--|------------|-------|--|
| Number of subjects | 79 | 79 | |
| Age categorical | | | |
| All patients who received at least 1 dose of trial medication in the re-induction or maintenance period. | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 74 | 74 | |
| From 65-84 years | 5 | 5 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| All patients who received at least 1 dose of trial medication in the re-induction or maintenance period. | | | |
| Units: years | | | |
| arithmetic mean | 43.0 | | |
| standard deviation | ± 14.9 | - | |
| Sex: Female, Male | | | |
| All patients who received at least 1 dose of trial medication in the re-induction or maintenance period. | | | |
| Units: Participants | | | |
| Female | 29 | 29 | |
| Male | 50 | 50 | |
| Race (NIH/OMB) | | | |
| All patients who received at least 1 dose of trial medication in the re-induction or maintenance period. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 1 | |
| Asian | 11 | 11 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 2 | 2 | |
| White | 65 | 65 | |
| More than one race | 0 | 0 | |

| | | | |
|--|----|----|--|
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB) | | | |
| All patients who received at least 1 dose of trial medication in the re-induction or maintenance period. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | |
| Not Hispanic or Latino | 78 | 78 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Spesolimab |
| Reporting group description: | |
| Patients with moderate-to-severe ulcerative colitis who completed treatment in previous spesolimab induction trials. Patients were treated according to their previous trial outcome. Those who completed treatment in the previous trials showing a clinical response (CR) directly received maintenance treatment, consisting of 300 mg solution for injection of spesolimab administered as subcutaneous (s.c.) injection q4w for 336 weeks. | |
| Patients who did not achieve a clinical response in the previous trials received multiple active doses of 1200 milligrams (mg) solution for infusion of spesolimab as intravenous (i.v.) infusion every 4 weeks (q4w) for 12 weeks, as re-induction treatment. If participants reached a clinical response at Week 12 of the re-induction treatment, they switched to the maintenance treatment receiving 300 mg solution of injection of spesolimab as subcutaneous (s.c.) injection q4w for up to 336 weeks. | |
| Subject analysis set title | 300 mg s.c. maintenance treatment [q4w] for 336 weeks |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| 300 mg solution for injection of spesolimab was administered as subcutaneous (s.c.) injection q4w for 336 weeks as maintenance treatment. This arm included participants who entered the maintenance treatment directly from the parent trial and participants who switched from the re-induction treatment. Participants who completed treatment in the parent trial and had a clinical response at week 12 (EOT) directly received maintenance treatment. Participants, who started re-induction treatment, could switch to maintenance treatment if they reached a clinical response at Week 12 of the re-induction period. Participants who experienced a disease flare during maintenance treatment were administered a single intravenous dose of spesolimab 1200 mg followed by an intensified subcutaneous maintenance dosing schedule with 600 mg q4w. | |

Primary: Exposure adjusted rate of subjects reporting a treatment emergent adverse event (TEAE) up to Week 336 of maintenance treatment

| | |
|--|---|
| End point title | Exposure adjusted rate of subjects reporting a treatment emergent adverse event (TEAE) up to Week 336 of maintenance treatment ^[1] |
| End point description: | |
| Exposure adjusted rate of subjects reporting a treatment emergent adverse event (TEAE) up to Week 336 of maintenance treatment. | |
| The exposure adjusted incidence rate (per 100 subject years) of a selected treatment emergent adverse event is defined as the number of subjects experiencing the adverse event per treatment group during time at risk divided by the total time of subjects at risk in that treatment group to contribute the event to the analysis multiplied by 100 (per 100 subject years). | |
| Safety analysis Set for maintenance treatment (SAF-MT): All subjects who received at least one dose of maintenance treatment in this extension trial. Only subjects receiving maintenance treatment were analysed for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Up to Week 336. | |

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: This endpoint has only been analyzed descriptively.

| | | | | |
|-------------------------------------|---|--|--|--|
| End point values | 300 mg s.c. maintenance treatment [q4w] for 336 weeks | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 34 | | | |
| Units: Events per 100 patient-years | | | | |

| | | | | |
|-------------------------|-------|--|--|--|
| number (not applicable) | 260.6 | | | |
|-------------------------|-------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with clinical remission at Week 336 of maintenance treatment

| | |
|--|---|
| End point title | Proportion of subjects with clinical remission at Week 336 of maintenance treatment |
| End point description: Proportion of subjects with clinical remission at Week 336 of maintenance treatment. Clinical remission was defined as rectal bleeding score (RBS) = 0, modified endoscopic subscore [mESS] ≤1, stool frequency score (SFS) = 0 or 1 and drop ≥1 from baseline, and modified mayo clinical score (MCS) ≤2. Since this trial was prematurely discontinued and no patient achieved the Week 336 visit, no data satisfied the reporting criteria, and the endpoint could not be analysed. | |
| End point type | Secondary |
| End point timeframe: Up to 336 weeks | |

| | | | | |
|-----------------------------|---|--|--|--|
| End point values | 300 mg s.c. maintenance treatment [q4w] for 336 weeks | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: Subjects | | | | |

Notes:

[2] - Since no subject achieved the Week 336 visit the endpoint could not be analysed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Re-induction period: up to 184 days for patients who did not participate in the maintenance treatment, up to 78 days for patients who continued with maintenance treatment.

Maintenance period: up to 1550 days.

Adverse event reporting additional description:

Safety analysis set for reinduction treatment (SAF-RT): All participants who received at least one dose of re-induction treatment in this extension period; Safety analysis set for maintenance treatment (SAF-MT): All participants who received at least one dose of maintenance treatment in this extension trial.

Arms are not mutually exclusive.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 26.0 |

Reporting groups

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|-----------------------|--|
| Reporting group title | 1200 mg i.v. re-induction treatment [q4w] for 12 weeks |
|-----------------------|--|

Reporting group description:

Participants who completed treatment in the parent trial, but did not have a clinical response at Week 12 (end of trial (EOT)), entered a 12-week spesolimab re-induction period, receiving multiple active doses of 1200 milligrams (mg) solution for infusion of spesolimab as intravenous (i.v.) infusion every 4 weeks (q4w) for 12 weeks (re-induction). If participants reached a clinical response at Week 12 of the re-induction treatment, they switched to the maintenance treatment receiving 300 mg solution of injection of spesolimab as subcutaneous (s.c.) injection q4w for up to 336 weeks. Participants who did not achieve a clinical response after 12 weeks of re-induction treatment were discontinued from treatment.

| | |
|-----------------------|---|
| Reporting group title | 300 mg s.c. maintenance treatment [q4w] for 336 weeks |
|-----------------------|---|

Reporting group description:

300 mg solution for injection of spesolimab was administered as subcutaneous (s.c.) injection q4w for 336 weeks as maintenance treatment. This arm included participants who entered the maintenance treatment directly from the parent trial and participants who switched from the re-induction treatment. Participants who completed treatment in the parent trial and had a clinical response at week 12 (EOT) directly received maintenance treatment. Participants, who started re-induction treatment, could switch to maintenance treatment if they reached a clinical response at Week 12 of the re-induction period. Participants who experienced a disease flare during maintenance treatment were administered a single intravenous dose of spesolimab 1200 mg followed by an intensified subcutaneous maintenance dosing schedule with 600 mg q4w.

| Serious adverse events | 1200 mg i.v. re-induction treatment [q4w] for 12 weeks | 300 mg s.c. maintenance treatment [q4w] for 336 weeks | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | 6 / 34 (17.65%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 34 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 2 / 34 (5.88%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| COVID-19 pneumonia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 34 (2.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | 1200 mg i.v. re-induction treatment [q4w] for 12 weeks | 300 mg s.c. maintenance treatment [q4w] for 336 weeks | |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 57 (24.56%) | 24 / 34 (70.59%) | |
| Investigations | | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 2 / 34 (5.88%) | |
| occurrences (all) | 1 | 2 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 2 / 34 (5.88%) | |
| occurrences (all) | 0 | 2 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 5 / 34 (14.71%) | |
| occurrences (all) | 0 | 9 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|--|--|--|
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 2 / 34 (5.88%) 2 | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 2 / 57 (3.51%) 2 | 5 / 34 (14.71%) 5 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Colitis ulcerative subjects affected / exposed occurrences (all) Anorectal discomfort subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 1 / 57 (1.75%) 1 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 1 / 57 (1.75%) 1 0 / 57 (0.00%) 0 | 2 / 34 (5.88%) 2 9 / 34 (26.47%) 13 2 / 34 (5.88%) 2 3 / 34 (8.82%) 3 3 / 34 (8.82%) 3 2 / 34 (5.88%) 5 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Upper respiratory tract inflammation subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 | 2 / 34 (5.88%) 2 2 / 34 (5.88%) 4 | |
| Skin and subcutaneous tissue disorders Dermatitis | | | |

| | | | |
|--|--|---|--|
| subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 2 / 57 (3.51%) 2 | 2 / 34 (5.88%) 2 2 / 34 (5.88%) 2 | |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 3 / 34 (8.82%) 3 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 5 / 57 (8.77%) 5 | 2 / 34 (5.88%) 2 | |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Viral infection subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 1 / 57 (1.75%) 1 7 / 57 (12.28%) 7 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 | 2 / 34 (5.88%) 3 2 / 34 (5.88%) 2 3 / 34 (8.82%) 3 2 / 34 (5.88%) 2 2 / 34 (5.88%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 11 June 2018 | Global Amendment 1: The following main changes were introduced by this amendment: Timing (days) was corrected for Visit 1, flare confirmation, and re-induction. Vital status collection timelines and timing of the assessments were clarified. Details for end of study (EOS) visit were clarified. Further endpoints were added to align with the TSAP. Steroid tapering instructions for budesonide MMX and beclomethasone dipropionate were added since they were previously missing. Criterion for withdrawal from trial treatment of patients not achieving clinical remission within the first 48 weeks of maintenance treatment was modified to consider the investigator's decision, based on individual patient history and available alternative treatment options. Instructions for s.c. trial drug administration were updated based on the results of trial 1368-0003. |
| 11 June 2018 | Global Amendment 1 (continued): Detailed instructions for monitoring and handling of systemic hypersensitivity reactions were added since they were previously missing. Instructions for permitted use of corticosteroids were clarified for clinical practice. Storage timelines for pharmacokinetics (PK) and anti-drug antibody (ADA) samples were corrected. Collected medical and surgical history was simplified since not all of this information was required for a roll-over trial. Timing of end of trial (EOT) and end of study (EOS) visits for prematurely discontinued patients was modified since a clarification was required. Baseline definitions for efficacy and safety were aligned. Exposure analysis plan for safety across projects with spesolimab given as rescue medication was aligned for harmonisation across projects. The expected number of patients was corrected. |
| 06 November 2018 | Global Amendment 2: The following main changes were introduced by this amendment: Further endpoint regarding faecal lactoferrin (FLF) was added since it had been missed in the previous version. Use of birth control for men able to father a child was removed from Inclusion Criterion #3 and from contraception requirements, to reflect changes in the IB. Restriction of sperm donation for male patients was removed to reflect changes in the IB. Adverse event (AE) monitoring instructions and definitions of adverse events of special interest (AESIs) were modified to remove cytokine release syndrome to reflect changes in the IB. Pre-treatment with steroids before next trial medication administration was permitted as secondary prophylaxis in patients who had experienced mild-to-moderate infusion reactions or anaphylactic reactions in the past to provide more clarity for use of steroids as secondary prophylaxis. |
| 14 November 2018 | Global Amendment 3: This amendment introduced a correction to Flow Chart 3. |

| | |
|------------------|--|
| 04 December 2019 | <p>Global Amendment 4: The following main changes were introduced by this amendment: Tuberculosis tests were introduced. The benefit-risk assessment section was re-phrased to reflect latest IB wording and BI project standard wording. Blood sampling frequency for PK, ADAs, and biomarkers was modified for reconciliation with planned data analysis. Clarification that patients not eligible to take part in trial 1368-0017 were to complete the follow-up visit 16 weeks after last dose in trial 1368-0004 or 1368-0005 Part 1 was added. Exceptions were added for application of exclusion criteria from the original induction trial (Exclusion Criterion #2) regarding:</p> <ul style="list-style-type: none"> - Disease limitation to the rectum (since it could have been met by patients with reduced colonic extension of their initial mucosal inflammation who responded to the induction treatment) and - Latent tuberculosis (since it was considered that these patients could benefit from the maintenance treatment in trial 1368-0017) |
| 04 December 2019 | <p>Global Amendment 4 (continued): The definition of disease flare was updated to align with expert experiences with other ulcerative colitis programmes. The dosing frequency for maintenance treatment was increased from a q12w interval to a q4w interval and the dose for intensified maintenance treatment after disease flare was increased from 300 mg to 600 mg spesolimab. This decision was taken since over 50% of the first 24 patients who rolled over into this trial experienced a relapse/flare during the first 6 months after switching from the induction to the maintenance treatment. This rate was higher than the rate observed with approved drugs for the same condition, which was considered to be related to a decrease in drug exposure below the threshold required to maintain maximum target engagement. It was considered that q4w dosing could maintain drug exposure in the therapeutic range. Since the s.c. injection interval in the intensified maintenance treatment could not be changed to q4w for trial-logistic reasons, it was decided to apply a higher dose of 600 mg to double the exposure compared to the original regimen. The proposed change was considered safe for the patients, since it was lower than the doses previously tested in healthy volunteers and ulcerative colitis patients</p> |
| 24 June 2020 | <p>Global Amendment 5: The following main changes were introduced by this amendment: The benefit-risk assessment was updated based on the results of induction trial 1368-0005. The criterion for patient withdrawal from trial treatment in case of >2 confirmed disease flares within a 12-month time period was changed to >1 confirmed flare during the trial, to allow discontinuation of patients with >1 confirmed flare. The criterion for patient withdrawal from trial treatment if continuation was not in the patient's best interest in the opinion of the investigator was added for clarification. The timing of electrocardiograms was corrected. The restriction period during which any biologic approved for ulcerative colitis was not allowed was clarified to provide a clear instruction about the end of restriction period. Timing of thyroid-stimulating hormone and haemoglobin A1c assessments was modified in the flow chart footnote to provide a specification.</p> |

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| 05 November 2020 | Global Amendment 6: The following main changes were introduced by this amendment: The frequency of stool sampling for faecal biomarker assessments until Visit M13 was reduced from every 12 to every 24 weeks for patients under maintenance treatment, to simplify the procedures of the trial and reduce the long-term burden for patients. The requirement of vital status collection for patients who discontinued trial medication before EOT was removed since it was not considered necessary for this long-term trial and the change was considered to reduce the burden of visits for these patients. The potential impact of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection was included in the benefit-risk assessment. |
| 23 May 2022 | Global Amendment 7: The following main changes were introduced by this amendment: The following main changes were introduced by this amendment: Peripheral neuropathy was included in the benefit-risk assessment and as an AESI, and a stopping rule for peripheral neuropathy was added, to reflect updates at project level. Tables specifying 2 obsolete product formulations were removed, to align with the current investigational medicinal product dossier. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Trial was prematurely ended due to the decision to discontinue the clinical development of spesolimab in inflammatory bowel disease. This decision was based on a lower-than-expected efficacy in previous clinical trials.

Notes: