



Clinical trial results:

An open label, long term safety trial of spesolimab treatment in patients with fistulising Crohn's disease who have completed previous spesolimab trials

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2019-001673-93 |
| Trial protocol | AT DE HU BE ES DK |
| Global end of trial date | 23 September 2022 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 30 September 2023 |
| First version publication date | 30 September 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 1368-0007 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04362254 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintrriage.rdg@boehringer-ingelheim.com |
| Scientific contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintrriage.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 | 21 November 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 May 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 September 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial were to evaluate the long-term safety and the long-term efficacy of spesolimab in patients with perianal fistulising Crohn's disease who had completed treatment in preceding parent trials.

Protection of trial subjects:

Only subjects that met all 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 | 25 May 2020 |
| 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: 3 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Worldwide total number of subjects | 12 |
| 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 months) | 0 |
| Children (2-11 years) | 0 |

| | |
|---------------------------|----|
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 12 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was an open-label, single group, long-term extension trial of approximately 89 weeks duration, which investigated the long-term safety and efficacy of spesolimab in patients with perianal fistulas due to Crohn's disease (CD) who had completed treatment in a parent spesolimab trial.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

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

Blinding implementation details:

This was an open label, single arm trial; therefore, no blinding was necessary.

Arms

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

Arm description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

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

Dosage and administration details:

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab.

| | |
|--|------------------------|
| Investigational medicinal product name | Spesolimab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

| Number of subjects in period 1 | Spesolimab |
|---------------------------------------|------------|
| Started | 12 |
| Completed | 0 |
| Not completed | 12 |
| Due to early termination of the trial | 10 |
| Adverse event, non-fatal | 1 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Spesolimab |
|-----------------------|------------|

Reporting group description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

| Reporting group values | Spesolimab | Total | |
|--|------------|-------|--|
| Number of subjects | 12 | 12 | |
| Age categorical | | | |
| The safety set (SAF) included all patients who received at least one dose of trial drug in the overall 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) | 12 | 12 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period. | | | |
| Units: years | | | |
| arithmetic mean | 37.1 | | |
| standard deviation | ± 10.2 | - | |
| Sex: Female, Male | | | |
| The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period. | | | |
| Units: Participants | | | |
| Female | 3 | 3 | |
| Male | 9 | 9 | |
| Race (NIH/OMB) | | | |
| The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 2 | 2 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 10 | 10 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |

| | | | |
|--|----|----|--|
| Ethnicity (NIH/OMB) | | | |
| The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 12 | 12 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Spesolimab |
| Reporting group description: | |
| During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks. | |
| Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks. | |

Primary: Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment

| | |
|---|--|
| End point title | Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment ^[1] |
| End point description: | |
| Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment. The incidence rate was calculated as Incidence rate = $100 \times \text{number of patients with TEAE} / \text{Total TEAE-specific time at risk}$. Where the Time at risk (for patients who experienced a TEAE) was calculated as Time at Risk (in subject years) = $((\text{date of onset of AE} - \text{study drug start date}) + 1 \text{ day}) / 365.25$ and Time at risk (for patients who did not experience a TEAE) Time at Risk (in subject years) = $((\text{date of the end of time at risk} - \text{study drug start date}) + 1 \text{ day}) / 365.25$. The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period. | |
| End point type | Primary |
| End point timeframe: | |
| First dose of Spesolimab in this trial through to the last dose of spesolimab + 16 weeks, up to 105 weeks. | |
| 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 comparison between groups was planned for this endpoint. | |

| End point values | Spesolimab | | | |
|---|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: Patients with TEAE per 100 patient years | | | | |
| number (not applicable) | 816.6 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with perianal fistula remission

| | |
|--|--|
| End point title | Proportion of patients with perianal fistula remission |
| End point description: | |
| Proportion of patients with perianal fistula remission at weeks 48 and 96. | |
| Perianal fistula remission was defined as closure of all external openings, i.e. no drainage and discharge | |

despite gentle finger compression, that were open and draining at baseline of the parent trial and closure of all external openings that were newly emerged during the parent trial or this trial.

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

End point timeframe:

Baseline, week 48 and 96 of treatment.

| End point values | Spesolimab | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |

Notes:

[2] - No data could be calculated for any subject.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with perianal fistula response

| | |
|-----------------|---|
| End point title | Proportion of patients with perianal fistula response |
|-----------------|---|

End point description:

Proportion of patients with perianal fistula response at weeks 48 and 96.

Perianal fistula response was defined as closure and no drainage and discharge despite gentle finger compression of at least 50% in number of external openings regardless of the onset time, compared with the number of open and drainage fistulas at baseline of the parent trial.

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

End point timeframe:

Baseline, week 48 and 96 of treatment.

| End point values | Spesolimab | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |

Notes:

[3] - No data could be calculated for any subject.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of Spesolimab through to the last dose of Spesolimab + 16 weeks, up to 105 weeks.

Adverse event reporting additional description:

The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Spesolimab |
|-----------------------|------------|

Reporting group description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

| Serious adverse events | Spesolimab | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Fistula | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Spesolimab | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 12 (91.67%) | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Intestinal anastomosis complication | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Seroma | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Inflammation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| occurrences (all) | 5 | | |
| Injection site reaction | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 2 | | |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |

| | | | |
|--|----------------------|--|--|
| Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Anal polyp subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Rectal stenosis subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Erythema subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Eczema subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Psychiatric disorders Panic attack subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Fistula | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Fistula discharge | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Muscle tightness | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 6 / 12 (50.00%) | | |
| occurrences (all) | 6 | | |
| Fungal infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 4 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Pustule | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 20 March 2020 | - Endpoints of endoscopic remission (secondary endpoint) and endoscopic response (further endpoint) were removed as no ileocolonoscopy was to be performed. The endoscopic score SES-CD was explored as further endpoint - Endpoint of clinical remission removed from secondary endpoints. The Crohn's Disease Activity Index (CDAI) score was explored as further endpoint as the patient population was expected to have low CDAI scores as per eligibility criteria (CDAI \leq 250) - The criteria for treatment discontinuation in case of flare/fistula relapse were changed to allow the investigator to decide whether there was clinical benefit for the patient instead of restricting the chance to continue to those who meet restricted definition of clinical response and to take a more global approach to clinical improvement of patients, as these patients may have had no other options. |
| 21 January 2021 | - Luminal inflammatory flare was differentiated from fistula relapse as patients who presented a luminal inflammatory flare without fistula relapse could receive antiinflammatory therapy as per Standard of Care (SOC) to treat luminal flare based on clinician judgement while continuing the same spesolimab maintenance dose - In case of restricted physical visits to the site during the COVID-19 pandemic the investigator could discuss with Boehringer Ingelheim to continue the trial treatment and trial medication could be shipped to the patient's home if acceptable according to local law and regulations |

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.

This trial was terminated early due to BI's decision to terminate the development of spesolimab in fistulising and fibrostenotic Crohn's disease.

Notes: