



Clinical trial results:

A Phase 3 Randomized, Double-blind, Placebo-controlled, Parallel-group Efficacy and Safety Study of SHP647 as Maintenance Therapy in Subjects With Moderate to Severe Crohn's Disease (CARMEN CD 307)

Summary

| | |
|--------------------------|--|
| EudraCT number | 2017-000617-23 |
| Trial protocol | IE GB NL AT LT CZ BE ES HU SK DE PT EE PL BG GR HR IT RO |
| Global end of trial date | 13 September 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 19 March 2022 |
| First version publication date | 19 March 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | SHP647-307 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03627091 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Shire |
| Sponsor organisation address | 300 Shire Way, Lexington, United States, MA 02421 |
| Public contact | Study Director, Shire, ClinicalTransparency@takeda.com |
| Scientific contact | Study Director, Shire, ClinicalTransparency@takeda.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 | 13 September 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 September 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy and safety of ontamalimab as maintenance treatment in subjects with moderate to severe Crohn's disease (CD).

Protection of trial subjects:

The study was conducted in accordance with current applicable industry regulations, International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996) and any updates, European Union (EU) Directive 2001/20/EC and its updates, the ethical principles in the Declaration of Helsinki, and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 06 February 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 57 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------------|
| Country: Number of subjects enrolled | Australia: 2 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 1 |
| Country: Number of subjects enrolled | Hungary: 2 |
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Japan: 1 |
| Country: Number of subjects enrolled | Mexico: 2 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Poland: 6 |
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Country: Number of subjects enrolled | South Africa: 2 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | Ukraine: 7 |
| Country: Number of subjects enrolled | United States: 2 |

| | |
|------------------------------------|----|
| Worldwide total number of subjects | 40 |
| EEA total number of subjects | 20 |

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) | 1 |
| Adults (18-64 years) | 38 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 33 sites between 06 February 2019 (first participant first visit) and 13 September 2021 (last participant last visit). 278 sites were initiated in this study, but only 33 sites had enrolled participants.

Pre-assignment

Screening details:

A total of 40 participants with moderate to severe CD who completed their participation in an induction study (either SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) and fulfilled the efficacy entry criteria of this study were enrolled and received study treatment in this 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 received matched placebo of ontamalimab subcutaneous (SC) injection using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks.

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received placebo matched to ontamalimab, injection, subcutaneously using a prefilled syringe.

| | |
|------------------|-------------------|
| Arm title | Ontamalimab 25 mg |
|------------------|-------------------|

Arm description:

Participants received 25 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Ontamalimab |
| Investigational medicinal product code | SHP647 |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received ontamalimab 25 mg, injection, subcutaneously using a prefilled syringe.

| | |
|------------------|-------------------|
| Arm title | Ontamalimab 75 mg |
|------------------|-------------------|

Arm description:

Participants received 75 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4

weeks for up to 52 weeks.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Ontamalimab |
| Investigational medicinal product code | SHP647 |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received ontamalimab 75 mg, injection, subcutaneously using a prefilled syringe.

| Number of subjects in period 1 | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|---------------------------------------|---------|-------------------|-------------------|
| Started | 19 | 10 | 11 |
| Completed | 7 | 4 | 6 |
| Not completed | 12 | 6 | 5 |
| Consent withdrawn by subject | 2 | - | 2 |
| Physician decision | 2 | - | - |
| Adverse event, non-fatal | - | - | 2 |
| Disease relapse | 7 | 5 | 1 |
| Site terminated by sponsor | - | 1 | - |
| Unspecified | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|---|-------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received matched placebo of ontamalimab subcutaneous (SC) injection using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |
| Reporting group title | Ontamalimab 25 mg |
| Reporting group description: | |
| Participants received 25 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |
| Reporting group title | Ontamalimab 75 mg |
| Reporting group description: | |
| Participants received 75 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |

| Reporting group values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg |
|------------------------|---------|-------------------|-------------------|
| Number of subjects | 19 | 10 | 11 |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|--------|---------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 37.7 | 38.4 | 45.8 |
| standard deviation | ± 14.26 | ± 7.18 | ± 14.85 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | 12 | 4 | 6 |
| Female | 7 | 6 | 5 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | 0 |
| Asian | 1 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 1 |
| Black or African American | 1 | 0 | 0 |
| White | 17 | 8 | 10 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 1 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 2 | 1 |
| Not Hispanic or Latino | 19 | 8 | 10 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 40 | | |

| | | | |
|---|----|--|--|
| Age Categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Male | 22 | | |
| Female | 18 | | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 1 | | |
| Asian | 1 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |
| Black or African American | 1 | | |
| White | 35 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 1 | | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 3 | | |
| Not Hispanic or Latino | 37 | | |
| Unknown or Not Reported | 0 | | |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received matched placebo of ontamalimab subcutaneous (SC) injection using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |
| Reporting group title | Ontamalimab 25 mg |
| Reporting group description: Participants received 25 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |
| Reporting group title | Ontamalimab 75 mg |
| Reporting group description: Participants received 75 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks. | |

Primary: Number of Participants With Clinical Remission at Week 52

| | |
|---|--|
| End point title | Number of Participants With Clinical Remission at Week 52 ^[1] |
| End point description: Clinical remission was defined by 2-item PRO sub-scores of average worst daily abdominal pain less than or equal to (\leq) 3 (based on 11 point numerical rating scale [NRS] ranging from 0 [no pain] to 10 [worst imaginable pain]); and average daily stool frequency \leq 2 of type 6/7 (very soft stools/liquid stools) as per the Bristol Stool Form Scale (BSFS) over the 7 most recent days. BSFS ranges from 1 (separate hard lumps, hard to pass), 2 (sausage-shaped, but lumpy), 3 (like a sausage but with cracks on the surface), 4 (like a sausage or snake, smooth and soft), 5 (soft blobs with clear-cut edges), 6 (fluffy pieces with ragged edges, a mushy stool), 7 (watery, no solid pieces, entirely liquid). Participants with missing data at Week 52 or discontinuation before Week 52 were considered failures. Number of participants with clinical remission at Week 52 were reported. Full analysis set (FAS) consisted of all randomized participants who had received at least 1 dose of study treatment. | |
| End point type | Primary |
| End point timeframe: At Week 52 | |
| 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: Due to the premature discontinuation of the study only descriptive data was planned to be analyzed for this endpoint. | |

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | | | | |
| Number analyzed | 2 | 3 | 5 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Enhanced Endoscopic Response at Week 52

| | |
|-----------------|--|
| End point title | Number of Participants With Enhanced Endoscopic Response at Week 52 ^[2] |
|-----------------|--|

End point description:

Enhanced endoscopic response was defined as a decrease in Simple Endoscopic Score for Crohn's disease (SES-CD) of at least 50 percent (%) from induction study (either SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29] baseline. The SES-CD considers ileum, right colon, transverse colon, left colon, rectum in terms of: size of ulcers, ulcerated surface, affected surface and presence of narrowing. Each graded from 0-3. Scale ranges from 0-56 with a higher score indicating greater severity of disease. Participants with missing data at Week 52 or who discontinued before Week 52 were considered non responders. Number of participants with enhanced endoscopic response at Week 52 were reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

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

End point timeframe:

At Week 52

Notes:

[2] - 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: Due to the premature discontinuation of the study only descriptive data was planned to be analyzed for this endpoint.

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 2 | 4 | 6 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Remission Based on Crohn's Disease Activity Index (CDAI) Score at Week 52

| | |
|-----------------|--|
| End point title | Number of Participants With Clinical Remission Based on Crohn's Disease Activity Index (CDAI) Score at Week 52 |
|-----------------|--|

End point description:

Clinical remission was defined as a CDAI score of < 150. CDAI assessed CD based on clinical signs/symptoms such as number of liquid stools, intensity of abdominal pain, general well-being (subjective), and presence of complications, use of antidiarrheal, presence of abdominal mass, physical examination and hematocrit (objective). CDAI score is equal to sum of weighted scores for subjective and objective items which range from 0-149 points: asymptomatic remission, 150-220 points: mild to moderate active CD, 221-450 points: moderate to severe active CD, > 451 points: severely active to fulminant disease. Higher score indicating more severity. Participants with missing data at Week 52 or who discontinued before Week 52 were considered failures. Number of participants with clinical remission as measured by CDAI at Week 52 were reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

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

End point timeframe:

At Week 52

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 8 | 4 | 7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Glucocorticoid-free Clinical Remission at Week 52

| | |
|-----------------|---|
| End point title | Number of Participants With Glucocorticoid-free Clinical Remission at Week 52 |
|-----------------|---|

End point description:

Glucocorticoid-free clinical remission was defined as clinical remission by 2-item PRO in addition to not requiring any treatment with glucocorticoids for at least 12 weeks prior to the Week 52 visit. Clinical remission was defined by 2-item PRO sub-scores of average worst daily abdominal pain ≤ 3 (based on 11 point NRS ranging from 0 [no pain] to 10 [worst imaginable pain]); and average daily stool frequency ≤ 2 of type 6/7 (very soft stools/liquid stools) as per the BSFS over the 7 most recent days. BSFS ranges from 1 (separate hard lumps, hard to pass), 2 (sausage-shaped, but lumpy), 3 (like a sausage but with cracks on the surface), 4 (like a sausage or snake, smooth and soft), 5 (soft blobs with clear-cut edges), 6 (fluffy pieces with ragged edges, a mushy stool), 7 (watery, no solid pieces, entirely liquid). FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

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

End point timeframe:

At Week 52

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 2 | 1 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Remission Defined by Crohn's Disease (CD) e-diary Sub-scores- at Week 52

| | |
|-----------------|---|
| End point title | Number of Participants With Clinical Remission Defined by Crohn's Disease (CD) e-diary Sub-scores- at Week 52 |
|-----------------|---|

End point description:

Clinical remission was defined by CD daily e-diary 2-item PRO subscores of average daily abdominal pain ≤ 1 (based on the 4 point scale, with scores ranging from 0 [none] to 3 [severe]) over 7 most recent days and average daily stool frequency ≤ 3 of type 6/7 (very soft stools/liquid stools) as per the BSFS over 7 most recent days. BSFS ranges from 1 (separate hard lumps, hard to pass), 2 (sausage-shaped, but lumpy), 3 (like a sausage but with cracks on the surface), 4 (like a sausage or snake, smooth and soft), 5 (soft blobs with clear-cut edges), 6 (fluffy pieces with ragged edges, a mushy stool), 7 (watery, no solid pieces, entirely liquid). Participants with missing data at Week 52 or who discontinued before Week 52 considered failures. Number of participants with clinical remission based on Crohn's Disease (CD) e-diary Sub-scores for abdominal pain was reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

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

End point timeframe:

At Week 52

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 2 | 3 | 7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Sustained Clinical Remission at Week 52

| | |
|-----------------|---|
| End point title | Number of Participants With Sustained Clinical Remission at Week 52 |
|-----------------|---|

End point description:

Sustained clinical remission was defined as clinical remission by 2-item PRO at both Week 52 visit and the maintenance baseline in this Study. Clinical remission was defined by 2-item PRO sub-scores of average worst daily abdominal pain less than or equal to (\leq) 3 (based on 11 point NRS ranging from 0 [no pain] to 10 [worst imaginable pain]); and average daily stool frequency ≤ 2 of type 6/7 (very soft stools/liquid stools) as per the BSFS over the 7 most recent days. BSFS ranges from 1 (separate hard lumps, hard to pass), 2 (sausage-shaped, but lumpy), 3 (like a sausage but with cracks on the surface), 4 (like a sausage or snake, smooth and soft), 5 (soft blobs with clear-cut edges), 6 (fluffy pieces with ragged edges, a mushy stool), 7 (watery, no solid pieces, entirely liquid). Number of participants with sustained clinical remission at Week 52 were reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

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

End point timeframe:

At Week 52

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 2 | 1 | 2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Sustained Enhanced Endoscopic Response at Week 52

| | |
|---|---|
| End point title | Number of Participants With Sustained Enhanced Endoscopic Response at Week 52 |
| End point description: Sustained enhanced endoscopic response was defined as enhanced endoscopic response at both Week 52 visit and the maintenance baseline in this study. Enhanced endoscopic response was defined as a decrease in SES-CD of at least 50 % from induction study (either SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) baseline. The SES-CD considers ileum, right colon, transverse colon, left colon, rectum in terms of: size of ulcers, ulcerated surface, affected surface and presence of narrowing. Each graded from 0-3. Scale ranges from 0-56 with a higher score indicating greater severity of disease. Number of participants with sustained enhanced endoscopic response at Week 52 were reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment. | |
| End point type | Secondary |
| End point timeframe: At Week 52 | |

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 1 | 2 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Remission Based on 2-item PRO With Enhanced Endoscopic Response at Week 52

| | |
|---|---|
| End point title | Number of Participants With Clinical Remission Based on 2-item PRO With Enhanced Endoscopic Response at Week 52 |
| End point description: Clinical remission was defined by 2-item PRO sub-scores of average worst daily abdominal pain ≤ 3 (based on 11-point NRS) over the 7 most recent days and average daily stool frequency ≤ 2 of Type 6/7 (very soft stools/liquid stools) as shown in the BSFS over the 7 most recent days. Participants with missing data at Week 52 or who discontinued before Week 52 were considered failures. Enhanced endoscopic response was defined as a decrease in SES-CD of at least 50% from induction study (SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29] baseline. Participants with missing | |

data at Week 52 or who discontinued before Week 52 were considered non-responders. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Week 52 | |

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 0 | 3 | 4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Complete Endoscopic Healing at Week 52

| | |
|-----------------|--|
| End point title | Number of Participants With Complete Endoscopic Healing at Week 52 |
|-----------------|--|

End point description:

Complete endoscopic healing was defined as SES-CD scale score from 0-2. The SES-CD considers ileum, right colon, transverse colon, left colon, rectum in terms of: size of ulcers, ulcerated surface, affected surface and presence of narrowing. Each graded from 0-3. Scale ranges from 0-56 with a higher score indicating greater severity of disease. Participants with missing data at Week 52 or who discontinued before Week 52 were considered failures. Number of participants with complete endoscopic healing at Week 52 were reported. FAS consisted of all randomized participants who had received at least 1 dose of study treatment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Week 52 | |

| End point values | Placebo | Ontamalimab 25 mg | Ontamalimab 75 mg | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 10 | 11 | |
| Units: Participants | 0 | 3 | 3 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to 56 weeks

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received matched placebo of ontamalimab subcutaneous (SC) injection using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Ontamalimab 75 mg |
|-----------------------|-------------------|

Reporting group description:

Participants received 75 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Ontamalimab 25 mg |
|-----------------------|-------------------|

Reporting group description:

Participants received 25 mg ontamalimab SC injection, using prefilled syringe on Day 1 Baseline Visit (Week 16 of the SHP647-305 [2017-000575-88] or SHP647-306 [2017-000576-29]) once every 4 weeks for up to 52 weeks.

| Serious adverse events | Placebo | Ontamalimab 75 mg | Ontamalimab 25 mg |
|---|----------------|-------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 2 / 11 (18.18%) | 0 / 10 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (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 |
| Gastrointestinal disorders | | | |
| Ileal perforation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| 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 | Ontamalimab 75 mg | Ontamalimab 25 mg |
|---|-----------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 19 (47.37%) | 8 / 11 (72.73%) | 5 / 10 (50.00%) |
| Vascular disorders | | | |
| Capillary fragility | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 2 / 11 (18.18%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Prostatic disorder subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 |
| Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Stress subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Procedural pain subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 2 | 1 / 11 (9.09%) 4 | 0 / 10 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 |

| | | | |
|--------------------------------------|-----------------|----------------|-----------------|
| Blood and lymphatic system disorders | | | |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all) | 3 | 1 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroduodenitis | | | |

| | | | |
|---|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 |
| Gastritis subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Skin disorder subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Eczema subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Dyshidrotic eczema subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 2 | 1 / 11 (9.09%) 1 | 1 / 10 (10.00%) 1 |
| Fistula subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 |
| Musculoskeletal stiffness | | | |

| | | | |
|------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Corona virus infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 28 August 2018 | Protocol Amendment 1: Updated the global fax number. Updated inclusion criterion 3b (ii) to indicate that subjects must have a decrease of at least 100 points in CDAI score from induction study baseline. Updated exclusion criterion 7 to indicate that subjects who developed enterovesical or enterovaginal fistulae during the induction study would be excluded. Updated exclusion criterion 12 to indicate that subjects meeting the few lab criteria would be excluded. Updated exclusion criterion 5 to indicate the exclusion of subjects who do not agree to postpone donation of any organ or tissue. Added statement that subjects who are withdrawn early from the study due to fulfilling the criteria for treatment failure also may be eligible to enter the long-term safety study. Updated key secondary endpoint to include the stipulated window for not requiring any treatment with glucocorticoids. Added describing risks and benefits of treatment. Added pregnancy to the list of reasons subject may be withdrawn from study treatment. Added language to specify that any antidiarrheal opiate drugs must be taken at stable doses for the duration of the study. |
| 22 November 2019 | Protocol Amendment 2: Updated language for reporting of product quality complaints. Added complete endoscopic healing will be measured by centrally read endoscopy. Revised exclusion criterion 4. Added that adverse events of special interest will be summarized by treatment group. Revised to extend window between Visit 14 and Visit 14 to 10 days. Added footnote for unscheduled assessment for calculating CDAI. Revised colonoscopy preparation may be done as colonoscopy procedure. Updated key secondary point. Added criteria of treatment failure as reason of subject withdrawal. Changed term 'protocol violations' to 'protocol deviations'. Updated to specify investigator may perform unscheduled CDAI assessment based on subject's reported symptoms. Changed 'very soft stools/liquid stools' to 'very soft stool/liquid stool frequency'. Updated method for calculating 2-item PRO and SES-CD score. Added ileocelectomy along with partial colectomy. Text updated to calculate CDAI scores. |
| 17 September 2020 | Protocol Amendment 3: Changed safety follow-up period from 16 weeks to 12 weeks. Added note after the implementation of Amendment 3, the participant's next scheduled visit will be the Week 52/ET visit, which should be conducted no later than 4 weeks from the participant's last study visit prior to the implementation of SHP647-304 Amendment 4. Updated pharmacokinetic assessments; removed health-related quality of life assessments. Updated footnotes 'c' and 'd'. Added footnote in case of a DTP situation, some procedures will be performed by remote visits via virtual communications and allow clinical laboratory assays to be done by local laboratory in case of issues related to COVID-19. Added footnote to specify that subjects performing home administrations consecutively for 3 months will need to perform liver function testing locally. Added language to clarify the early termination of this study by the sponsor, colonoscopy is optional for subjects who received less than 52 weeks of treatment. Addition of details around DTP program/provision for home administration of investigational product. Removed other secondary objectives and text regarding treatment failures. Added text on allowing continued treatment with ontamalimab for subjects benefiting. Added text on allowing study program to be stopped in case of no clinical efficacy. Updated participant's maximum study duration. |

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.

The study was closed early as the sponsor discontinued the ontamalimab clinical trial program in CD for reasons unrelated to safety or efficacy.

Notes: