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 (<=) 3 (based on 11 point numerical rating scale [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 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 (<=) 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	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Prostatic disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 19 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 19 (5.26%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	4	0
Paraesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	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	0 / 19 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dyshidrotic eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Fistula			
subjects affected / exposed	1 / 19 (5.26%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	1 / 19 (5.26%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	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 ileocolectomy 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: