Clinical trial results:
A Phase 3 Randomized, Double-blind, Placebo controlled, Parallel group Efficacy and Safety Study of SHP647 as Induction Therapy in Subjects With Moderate to Severe Crohn's Disease (CARMEN CD 306)

Summary

EudraCT number	2017-000576-29
Trial protocol	IE BE HU SK ES PT EE BG GR
Global end of trial date	18 August 2020

Results information

Result version number	v1 (current)
This version publication date	03 May 2021
First version publication date	03 May 2021

Trial information

Trial identification

Sponsor protocol code	SHP647-306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03566823
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	18 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 August 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of ontamalimab in subjects with moderate to severe Crohn's disease (CD) in inducing clinical remission based on 2-item patient-reported outcome (PRO) (abdominal pain severity and very soft stool/liquid stool frequency) and inducing endoscopic response based on centrally read colonoscopy.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996), the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	34
EEA total number of subjects	15

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)	34
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 25 sites in the Unites States, Belgium, Bosnia and Herzegovina, Colombia, Hungary, Japan, Mexico, Slovakia, Republic of Korea, Spain and Ukraine between 17 July 2018 (first subject first visit) and 18 August 2020 (last subject last visit).

Pre-assignment

Screening details:

A total of 34 subjects were enrolled into the study, of which 27 subjects completed the study. Other secondary endpoints were not analyzed due to early discontinuation of the study for reasons unrelated to safety.

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:

Subjects received ontamalimab matching-placebo, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.

Arm type	Placebo
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:

Subjects received placebo matched to ontamalimab SC injection, using a PFS.

Arm title	Ontamalimab 25 mg

Arm description:

Subjects received ontamalimab 25 milligram (mg), injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.

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:

Subjects received 25 mg of ontamalimab SC injection, using a PFS.

Arm title	Ontamalimab 75 mg

Arm description:

Subjects received ontamalimab 75 mg, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.

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:

Subjects received 75 mg of ontamalimab SC injection, using a PFS.

Number of subjects in period 1	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg
Started	6	15	13
Completed	4	12	11
Not completed	2	3	2
Consent withdrawn by subject	1	2	-
Adverse event, non-fatal	1	-	2
Lack of efficacy	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received ontamalimab matching-placebo, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 25 mg
Reporting group description:	
Subjects received ontamalimab 25 milligram (mg), injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 75 mg
Reporting group description:	
Subjects received ontamalimab 75 mg, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	

Reporting group values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg
Number of subjects	6	15	13
Age categorical Units: subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	15	13
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	42.4	37.5	39.1
standard deviation	± 13.60	± 10.20	± 12.74
Sex: Female, Male Units: subjects			
Female	2	8	5
Male	4	7	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	2	0
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	1	0	1
White	3	12	11
More than one race	0	0	0
Unknown or Not Reported	2	0	0
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	2	1	1
Not Hispanic or Latino	4	14	12
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	34		
Age categorical Units: subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	34		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: subjects			
Female	15		
Male	19		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	2		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	2		
White	26		
More than one race	0		
Unknown or Not Reported	2		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	30		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received ontamalimab matching-placebo, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 25 mg
Reporting group description:	
Subjects received ontamalimab 25 milligram (mg), injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 75 mg
Reporting group description:	
Subjects received ontamalimab 75 mg, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	

Primary: Number of Subjects With Clinical Remission Based on 2-item Patient-reported Outcome (PRO) at Week 16

End point title	Number of Subjects With Clinical Remission Based on 2-item Patient-reported Outcome (PRO) at Week 16[1]
End point description:	
Clinical remission was defined by 2-item PRO subs-cores 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). Subjects with missing data at Week 16 or discontinuation before Week 16 were considered failures. Number of subjects with clinical remission were reported. The full analysis set (FAS) consisted of all subjects in the randomized set who had received at least 1 dose of IP.	
End point type	Primary
End point timeframe:	
At Week 16	
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: 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	6	15	13	
Units: Subjects	3	5	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Endoscopic Response at Week 16

End point title	Number of Subjects With Endoscopic Response at Week 16[2]

End point description:

Endoscopic response was defined as a decrease in Simple Endoscopic Score for Crohn's disease (SES-CD) of at least 25 percent (%) from 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. Subjects with missing data at Week 16 or who discontinued before Week 16 were considered failures. Number of subjects with endoscopic response were reported. The FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

End point type	Primary

End point timeframe:

At Week 16

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: 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	6	15	13	
Units: Subjects	2	10	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Remission Based on Crohn's Disease Activity Index (CDAI) Score at Week 16

End point title	Number of Subjects With Clinical Remission Based on Crohn's Disease Activity Index (CDAI) Score at Week 16

End point description:

Clinical remission was defined as a CDAI score of <150. CDAI assesses 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. Number of subjects with clinical remission as measured by CDAI were reported. The FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	4	8	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Enhanced Endoscopic Response at Week 16

End point title	Number of Subjects With Enhanced Endoscopic Response at Week 16

End point description:

Enhanced endoscopic response was defined as a decrease in SES-CD by matching segments of at least 50% from 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. Subjects with missing data at Week 16 or who discontinued before Week 16 were considered non-responders. Number of subjects with enhanced endoscopic response were reported. The FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	2	5	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Remission Based on 2-item PRO With 4-point Scale for Abdominal Pain at Week 16

End point title	Number of Subjects With Clinical Remission Based on 2-item PRO With 4-point Scale for Abdominal Pain at Week 16

End point description:

Clinical remission was defined by 2-item PRO subs-cores of average daily abdominal pain <=1 (based on the 4 point scale, with scores ranging from 0 [none] to 3 [severe]) over the 7 most recent days and average daily stool frequency <=3 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). Subjects with missing data at Week 16 or who discontinued before Week 16 were considered failures. Number of subjects with enhanced endoscopic response were reported. The FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	3	6	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Response Based on 2-item PRO With 2 Criteria at Week 16

End point title	Number of Subjects With Clinical Response Based on 2-item PRO With 2 Criteria at Week 16

End point description:

Clinical response was measured by 2-item PRO; defined as meeting at least 1 of the 2 criteria: 1)A decrease of >=30%and at least 2points from baseline in the average daily worst abdominal pain over the 7most recent days, with the average daily stool frequency of type 6/7(very soft/liquid stools)either a)not worsening from baseline and/or b)average daily stool frequency <=2 of type 6/7 as per the BSFS over the 7most recent days; 2)A decrease of >=30%from baseline in average daily stool frequency of type 6/7(very soft/liquid stools)as per the BSFS over the 7most recent days, with the average daily worst abdominal pain either a)not worsening from baseline and/or b)worst daily abdominal pain <=3(based on 11-point NRS)over the 7most recent days. Subjects with missing data or who discontinued at/before Week16 were considered failures. Number of subjects with clinical response were reported. The FAS consisted of all subjects in the randomized set who had received at least 1dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	5	11	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Remission Based on 2-Item PRO With Endoscopic Response at Week 16

End point title	Number of Subjects With Clinical Remission Based on 2-Item

	PRO With Endoscopic Response at Week 16

End point description:

Clinical remission was defined by 2-item PRO subs-cores of average worst daily abdominal pain <=3(based on 11point 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 perBSFS ranging from type1(separate hard lumps-like stools)to type7(entirely liquid stools)over the 7most recent days. Endoscopic response was defined as a decrease in SES-CDof at least 25%from baseline. 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 from0-3. Scale ranges from0-56 with a higher score indicating greater severity of disease. Subjects with missing data or who discontinued at/before Week16 were considered failures. Number of subjects with clinical remission with endoscopic response were reported. The FAS consisted of all subjects in the randomized set who had received at least 1dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	1	4	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Complete Endoscopic Healing at Week 16

End point title	Number of Subjects With Complete Endoscopic Healing at Week 16

End point description:

Clinical remission was defined by 2-item PRO subs-cores 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 <=2of type 6/7 (very soft stools/liquid stools)as per BSFS ranging from type1 (separate hard lumps-like stools) to type7 (entirely liquid stools) over the 7 most recent days. Endoscopic response was defined as a decrease in SES-CD of at least 25% from baseline. 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. Subjects with missing data or who discontinued at/before Week16 were considered failures. Number of subjects with complete endoscopic healing were reported. The FAS consisted of all subjects in the randomized set who had received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	15	13	
Units: Subjects	1	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Response as Measured by CDAI-100 at Week 16

End point title	Number of Subjects With Clinical Response as Measured by CDAI-100 at Week 16

End point description:

Clinical response is measured by at least a 100-point reduction in the CDAI from baseline (CDAI-100 response). CDAI assesses 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. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[3]	0[4]	0[5]	
Units: Subjects				

Notes:

[3] - Data collection and analysis for this endpoint was not performed due to study termination.

[4] - Data collection and analysis for this endpoint was not performed due to study termination.

[5] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Response as Measured by CDAI-70 at Week 16

End point title	Number of Subjects With Clinical Response as Measured by CDAI-70 at Week 16

End point description:

Clinical response is measured by at least a 70-point reduction in the CDAI from baseline (CDAI-70 response). CDAI assesses 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. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: Subjects				

Notes:

[6] - Data collection and analysis for this endpoint was not performed due to study termination.

[7] - Data collection and analysis for this endpoint was not performed due to study termination.

[8] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Remission Over Time

End point title	Number of Subjects With Clinical Remission Over Time

End point description:

Clinical remission is defined by 2-item PRO subs-cores of average worst daily abdominal pain (based on 11 point NRS ranging from 0 [no pain] to 10 [worst imaginable pain]); and average daily stool frequency of type 6/7 (very soft stools/liquid stools) as per 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). Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[9]	0[10]	0[11]	
Units: Subjects				

Notes:

[9] - Data collection and analysis for this endpoint was not performed due to study termination.

[10] - Data collection and analysis for this endpoint was not performed due to study termination.

[11] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Individual and Total Sign/Symptom Score Based on Subjects Daily Electronic Diary (e-diary) Entries

End point title	Change From Baseline in Individual and Total Sign/Symptom Score Based on Subjects Daily Electronic Diary (e-diary) Entries

End point description:

CD clinical signs and symptoms includes total stool frequency, rectal bleeding frequency, rectal urgency frequency, nausea severity, vomiting frequency, and rectal incontinence frequency. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: Subjects				

Notes:

[12] - Data collection and analysis for this endpoint was not performed due to study termination.

[13] - Data collection and analysis for this endpoint was not performed due to study termination.

[14] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Endoscopic Healing at Week 16

End point title	Number of Subjects With Endoscopic Healing at Week 16

End point description:

Endoscopic healing is measured by SES-CD <=4 and at least 2-point reduction versus baseline and no sub-score >1 in any individual variable. 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. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: Subjects				

Notes:

[15] - Data collection and analysis for this endpoint was not performed due to study termination.

[16] - Data collection and analysis for this endpoint was not performed due to study termination.

[17] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total (Absolute) Score at Weeks 8, 12 and 16

End point title	Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total (Absolute) Score at Weeks 8, 12 and 16

End point description:

The IBDQ is a psychometrically validated PRO instrument for measuring the disease-specific health-related quality of life (HRQL) in subjects with IBD, including CD. The IBDQ consists of 32 items, which are grouped into 4 domains and scored as: bowel function (10 to 70), systemic symptoms (5 to 35), emotional status (12 to 84), and social function (5 to 35). The total IBDQ score ranges from 32 to 224. For the total score and each domain, a higher score indicates better HRQL. A score of at least 170 corresponds to clinical remission and an increase of at least 16 points is considered to indicate a clinically meaningful improvement. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 12 and 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[18]	0[19]	0[20]	
Units: Subjects				

Notes:

[18] - Data collection and analysis for this endpoint was not performed due to study termination.

[19] - Data collection and analysis for this endpoint was not performed due to study termination.

[20] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form-36 Health Survey (SF-36) Scores at Week 16

End point title	Change From Baseline in Short Form-36 Health Survey (SF-36) Scores at Week 16

End point description:

The SF-36, version 2 is a generic quality-of-life instrument that has been widely used to assess HRQL of subjects. The SF-36 consists of 36 items that are aggregated into 8 multi-item scales (physical functioning, role – physical, bodily pain, general health, vitality, social functioning, role – emotional, and

mental health), with scores ranging from 0 to 100. Higher scores indicate better HRQL. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[21]	0[22]	0[23]	
Units: Subjects				

Notes:

[21] - Data collection and analysis for this endpoint was not performed due to study termination.

[22] - Data collection and analysis for this endpoint was not performed due to study termination.

[23] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Based on Incidence of All-cause Hospitalizations

End point title	Number of Subjects Based on Incidence of All-cause Hospitalizations

End point description:

Incidence of all cause hospitalizations was planned to be assessed. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline up to Week 32

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	0[25]	0[26]	
Units: Subjects				

Notes:

[24] - Data collection and analysis for this endpoint was not performed due to study termination.

[25] - Data collection and analysis for this endpoint was not performed due to study termination.

[26] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Based on Total Inpatient Days

End point title	Number of Subjects Based on Total Inpatient Days

End point description:

Total inpatient days were planed to be assessed. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline up to Week 32

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[27]	0[28]	0[29]	
Units: Subjects				

Notes:

[27] - Data collection and analysis for this endpoint was not performed due to study termination.

[28] - Data collection and analysis for this endpoint was not performed due to study termination.

[29] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Based on Incidence of CD-related Surgeries and Other Surgical Procedures

End point title	Number of Subjects Based on Incidence of CD-related Surgeries and Other Surgical Procedures

End point description:

Incidence of CD-related surgeries and other surgical procedures were planned to be recorded. Study terminated early for reasons unrelated to safety. Hence, for this endpoint, the planned data collection and analysis was not performed.

End point type	Secondary

End point timeframe:

Baseline up to Week 32

End point values	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[30]	0[31]	0[32]	
Units: Subjects				

Notes:

[30] - Data collection and analysis for this endpoint was not performed due to study termination.

[31] - Data collection and analysis for this endpoint was not performed due to study termination.

[32] - Data collection and analysis for this endpoint was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From screening up to safety follow-up period (Week 32)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received ontamalimab matching-placebo, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 25 mg
Reporting group description:	
Subjects received ontamalimab 25 mg, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	
Reporting group title	Ontamalimab 75 mg
Reporting group description:	
Subjects received ontamalimab 75 mg, injection, subcutaneously using a prefilled syringe on Week 0 (Day 1), Week 4, Week 8, and Week 12 in a 16-week treatment period.	

Serious adverse events	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	2 / 13 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal stenosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (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

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

Non-serious adverse events	Placebo	Ontamalimab 25 mg	Ontamalimab 75 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 15 (40.00%)	5 / 13 (38.46%)
Investigations			
Pain threshold decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Chest injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Memory impairment			

subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Anal fistula			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Crohn's disease			
subjects affected / exposed	2 / 6 (33.33%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Large intestinal stenosis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus generalised			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Spondylitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Fungal skin infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gingival abscess			
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Ureteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2018	Protocol Amendment 1: Updated inclusion criteria to collect additional data for abdominal pain at study entry using the 0-3 CDAI severity scale. Updated exclusion criteria to exclude subjects with non steroidal anti-inflammatory drug-induced colitis, any history of positive tuberculosis (TB) and cirrhosis with or without decompensation; to clarify that subjects with positive hepatitis B core antibody (HBcAb), without hepatitis B virus (HBV) DNA and chronic hepatitis C virus (HCV), without HCV RNA may be eligible for the study. Added new new exclusion criterion to clarify that documentation of HIV status should be performed within 6 months of screening. Added text to clarify that concomitant antidiarrheal opiate drugs were permitted if taken at stable doses for the duration of the study, with dose reduction or discontinuation allowed only if required due to clinical improvement or adverse event. Added new section to provide appropriate guidance on subjects who have been enrolled with elevated liver function test or who have elevated liver function test(s) during the study.
22 November 2019	Protocol Amendment 2: Revised exclusion criterion to clarify that subjects with obstructive colonic stricture were to be excluded if it was clinically significant. Revised text to clarify the allowed doses of steroids. Added text to address FDA recommendation to evaluate the risk of hypersensitivity reactions in the Phase 3 studies and aid in the collection of relevant safety data. Updated the sample volume needed for the serum chemistry test and for the pharmacokinetic assessment.

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 terminated as the sponsor discontinued the ontamalimab clinical trial program in ulcerative colitis and CD for reasons unrelated to safety.

Notes: