Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Assess the Efficacy and Safety of Etrasimod in Subjects with Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2018-003985-15
Trial protocol	SK BE DE LV AT NL LT PT FR EE HU DK CZ PL BG ES HR IT RO
Global end of trial date	23 February 2022

Results information

Result version number	v1 (current)
This version publication date	31 August 2022
First version publication date	31 August 2022

Trial information

Trial identification

Sponsor protocol code	APD334-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03945188
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Arena Pharmaceuticals, a wholly owned subsidiary of Pfizer
Sponsor organisation address	6154 Nancy Ridge Drive, San Diego, United States,
Public contact	Fabio Cataldi, Arena Pharmaceuticals, Inc., 001 8584537200, ct.gov@arenapharm.com
Scientific contact	Fabio Cataldi, Arena Pharmaceuticals, Inc., 001 8584537200, ct.gov@arenapharm.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002713-PIP01-19
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	10 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of etrasimod on clinical remission in participants with moderately to severely active ulcerative colitis (UC) after 12 and 52 weeks of treatment.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Council for Harmonisation Guidelines for Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Estonia: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	India: 20
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	United States: 78
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Bulgaria: 12

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Belarus: 22
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Georgia: 37
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Moldova, Republic of: 16
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Russian Federation: 36
Country: Number of subjects enrolled	Serbia: 4
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	Ukraine: 37
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	433
EEA total number of subjects	151

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)	405
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with moderately to severely active ulcerative colitis (UC) were enrolled in this study. Eligible participants were randomized in a 2:1 ratio to receive either etrasimod 2 milligrams (mg) once daily or matching placebo once daily for up to 52 weeks.

Pre-assignment

Screening details:

The study included a Screening Period (up to 28 days), a 12-Week Treatment Period (induction) followed by a 40-Week Treatment Period (maintenance; for which no re-randomization took place), and a 2-Week and 4-Week Follow-Up Period.

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	Etrasimod 2 mg

Arm description:

Etrasimod 2 mg was administered orally once daily for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Etrasimod
Investigational medicinal product code	
Other name	APD334
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One etrasimod tablet was to be taken each day (with water, either with or without food).

Arm title	Placebo

Arm description:

Placebo was administered orally once daily for up to 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One matching placebo tablet was to be taken each day (with water, either with or without food).

Number of subjects in period 1	Etrasimod 2 mg	Placebo
Started	289	144
Completed	161	46
Not completed	128	98
Physician decision	2	2
Withdrawal by participant or parent/guardian	24	10
Adverse event, non-fatal	10	5
Pregnancy	2	-
Unspecified	2	2
Disease worsening	79	73
Lost to follow-up	1	2
Lack of efficacy	7	4
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Etrasimod 2 mg
Reporting group description:	
Etrasimod 2 mg was administered orally once daily for up to 52 weeks.	
Reporting group title	Placebo
Reporting group description:	
Placebo was administered orally once daily for up to 52 weeks.	

Reporting group values	Etrasimod 2 mg	Placebo	Total
Number of subjects	289	144	433
Age categorical Units: Subjects			
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	272	133	405
From 65-84 years	17	10	27
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.2	38.9	
standard deviation	± 13.97	± 14.04	-
Gender categorical Units: Subjects			
Female	137	56	193
Male	152	88	240
Race Units: Subjects			
White	256	129	385
Black or African American	6	3	9
Asian	22	9	31
American Indian or Alaska Native	1	3	4
Not Reported	4	0	4

End points

End points reporting groups

Reporting group title	Etrasimod 2 mg
Reporting group description: Etrasimod 2 mg was administered orally once daily for up to 52 weeks.	
Reporting group title	Placebo
Reporting group description: Placebo was administered orally once daily for up to 52 weeks.	

Primary: Percentage of participants achieving clinical remission at Week 12

End point title	Percentage of participants achieving clinical remission at Week 12
End point description: Clinical remission was based on the modified Mayo score (MMS). The MMS is a composite score of 3 assessments consisting of participant-reported symptoms using daily eDiary and centrally read endoscopy: stool frequency (SF), rectal bleeding (RB) and endoscopic score (ES). Clinical remission was defined as SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, and ES ≤ 1 (excluding friability). Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the Full Analysis Set (FAS, consisting of all randomized participants who received at least 1 dose of study treatment) with actual Baseline MMS 5 to 9.	
End point type	Primary
End point timeframe: At Week 12	

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	27.0	7.4		

Statistical analyses

Statistical analysis title	Clinical Remission at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	12.88
upper limit	26.63

Primary: Percentage of participants achieving clinical remission at Week 52

End point title	Percentage of participants achieving clinical remission at Week 52

End point description:

Clinical remission was based on the MMS which is a composite score of 3 assessments: SF, RB and ES. Clinical remission was defined as SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, and ES ≤ 1 (excluding friability). Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Primary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	32.1	6.7		

Statistical analyses

Statistical analysis title	Clinical Remission at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.42
upper limit	32.36

Secondary: Percentage of participants achieving endoscopic improvement at Week 12

End point title	Percentage of participants achieving endoscopic improvement at Week 12

End point description:

Endoscopic improvement was defined as an ES ≤ 1 (excluding friability). The ES ranged from 0 to 3 (where 0 = normal/inactive disease and 3 = severe disease). Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	35.0	14.1		

Statistical analyses

Statistical analysis title	Endoscopic Improvement at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.03
upper limit	29.32

Secondary: Percentage of participants achieving endoscopic improvement at Week 52

End point title	Percentage of participants achieving endoscopic improvement at Week 52

End point description:

Endoscopic improvement was defined as an ES ≤ 1 (excluding friability). The ES ranged from 0 to 3 (where 0 = normal/inactive disease and 3 = severe disease). Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	37.2	10.4		

Statistical analyses

Statistical analysis title	Endoscopic Improvement at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.99
upper limit	34.39

Secondary: Percentage of participants achieving symptomatic remission at Week 12

End point title	Percentage of participants achieving symptomatic remission at Week 12

End point description:

Symptomatic remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline) and RB subscore = 0. The SF subscore ranged from 0 to 3 (where 0 = normal number of stools and 3 = at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0 = no blood and 3 = blood alone passes). Higher scores indicate more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	46.0	21.5		

Statistical analyses

Statistical analysis title	Symptomatic Remission at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.46
upper limit	33.63

Secondary: Percentage of participants achieving symptomatic remission at Week 52

End point title	Percentage of participants achieving symptomatic remission at Week 52

End point description:

Symptomatic remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline) and RB subscore = 0. The SF subscore ranged from 0 to 3 (where 0 = normal number of stools and 3 = at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0 = no blood and 3 = blood alone passes). Higher scores indicate more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	43.4	18.5		

Statistical analyses

Statistical analysis title	Symptomatic Remission at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.17
upper limit	33.6

Secondary: Percentage of participants with mucosal healing at Week 12

End point title	Percentage of participants with mucosal healing at Week 12

End point description:

Mucosal healing was defined as an ES ≤ 1 (excluding friability) with histologic remission measured by a Geboes Index score < 2.0. The ES ranged from 0 to 3 (where 0 = normal/inactive disease and 3 = severe disease). The Geboes score grading system is a validated score for evaluating histologic disease activity in UC as follows: grade 0 = structural and architectural changes; grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher Geboes score indicates more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	21.2	4.4		

Statistical analyses

Statistical analysis title	Mucosal Healing at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.78
upper limit	22.98

Secondary: Percentage of participants with mucosal healing at Week 52

End point title	Percentage of participants with mucosal healing at Week 52

End point description:

Mucosal healing was defined as an ES ≤ 1 (excluding friability) with histologic remission measured by a Geboes Index score < 2.0. The ES ranged from 0 to 3 (where 0 = normal/inactive disease and 3 = severe disease). The Geboes score grading system is a validated score for evaluating histologic disease activity in UC as follows: grade 0 = structural and architectural changes; grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher Geboes score indicates more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	26.6	8.1		

Statistical analyses

Statistical analysis title	Mucosal Healing at Week 52
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	18.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.39
upper limit	25.39

Secondary: Percentage of participants achieving corticosteroid-free clinical remission at Week 52

End point title	Percentage of participants achieving corticosteroid-free clinical remission at Week 52

End point description:

Corticosteroid-free clinical remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, ES ≤ 1 (excluding friability), and have not received corticosteroids for ≥ 12 weeks in the 40-Week Treatment Period. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	32.1	6.7		

Statistical analyses

Statistical analysis title	Corticosteroid-Free Clinical Remission
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	18.42
upper limit	32.36

Secondary: Percentage of participants achieving sustained clinical remission at both Weeks 12 and 52

End point title	Percentage of participants achieving sustained clinical remission at both Weeks 12 and 52

End point description:

Sustained clinical remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, and ES ≤ 1 (excluding friability) at both Week 12 and Week 52. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 12 and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	17.9	2.2		

Statistical analyses

Statistical analysis title	Sustained Clinical Remission
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.66
upper limit	21.03

Secondary: Percentage of participants achieving clinical response at Week 12	
End point title	Percentage of participants achieving clinical response at Week 12

End point description:

Clinical response was based on the MMS which is a composite score of 3 assessments: SF, RB and ES. Clinical response was defined as a ≥ 2-point and ≥ 30% decrease from Baseline MMS, and a ≥ 1-point decrease from Baseline in RB subscore or an absolute RB subscore ≤ 1. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	62.4	34.1		

Statistical analyses

Statistical analysis title	Clinical Response at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.51
upper limit	38.02

Secondary: Percentage of participants achieving clinical response at Week 52	
End point title	Percentage of participants achieving clinical response at Week 52

End point description:

Clinical response was based on the MMS which is a composite score of 3 assessments: SF, RB and ES. Clinical response was defined as a ≥ 2-point and ≥ 30% decrease from Baseline MMS, and a ≥ 1-point

decrease from Baseline in RB subscore or an absolute RB sub-score ≤ 1. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	48.2	23.0		

Statistical analyses

Statistical analysis title	Clinical Response at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.79
upper limit	34.07

Secondary: Percentage of participants achieving clinical response at both Weeks 12 and 52

End point title	Percentage of participants achieving clinical response at both Weeks 12 and 52

End point description:

Clinical response was based on the MMS which is a composite score of 3 assessments: SF, RB and ES. Clinical response was defined as a ≥ 2-point and ≥ 30% decrease from Baseline MMS, and a ≥ 1-point decrease from Baseline in RB subscore or an absolute RB subscore ≤ 1. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 12 and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	44.9	18.5		

Statistical analyses

Statistical analysis title	Clinical Response at Both Weeks 12 and 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.48
upper limit	34.84

Secondary: Percentage of participants with mucosal healing at both Weeks 12 and 52

End point title	Percentage of participants with mucosal healing at both Weeks 12 and 52

End point description:

Mucosal healing was defined as an ES ≤ 1 (excluding friability) with histologic remission measured by a Geboes Index score < 2.0. The ES ranged from 0 to 3 (where 0 = normal/inactive disease and 3 = severe disease). The Geboes score grading system is a validated score for evaluating histologic disease activity in UC as follows: grade 0 = structural and architectural changes; grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher Geboes score indicates more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 12 and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	13.5	2.2		

Statistical analyses

Statistical analysis title	Mucosal Healing at Both Weeks 12 and 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	11.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.49
upper limit	16.14

Secondary: Percentage of participants achieving endoscopic normalization at Week 12

End point title	Percentage of participants achieving endoscopic normalization at Week 12

End point description:

Endoscopic normalization was defined as an ES = 0. The ES ranged from 0 to 3 (where 0= normal/inactive disease and 3= severe disease). Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	14.6	4.4		

Statistical analyses

Statistical analysis title	Endoscopic Normalization at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	10.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.73
upper limit	15.73

Secondary: Percentage of participants achieving endoscopic normalization at Week 52

End point title	Percentage of participants achieving endoscopic normalization at Week 52
End point description:	
Endoscopic normalization was defined as an ES = 0. The ES ranged from 0 to 3 (where 0= normal/inactive disease and 3= severe disease). Analysis was performed using the FAS with actual Baseline MMS 5 to 9.	
End point type	Secondary
End point timeframe:	
At Week 52	

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	26.3	5.9		

Statistical analyses

Statistical analysis title	Endoscopic Normalization at Week 52
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.79
upper limit	26.98

Secondary: Percentage of participants achieving endoscopic normalization at both Weeks 12 and 52

End point title	Percentage of participants achieving endoscopic normalization at both Weeks 12 and 52

End point description:

Endoscopic normalization was defined as an ES = 0. The ES ranged from 0 to 3 (where 0= normal/inactive disease and 3= severe disease). Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 12 and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)	10.6	1.5		

Statistical analyses

Statistical analysis title	Endoscopic Normalization at Both Weeks 12 and 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	9.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.93
upper limit	13.38

Secondary: Percentage of participants achieving symptomatic remission by study visit

End point title	Percentage of participants achieving symptomatic remission by study visit

End point description:

Symptomatic remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline) and RB subscore = 0. The SF subscore ranged from 0 to 3 (where 0 = normal number of stools and 3 = at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0 = no blood and 3 = blood alone passes). Higher scores indicate more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 16, 20, 24, 32, 40, and 48

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)				
Week 2	15.3	8.9		
Week 4	28.1	13.3		
Week 8	37.6	20.7		
Week 16	43.1	21.5		
Week 20	43.8	20.0		
Week 24	44.9	23.7		
Week 32	44.5	18.5		
Week 40	42.0	18.5		
Week 48	42.0	15.6		

Statistical analyses

Statistical analysis title	Symptomatic Remission At Week 2
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	6.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	12.95

Statistical analysis title	Symptomatic Remission At Week 4
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.32
upper limit	22.74

Statistical analysis title	Symptomatic Remission At Week 8
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.06
upper limit	25.63

Statistical analysis title	Symptomatic Remission At Week 16

Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.71
upper limit	30.61

Statistical analysis title	Symptomatic Remission At Week 20
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.98
upper limit	32.51

Statistical analysis title	Symptomatic Remission At Week 24
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.83
upper limit	30.24

Statistical analysis title	Symptomatic Remission At Week 32
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.08
upper limit	34.56

Statistical analysis title	Symptomatic Remission At Week 40
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.8
upper limit	32.14

Statistical analysis title	Symptomatic Remission At Week 48
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.92
upper limit	34.82

Secondary: Percentage of participants achieving complete symptomatic remission by study visit

End point title	Percentage of participants achieving complete symptomatic remission by study visit

End point description:

Complete symptomatic remission was defined as an SF subscore = 0 and RB subscore = 0. The SF subscore ranged from 0 to 3 (where 0 = normal number of stools and 3 = at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0 = no blood and 3 = blood alone passes). Higher scores indicate more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48 and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)				
Week 2	5.8	2.2		
Week 4	11.3	4.4		
Week 8	16.8	6.7		
Week 12	23.0	6.7		
Week 16	21.2	5.9		
Week 20	22.3	4.4		
Week 24	22.3	8.1		
Week 32	23.0	3.0		
Week 40	21.2	5.9		
Week 48	19.7	2.2		
Week 52	24.5	4.4		

Statistical analyses

Statistical analysis title	Complete Symptomatic Remission at Week 2
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	3.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	7.3

Statistical analysis title	Complete Symptomatic Remission at Week 4
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	6.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	11.9

Statistical analysis title	Complete Symptomatic Remission at Week 8
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	10.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.09
upper limit	16.2

Statistical analysis title	Complete Symptomatic Remission at Week 12
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.89
upper limit	22.83

Statistical analysis title	Complete Symptomatic Remission at Week 16
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.23
upper limit	21.52

Statistical analysis title	Complete Symptomatic Remission at Week 20
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.85
upper limit	23.75

Statistical analysis title	Complete Symptomatic Remission at Week 24

Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	14.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.45
upper limit	21.04

Statistical analysis title	Complete Symptomatic Remission at Week 32
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.25
upper limit	25.81

Statistical analysis title	Complete Symptomatic Remission at Week 40
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.91
upper limit	21.35

Statistical analysis title	Complete Symptomatic Remission at Week 48
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.16
upper limit	22.87

Statistical analysis title	Complete Symptomatic Remission at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.75
upper limit	25.98

Secondary: Percentage of participants achieving non-invasive clinical response by study visit

End point title	Percentage of participants achieving non-invasive clinical response by study visit

End point description:

Non-invasive clinical response was defined as a ≥ 30% decrease from Baseline in composite RB and SF subscores, and a ≥ 1-point decrease from Baseline in RB subscore or RB subscore ≤ 1. The SF subscore ranged from 0 to 3 (where 0 = normal number of stools and 3 = at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0 = no blood and 3 = blood alone passes). The composite RB and SF score range was from 0 to 6, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48, and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)				
Week 2	38.3	33.3		
Week 4	56.2	39.3		
Week 8	63.1	43.0		
Week 12	65.7	42.2		
Week 16	55.5	30.4		
Week 20	57.3	28.1		
Week 24	56.6	30.4		
Week 32	54.0	25.2		
Week 40	51.5	23.0		
Week 48	51.1	21.5		
Week 52	50.4	23.7		

Statistical analyses

Statistical analysis title	Non-invasive Clinical Response at Week 2
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.336
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	4.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.01
upper limit	14.68

Statistical analysis title	Non-invasive Clinical Response at Week 4
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	7.06
upper limit	27.15

Statistical analysis title	Non-invasive Clinical Response at Week 8
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.15
upper limit	30.19

Statistical analysis title	Non-invasive Clinical Response at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.45
upper limit	33.43

Statistical analysis title	Non-invasive Clinical Response at Week 16
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.67
upper limit	34.83

Statistical analysis title	Non-invasive Clinical Response at Week 20
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.77
upper limit	38.64

Statistical analysis title	Non-invasive Clinical Response at Week 24
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.47
upper limit	35.69

Statistical analysis title	Non-invasive Clinical Response at Week 32

Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.35
upper limit	38.02

Statistical analysis title	Non-invasive Clinical Response at Week 40
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.3
upper limit	37.55

Statistical analysis title	Non-invasive Clinical Response at Week 48
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.55
upper limit	38.64

Statistical analysis title	Non-invasive Clinical Response at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.18
upper limit	35.68

Secondary: Percentage of participants achieving symptomatic response by study visit

End point title	Percentage of participants achieving symptomatic response by study visit

End point description:

Symptomatic response was defined as a ≥ 30% decrease from Baseline in composite RB and SF subscores. The SF subscore ranged from 0 to 3 (where 0= normal number of stools and 3= at least 5 stools more than normal) and RB subscore ranged from 0 to 3 (where 0= no blood and 3= blood alone passes). The composite RB and SF score range was from 0 to 6, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48, and 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	135		
Units: Percentage of participants				
number (not applicable)				
Week 2	39.4	33.3		
Week 4	57.3	40.0		
Week 8	64.6	43.7		
Week 12	66.4	42.2		
Week 16	55.5	31.1		
Week 20	57.7	28.1		
Week 24	56.9	30.4		
Week 32	54.7	25.2		
Week 40	51.8	23.0		
Week 48	51.5	21.5		
Week 52	50.7	23.7		

Statistical analyses

Statistical analysis title	Symptomatic Response at Week 2
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.96
upper limit	15.81

Statistical analysis title	Symptomatic Response at Week 4
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.48
upper limit	27.53

Statistical analysis title	Symptomatic Response at Week 8
Comparison groups	Etrasimod 2 mg v Placebo

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.92
upper limit	30.94

Statistical analysis title	Symptomatic Response at Week 12
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.15
upper limit	34.1

Statistical analysis title	Symptomatic Response at Week 16
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.89
upper limit	34.13

Statistical analysis title	Symptomatic Response at Week 20

Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.13
upper limit	39.01

Statistical analysis title	Symptomatic Response at Week 24
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.88
upper limit	36.02

Statistical analysis title	Symptomatic Response at Week 32
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.01
upper limit	38.68

Statistical analysis title	Symptomatic Response at Week 40
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.71
upper limit	37.95

Statistical analysis title	Symptomatic Response at Week 48
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.97
upper limit	39.03

Statistical analysis title	Symptomatic Response at Week 52
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.6
upper limit	36.07

Secondary: Percentage of participants achieving 4-week corticosteroid-free clinical remission at Week 52 among participants receiving corticosteroids at Baseline

End point title	Percentage of participants achieving 4-week corticosteroid-free clinical remission at Week 52 among participants receiving corticosteroids at Baseline

End point description:

Four-week corticosteroid-free clinical remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, and ES ≤ 1, and have not received corticosteroids for ≥ 4 weeks in the 40-Week Treatment Period. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9. Only participants receiving corticosteroids at study entry and who had not been receiving corticosteroids for ≥ 4 weeks prior to Week 52 were included in this analysis.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	40		
Units: Percentage of participants				
number (not applicable)	31.0	7.5		

Statistical analyses

Statistical analysis title	4-Week Corticosteroid-Free Clinical Remission
Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	35.9

Secondary: Percentage of participants achieving clinical remission at Week 52 among participants in clinical response at Week 12

End point title	Percentage of participants achieving clinical remission at Week 52 among participants in clinical response at Week 12

End point description:

Clinical remission and clinical response were based on the MMS which is a composite of 3 assessments: SF, RB and ES. Clinical remission was defined as an SF subscore = 0 (or = 1 with a ≥ 1-point decrease from Baseline), RB subscore = 0, and ES ≤ 1 (excluding friability). Clinical response was defined as a ≥ 2-point and ≥ 30% decrease from Baseline MMS, and a ≥ 1-point decrease from Baseline in RB subscore or an absolute RB subscore ≤ 1. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. Analysis was performed using the FAS with actual Baseline MMS 5 to 9.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Etrasimod 2 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	46		
Units: Percentage of participants				
number (not applicable)	49.1	17.4		

Statistical analyses

Statistical analysis title	Clinical Remission at Week 52

Statistical analysis description:

Clinical remission at Week 52 among participants in clinical response at Week 12

Comparison groups	Etrasimod 2 mg v Placebo
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	31.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.45
upper limit	45.28

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 56 weeks (12-Week and 40-Week Treatment Periods plus Follow-up). Treatment-emergent adverse events (TEAEs) were collected from first dose of study treatment up to 30 days following discontinuation of the study treatment.

Adverse event reporting additional description:

TEAEs, defined as those adverse events that started or worsened in severity after the first dose of study treatment, are reported for the Safety Population which included all randomized participants who received at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo was administered orally once daily for up to 52 weeks.

Reporting group title	Etrasimod 2 mg

Reporting group description:

Etrasimod 2 mg was administered orally once daily for up to 52 weeks.

Serious adverse events	Placebo	Etrasimod 2 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 144 (6.25%)	20 / 289 (6.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Breast conserving surgery			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Intracranial pressure increased			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Anembryonic gestation			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	3 / 144 (2.08%)	6 / 289 (2.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal prolapse syndrome			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Campylobacter infection			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Etrasimod 2 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 144 (53.47%)	204 / 289 (70.59%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 144 (0.69%)	8 / 289 (2.77%)	
occurrences (all)	1	8	
Hypertensive crisis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

Varicose vein			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Deep vein thrombosis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 144 (4.17%)	14 / 289 (4.84%)	
occurrences (all)	7	15	
Asthenia			
subjects affected / exposed	2 / 144 (1.39%)	7 / 289 (2.42%)	
occurrences (all)	2	7	
Fatigue			
subjects affected / exposed	2 / 144 (1.39%)	5 / 289 (1.73%)	
occurrences (all)	3	6	
Chest discomfort			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Pain			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Peripheral swelling			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Vaccination site pain			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	3	
Discomfort			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Drug intolerance			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 144 (1.39%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Chest pain			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Infusion site reaction			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 144 (1.39%)	0 / 289 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Endometriosis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Heavy menstrual bleeding			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Amenorrhoea			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Penile curvature			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Dyspnoea exertional			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Cough			
subjects affected / exposed	2 / 144 (1.39%)	2 / 289 (0.69%)	
occurrences (all)	2	2	
Dyspnoea			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Nasal congestion			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 144 (0.00%)	4 / 289 (1.38%)	
occurrences (all)	0	4	
Pulmonary mass			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Bronchial obstruction			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			

subjects affected / exposed	2 / 144 (1.39%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Epistaxis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Obstructive airways disorder			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Painful respiration			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Sinus congestion			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Agitation			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Depression			

subjects affected / exposed	2 / 144 (1.39%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Sleep disorder			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 144 (0.69%)	5 / 289 (1.73%)	
occurrences (all)	1	5	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 144 (1.39%)	8 / 289 (2.77%)	
occurrences (all)	2	12	
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 144 (1.39%)	5 / 289 (1.73%)	
occurrences (all)	2	5	
Transaminases increased			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	4	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 144 (2.08%)	3 / 289 (1.04%)	
occurrences (all)	3	5	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 144 (0.69%)	3 / 289 (1.04%)	
occurrences (all)	1	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Serum ferritin decreased			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Blood triglycerides increased			

subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Lymphocyte count decreased			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Hepatic enzyme increased			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Blood cholesterol increased			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Weight increased			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Blood glucose increased			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Blood iron decreased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Haemoglobin decreased			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
C-reactive protein increased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Blood triglycerides abnormal			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Blood thyroid stimulating hormone			

increased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
International normalised ratio increased			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Urine ketone body			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Forced expiratory volume decreased			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Bacterial test positive			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Spirometry abnormal			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
FEV1/FVC ratio decreased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Lung diffusion test decreased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Prothrombin time prolonged			

subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Pulmonary arterial pressure decreased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Arthropod sting			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Injury corneal			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Patella fracture			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Post lumbar puncture syndrome			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Vaccination complication			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Peripheral nerve injury			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Lower limb fracture			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Atrioventricular block first degree			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Bradycardia			
subjects affected / exposed	0 / 144 (0.00%)	4 / 289 (1.38%)	
occurrences (all)	0	4	
Atrioventricular block second degree			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

Palpitations			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 144 (4.86%)	24 / 289 (8.30%)	
occurrences (all)	12	36	
Dizziness			
subjects affected / exposed	1 / 144 (0.69%)	15 / 289 (5.19%)	
occurrences (all)	1	17	
Head discomfort			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Migraine			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	8	
Carotid arteriosclerosis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Parkinson's disease			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Post herpetic neuralgia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Asterixis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Dizziness exertional			

subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Tension headache			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Dizziness postural			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 144 (9.72%)	24 / 289 (8.30%)	
occurrences (all)	17	31	
Iron deficiency anaemia			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Thrombocytosis			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Hypocoagulable state			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Vision blurred			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	3	
Cataract			
subjects affected / exposed	1 / 144 (0.69%)	3 / 289 (1.04%)	
occurrences (all)	1	3	
Myopia			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Amblyopia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Astigmatism			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Blepharitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Eyelid pain			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Eyelid cyst			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Macular oedema			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

Eye swelling			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Keratitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Uveitis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Retinal haemorrhage			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Maculopathy			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	10 / 144 (6.94%)	17 / 289 (5.88%)	
occurrences (all)	10	18	
Nausea			
subjects affected / exposed	2 / 144 (1.39%)	9 / 289 (3.11%)	
occurrences (all)	2	11	
Diarrhoea			
subjects affected / exposed	1 / 144 (0.69%)	5 / 289 (1.73%)	
occurrences (all)	1	5	
Flatulence			

subjects affected / exposed	0 / 144 (0.00%)	6 / 289 (2.08%)	
occurrences (all)	0	6	
Abdominal pain			
subjects affected / exposed	5 / 144 (3.47%)	11 / 289 (3.81%)	
occurrences (all)	6	13	
Abdominal distension			
subjects affected / exposed	3 / 144 (2.08%)	4 / 289 (1.38%)	
occurrences (all)	4	5	
Haemorrhoids			
subjects affected / exposed	0 / 144 (0.00%)	7 / 289 (2.42%)	
occurrences (all)	0	8	
Vomiting			
subjects affected / exposed	0 / 144 (0.00%)	5 / 289 (1.73%)	
occurrences (all)	0	5	
Dyspepsia			
subjects affected / exposed	2 / 144 (1.39%)	3 / 289 (1.04%)	
occurrences (all)	2	3	
Constipation			
subjects affected / exposed	1 / 144 (0.69%)	4 / 289 (1.38%)	
occurrences (all)	1	4	
Abdominal pain lower			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Anal pruritus			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	3	
Gastritis			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	3	
Aphthous ulcer			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Abdominal pain upper			

subjects affected / exposed	3 / 144 (2.08%)	1 / 289 (0.35%)	
occurrences (all)	3	1	
Abdominal tenderness			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Proctalgia			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Large intestine polyp			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Anal fissure			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Diverticulum intestinal			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Enteritis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	2	
Epigastric discomfort			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Eructation			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Melaena			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	2	
Inguinal hernia			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Mucosal prolapse syndrome			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Rectal tenesmus			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Paraesthesia oral			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Rectal polyp			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Small intestine polyp			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Tooth impacted			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Umbilical hernia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Defaecation urgency			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Food poisoning			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	3 / 144 (2.08%)	0 / 289 (0.00%)	
occurrences (all)	4	0	
Hepatobiliary disorders			

Hyperbilirubinaemia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Cholestasis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Cholangitis sclerosing			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Primary biliary cholangitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 144 (0.69%)	3 / 289 (1.04%)	
occurrences (all)	2	3	
Acne			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	3 / 144 (2.08%)	5 / 289 (1.73%)	
occurrences (all)	4	5	
Erythema			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Eczema			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Night sweats			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Alopecia scarring			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Psoriasis			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	2 / 144 (1.39%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Ecchymosis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Ephelides			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Purpura senile			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Xanthelasma			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

Pollakiuria			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Chromaturia			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Renal cyst			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Micturition frequency decreased			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Renal impairment			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Urine abnormality			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Cushingoid			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Autoimmune thyroiditis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Thyroid cyst			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 144 (2.08%)	13 / 289 (4.50%)	
occurrences (all)	3	16	
Back pain			
subjects affected / exposed	3 / 144 (2.08%)	7 / 289 (2.42%)	
occurrences (all)	4	7	
Neck pain			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	4	
Muscle spasms			
subjects affected / exposed	0 / 144 (0.00%)	5 / 289 (1.73%)	
occurrences (all)	0	5	
Osteoarthritis			
subjects affected / exposed	1 / 144 (0.69%)	3 / 289 (1.04%)	
occurrences (all)	1	3	
Pain in extremity			
subjects affected / exposed	2 / 144 (1.39%)	2 / 289 (0.69%)	
occurrences (all)	2	2	
Tendonitis			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Ankle deformity			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Joint stiffness			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Arthropathy			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Groin pain			

subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Muscle twitching			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Periarthritis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Osteochondrosis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Spondyloarthropathy			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Flank pain			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Limb mass			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 144 (5.56%)	19 / 289 (6.57%)	
occurrences (all)	8	29	

Respiratory tract infection viral			
subjects affected / exposed	2 / 144 (1.39%)	6 / 289 (2.08%)	
occurrences (all)	2	6	
Urinary tract infection			
subjects affected / exposed	3 / 144 (2.08%)	6 / 289 (2.08%)	
occurrences (all)	3	8	
COVID-19 pneumonia			
subjects affected / exposed	1 / 144 (0.69%)	4 / 289 (1.38%)	
occurrences (all)	1	4	
Cystitis			
subjects affected / exposed	0 / 144 (0.00%)	4 / 289 (1.38%)	
occurrences (all)	0	4	
Bronchitis			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	3	
Pharyngitis			
subjects affected / exposed	0 / 144 (0.00%)	3 / 289 (1.04%)	
occurrences (all)	0	4	
Nasopharyngitis			
subjects affected / exposed	4 / 144 (2.78%)	3 / 289 (1.04%)	
occurrences (all)	4	3	
Anal abscess			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	2 / 144 (1.39%)	3 / 289 (1.04%)	
occurrences (all)	3	4	
Herpes zoster			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Candida infection			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Hordeolum			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	

Oral herpes			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Pustule			
subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Conjunctivitis			
subjects affected / exposed	4 / 144 (2.78%)	1 / 289 (0.35%)	
occurrences (all)	6	1	
Abscess limb			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Acne pustular			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Helicobacter infection			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Clostridium difficile infection			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Liver abscess			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Helminthic infection			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Pneumonia viral			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Pulpitis dental			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	

Respiratory tract infection			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Tinea infection			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Ear infection staphylococcal			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Tracheitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Vulval abscess			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

Gastroenteritis viral			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Tuberculosis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 144 (0.69%)	4 / 289 (1.38%)	
occurrences (all)	1	4	
Hypercholesterolaemia			
subjects affected / exposed	0 / 144 (0.00%)	6 / 289 (2.08%)	
occurrences (all)	0	6	
Decreased appetite			
subjects affected / exposed	1 / 144 (0.69%)	1 / 289 (0.35%)	
occurrences (all)	1	1	
Vitamin D deficiency			

subjects affected / exposed	0 / 144 (0.00%)	2 / 289 (0.69%)	
occurrences (all)	0	2	
Dehydration			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Iron deficiency			
subjects affected / exposed	1 / 144 (0.69%)	2 / 289 (0.69%)	
occurrences (all)	1	2	
Diabetes mellitus			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 289 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	
Lipomatosis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2019	Amendment 1.0: Changed stratification factor from failed biologic or Janus kinase (JAK) inhibitor therapy to naïve to biologic or JAK inhibitor therapy; updated inclusion/exclusion criteria for hematological function, prior medication, and hospitalization for UC; added a section "Guidance for Cardiac Monitoring Following Treatment Initiation or Re-Initiation" and added a 12-lead electrocardiogramn (ECG) at Week 12 and Week 52; updated safety precautions for cardiovascular events; renamed the analysis sets; added a section on subgroup analyses.
20 December 2019	Amendment 2.0: Updated entry criteria for open-label extension (OLE) study for participants who experience UC worsening after Week 12 and prior to Week 52. Amendment provided additional guidance to the Investigator regarding required endoscopic evaluation to confirm eligibility for OLE prior to Week 52. Updated eligibility criteria (list of prior therapy failures or non-response, contraception use, cardiovascular disease history, and prior therapy washout period); added a 4-Week Follow-Up Visit; provided additional instructions for safety monitoring related to 12-lead ECG, pulmonary function tests (PFTs), ophthalmoscopy and optical coherence tomography (OCT), and Quantiferon tuberculosis Gold and tuberculin skin tests.
07 February 2020	Amendment 3.0: Provided clarification and further instructions for tuberculosis testing and updated the tuberculosis screening questionnaire; updated entry criteria for enrollment in the OLE study; added lack of efficacy as a reason a participant may discontinue from double-blind treatment. Added that if the Early Termination or Study Completion visit is ≥ 2 weeks after the last dose of study treatment, the 2-Week Follow-Up visit is not required; however, the 4-Week Follow-up visit should be scheduled and completed. If the Early Termination or Study Completion visit is ≥ 4 weeks after the last dose of study treatment, the 4-Week Follow-Up visit is not required.
22 December 2020	Amendment 4.0: Updated the participant enrollment number and guidance for conducting virtual and offsite visits; added information on anti-arrhythmic drugs to prohibited concomitant therapies; updated the corticosteroid-free remission secondary endpoint; updated language regarding timing of screening OCTs and PFTs; added an exclusion criterion covering treatment with topical rectal Chinese medicine, enemas, or suppositories.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported