



Clinical trial results:

A Phase III, Double-Blind, Placebo-Controlled, Multicenter Study of the Efficacy and Safety of Etrolizumab During Induction and Maintenance in Patients With Moderate to Severe Active Ulcerative Colitis who are Refractory to or Intolerant of TNF Inhibitors.

Summary

EudraCT number	2013-004278-88
Trial protocol	LT GR DE CZ DK BE HU AT ES NL IT FR PL
Global end of trial date	16 April 2020

Results information

Result version number	v1
This version publication date	25 April 2021
First version publication date	25 April 2021

Trial information

Trial identification

Sponsor protocol code	GA28950
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02100696
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of Etrolizumab

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

All subjects were on immunosuppressants and/or corticosteroids.

Evidence for comparator: -

Actual start date of recruitment	21 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Australia: 22
Country: Number of subjects enrolled	Austria: 16
Country: Number of subjects enrolled	Belgium: 29
Country: Number of subjects enrolled	Brazil: 24
Country: Number of subjects enrolled	Canada: 41
Country: Number of subjects enrolled	Switzerland: 9
Country: Number of subjects enrolled	Czechia: 39
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	France: 71
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 43
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Lithuania: 6

Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	United States: 107
Worldwide total number of subjects	609
EEA total number of subjects	344

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	580
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 184 centers in 24 countries.

Pre-assignment

Screening details:

A total of 609 subjects were enrolled into the Induction phase of this study and the entire study. A subset (259) of these subjects moved into the Maintenance phase of this study.

Period 1

Period 1 title	Induction Phase
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)

Arm description:

Participants assigned to this arm will receive treatment with open-label etrolizumab 105 milligrams (mg) subcutaneous (SC) injection once every 4 weeks (Q4W) for 14 weeks during the induction phase.

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

Dosage and administration details:

105mg once every 4 weeks

Arm title	Cohort 2: Placebo (Double-Blind Induction Phase)
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Arm description:

Participants randomized to this arm will receive treatment with double-blind placebo SC injection Q4W for 14 weeks during the induction phase.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matched to Etrolizumab

Arm title	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
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Arm description:

Participants randomized to this arm will receive treatment with double-blind etrolizumab 105 mg SC injection Q4W for 14 weeks during the induction phase.

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

Dosage and administration details:

105mg once every 4 weeks

Number of subjects in period 1	Cohort 1: Etrolizumab (Open- Label Induction (OLI) Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Started	130	95	384
Completed	115	90	358
Not completed	15	5	26
Consent withdrawn by subject	8	2	13
Physician decision	1	-	2
Adverse event, non-fatal	-	-	1
Multiple Reasons	5	2	8
Lost to follow-up	1	-	1
Protocol deviation	-	1	1

Period 2

Period 2 title	Maintenance Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Responders: Placebo (Maintenance Phase)

Arm description:

Participants who received placebo during the induction phase, Cohort 2: Placebo (Double-Blind Induction Phase), and achieve a clinical response with placebo at Week 14 will continue to receive blinded placebo from Week 16 up to Week 66 during the maintenance phase.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matched to Etrolizumab

Arm title	Etrolizumab Responders: Placebo (Maintenance Phase)
Arm description:	
Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive placebo SC injection Q4W from Week 16 up to Week 66.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Matched to Etrolizumab	
Arm title	Etrolizumab Responders: Etrolizumab (Maintenance Phase)

Arm description:	
Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive etrolizumab 105 mg SC injection Q4W from Week 16 up to Week 66.	
Arm type	Experimental
Investigational medicinal product name	Etrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
105mg once every 4 weeks	

Number of subjects in period 2 ^[1]	Placebo Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)
Started	27	115	117
Completed	26	106	112
Not completed	1	9	5
Consent withdrawn by subject	1	4	2
Physician decision	-	1	-
Adverse event, non-fatal	-	-	2
Multiple Reasons	-	2	1
Lost to follow-up	-	1	-
Protocol deviation	-	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of the 609 subjects that enrolled into the Induction phase of this study and entire study, a subset (259) subjects moved into the Maintenance phase.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)
Reporting group description:	
Participants assigned to this arm will receive treatment with open-label etrolizumab 105 milligrams (mg) subcutaneous (SC) injection once every 4 weeks (Q4W) for 14 weeks during the induction phase.	
Reporting group title	Cohort 2: Placebo (Double-Blind Induction Phase)
Reporting group description:	
Participants randomized to this arm will receive treatment with double-blind placebo SC injection Q4W for 14 weeks during the induction phase.	
Reporting group title	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Reporting group description:	
Participants randomized to this arm will receive treatment with double-blind etrolizumab 105 mg SC injection Q4W for 14 weeks during the induction phase.	

Reporting group values	Cohort 1: Etrolizumab (Open- Label Induction (OLI) Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects	130	95	384
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	123	90	367
From 65-84 years	7	5	17
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	39.5	38.8	40.7
standard deviation	± 13.5	± 13.9	± 13.3
Sex: Female, Male Units: Participants			
Female	52	41	160
Male	78	54	224
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	4	5	30
Not Hispanic or Latino	118	76	321
Not Reported or Unknown	8	14	33
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	6	5	26

Black or African American	3	1	6
White	109	73	304
Other	12	15	48
American Indian or Alaska Native	0	1	0

Reporting group values	Total		
Number of subjects	609		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	580		
From 65-84 years	29		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	253		
Male	356		
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	39		
Not Hispanic or Latino	515		
Not Reported or Unknown	55		
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	37		
Black or African American	10		
White	486		
Other	75		
American Indian or Alaska Native	1		

End points

End points reporting groups

Reporting group title	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)
Reporting group description: Participants assigned to this arm will receive treatment with open-label etrolizumab 105 milligrams (mg) subcutaneous (SC) injection once every 4 weeks (Q4W) for 14 weeks during the induction phase.	
Reporting group title	Cohort 2: Placebo (Double-Blind Induction Phase)
Reporting group description: Participants randomized to this arm will receive treatment with double-blind placebo SC injection Q4W for 14 weeks during the induction phase.	
Reporting group title	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Reporting group description: Participants randomized to this arm will receive treatment with double-blind etrolizumab 105 mg SC injection Q4W for 14 weeks during the induction phase.	
Reporting group title	Placebo Responders: Placebo (Maintenance Phase)
Reporting group description: Participants who received placebo during the induction phase, Cohort 2: Placebo (Double-Blind Induction Phase), and achieve a clinical response with placebo at Week 14 will continue to receive blinded placebo from Week 16 up to Week 66 during the maintenance phase.	
Reporting group title	Etrolizumab Responders: Placebo (Maintenance Phase)
Reporting group description: Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive placebo SC injection Q4W from Week 16 up to Week 66.	
Reporting group title	Etrolizumab Responders: Etrolizumab (Maintenance Phase)
Reporting group description: Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive etrolizumab 105 mg SC injection Q4W from Week 16 up to Week 66.	
Subject analysis set title	Cohort 1: Etro (OLI Phase) + Cohort 2: Etro (DB Ind Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cohort 1: Participants assigned to this arm will receive treatment with open-label etrolizumab 105 milligrams (mg) subcutaneous (SC) injection once every 4 weeks (Q4W) for 14 weeks during the induction phase. Cohort 2: Participants randomized to this arm will receive treatment with double-blind etrolizumab 105 mg SC injection Q4W for 14 weeks during the induction phase. Subjects in this arm did not enter into the Maintenance phase of the study.	
Subject analysis set title	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive placebo SC injection Q4W from Week 16 up to Week 66.	
Subject analysis set title	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive etrolizumab 105 mg SC injection Q4W from Week 16 up to Week 66.	

responders re-randomized to this arm will receive etrolizumab SC injection Q4W from Week 16 up to Week 66.

Primary: Induction Phase: Percentage of Subjects with Remission at Week 14, as Determined by the Mayo Clinic Score (MCS)

End point title	Induction Phase: Percentage of Subjects with Remission at Week 14, as Determined by the Mayo Clinic Score (MCS) ^[1]
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End point description:

The Mayo Clinic Score (MCS) ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores \leq 1 and a rectal bleeding subscore of 0.

End point type	Primary
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End point timeframe:

Week 14

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	384		
Units: Percentage of Subjects				
number (not applicable)	6.3	18.5		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	479
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0033
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted difference in response rates
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.95
upper limit	17.67

Primary: Maintenance Phase: Percentage of Subjects with Remission at Week 66

Among Subjects Who Had Achieved a Clinical Response at Week 14, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Remission at Week 66 Among Subjects Who Had Achieved a Clinical Response at Week 14, as Determined by the MCS
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End point description:

The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores ≤ 1 and a rectal bleeding subscore of 0. Clinical Response is MCS with ≥ 3 -point decrease and 30% reduction from baseline as well as ≥ 1 -point decrease in rectal bleeding subscore or an absolute rectal bleeding score of 0 or 1.

End point type	Primary
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End point timeframe:

Week 66

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	114	112		
Units: Percentage of Subjects				
number (not applicable)	20.2	24.1		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4956
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.13
upper limit	14.56

Secondary: Induction Phase: Percentage of Subjects with Clinical Remission at Week 14, as Determined by the MCS

End point title	Induction Phase: Percentage of Subjects with Clinical
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End point description:

The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Clinical Remission is MCS ≤ 2 with individual subscores ≤ 1 .

End point type	Secondary
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End point timeframe:

Week 14

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	384		
Units: Percentage of Subjects				
number (not applicable)	6.3	18.8		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	479
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0028
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.19
upper limit	17.94

Secondary: Induction Phase: Percentage of Subjects with Clinical Response at Week 14, as Determined by the MCS

End point title	Induction Phase: Percentage of Subjects with Clinical Response at Week 14, as Determined by the MCS ^[3]
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End point description:

The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores ≤ 1 and a rectal bleeding subscore of 0. Clinical Response is MCS with ≥ 3 -point decrease and

30% reduction from baseline as well as ≥ 1 -point decrease in rectal bleeding subscore or an absolute rectal bleeding score of 0 or 1.

End point type	Secondary
End point timeframe:	
Week 14	

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	384		
Units: Percentage of Subjects				
number (not applicable)	31.6	45.8		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	479
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0121
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.21
upper limit	24.14

Secondary: Induction Phase: Percentage of Subjects with Improvement from Baseline in Endoscopic Appearance of the Mucosa at Week 14, as Determined by the MCS Endoscopic Subscore

End point title	Induction Phase: Percentage of Subjects with Improvement from Baseline in Endoscopic Appearance of the Mucosa at Week 14, as Determined by the MCS Endoscopic Subscore ^[4]
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Improvement in endoscopic appearance of the mucosa is Endoscopy subscore ≤ 1 .
End point type	Secondary

End point timeframe:

Baseline and Week 14

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	384		
Units: Percentage of Subjects				
number (not applicable)	25.3	33.3		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	479
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1204
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	17.22

Secondary: Induction Phase: Percentage of Subjects with Endoscopic Remission at Week 14, as Determined by the MCS Endoscopic Subscore

End point title	Induction Phase: Percentage of Subjects with Endoscopic Remission at Week 14, as Determined by the MCS Endoscopic Subscore ^[5]
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Endoscopic Remission is Endoscopy subscore = 0.
End point type	Secondary
End point timeframe:	
Week 14	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	384		
Units: Percentage of Subjects				
number (not applicable)	9.5	17.2		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	479
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0647
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	13.66

Secondary: Induction Phase: Percentage of Subjects with Histologic Remission at Week 14, as Determined by the Nancy Histological Index

End point title	Induction Phase: Percentage of Subjects with Histologic Remission at Week 14, as Determined by the Nancy Histological Index ^[6]
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End point description:

Nancy Histological Index (NHI) is a 5-level classification ranging from grade 0 (No histologically significant disease) to grade 4 (severely active disease). Histologic remission is defined as a Nancy Histological Index of 0 or 1.

End point type	Secondary
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End point timeframe:

Week 14

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	310		
Units: Percentage of Subjects				
number (not applicable)	25.0	29.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.392
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.78
upper limit	14.69

Secondary: Induction Phase: Change from Baseline to Week 6 in MCS Rectal Bleed Subscore

End point title	Induction Phase: Change from Baseline to Week 6 in MCS Rectal Bleed Subscore ^[7]
End point description:	
Rectal bleeding data were collected via the subject's diaries and each day a subject provided a score from 0 to 3 according to the following definitions: 0 = no blood in the stool; 1 = streaks of blood with stool less than half the time; 2 = obvious blood with stool most of the time; 3 = blood alone passed. The Mayo Clinic Score (MCS) rectal bleeding subscore was calculated as the worst value of three days of daily diary scores closest to anchor dates at baseline and post-baseline. The data was considered non-parametric and was reported using RANK analysis of covariance (ANCOVA). Subjects were stratified by concomitant treatment with corticosteroids or immunosuppressants at randomization and disease activity measured during screening (MCS ≤9/MCS ≥10); the model adjusted for these stratification factors along with the baseline rectal bleeding (RB) subscore.	
End point type	Secondary
End point timeframe:	
Baseline and Week 6	

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	383		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.4 (± 0.8)	-0.7 (± 0.9)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	477
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0029
Method	ANCOVA
Parameter estimate	Difference in Unadjusted Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0

Secondary: Induction Phase: Change from Baseline to Week 6 in MCS Stool Frequency Subscore

End point title	Induction Phase: Change from Baseline to Week 6 in MCS Stool Frequency Subscore ^[8]
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End point description:

Stool frequency data were collected via the subject's diaries and each day a subject provided a score from 0 to 3 according to the following definitions: 0 = normal number of stools; 1 = 1 to 2 more stools than normal; 2 = 3 to 4 more stools than normal; 3 = 5 or more stools than normal. The Mayo Clinic Score (MCS) stool frequency subscore was calculated as the average of three days daily diary scores closest to anchor dates at baseline and post-baseline. The data was considered non-parametric and was reported using RANK analysis of covariance (ANCOVA). Subjects were stratified by concomitant treatment with corticosteroids or immunosuppressants at randomization and disease activity measured during screening (MCS ≤9/MCS ≥10); the model adjusted for these stratification factors along with the baseline stool frequency (SF) subscore.

End point type	Secondary
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End point timeframe:

Baseline and Week 6

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	383		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.5 (± 0.9)	-0.6 (± 1.0)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	477
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1124
Method	ANCOVA
Parameter estimate	Difference in Unadjusted Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.1

Secondary: Induction Phase: Change from Baseline to Week 14 in UC Bowel Movement Signs and Symptoms, as Assessed by the Ulcerative Colitis Patient-Reported Outcome Signs and Symptoms (UC-PRO/SS) Questionnaire

End point title	Induction Phase: Change from Baseline to Week 14 in UC Bowel Movement Signs and Symptoms, as Assessed by the Ulcerative Colitis Patient-Reported Outcome Signs and Symptoms (UC-PRO/SS) Questionnaire ^[9]
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End point description:

The UC-PRO questionnaire is collected in the e-diary and completed by subjects for at least 9-12 consecutive days prior to a study visit. The UC-PRO is being reported in three domains; two domains are key endpoints and reported as UC-PRO Signs and Symptoms (UC-PRO/SS). The bowel domain score ranges from 0-27, with a higher score indicating a worse disease state.

End point type	Secondary
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End point timeframe:

Baseline and Week 14

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	272		
Units: Score on a Scale				
least squares mean (standard error)	-3.6 (± 0.6)	-5.2 (± 0.3)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0163
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-0.3

Secondary: Induction Phase: Change from Baseline to Week 14 in UC Functional Symptoms, as Assessed by the UC-PRO/SS Questionnaire

End point title	Induction Phase: Change from Baseline to Week 14 in UC Functional Symptoms, as Assessed by the UC-PRO/SS Questionnaire ^[10]
End point description:	The UC-PRO questionnaire is collected in the e-diary and completed by subjects for at least 9-12 consecutive days prior to a study visit. The UC-PRO is being reported in three domains; two domains are key endpoints and reported as UC-PRO Signs and Symptoms (UC-PRO/SS). The functional (abdominal symptoms) domain score ranges from 0-12, with a higher score indicating a worse disease state.
End point type	Secondary
End point timeframe:	
Baseline and Week 14	

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	272		
Units: Score on a Scale				
least squares mean (standard error)	-1.1 (± 0.2)	-1.5 (± 0.1)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0726
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0

Secondary: Induction Phase: Change from Baseline to Week 14 in Health-Related Quality of Life, as Assessed by the Overall Score of the Inflammatory Bowel Disease Questionnaire (IBDQ)

End point title	Induction Phase: Change from Baseline to Week 14 in Health-Related Quality of Life, as Assessed by the Overall Score of the Inflammatory Bowel Disease Questionnaire (IBDQ) ^[11]
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End point description:

The IBDQ is used to assess subject's health-related quality of life (QOL). The 32-item questionnaire contains four domains: bowel symptoms (10 items), systemic symptoms (5 items), emotional function (12 items), and social function (5 items). The items are scored on a 7-point Likert scale with a higher score indicating better health-related QOL.

End point type	Secondary
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End point timeframe:

Baseline and Week 14

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This analysis was only performed on the 'Induction phase' arms and hence why not all arms are presented.

End point values	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	293		
Units: Adjusted Mean				
number (not applicable)	28.4	37.4		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Cohort 2: Placebo (Double-Blind Induction Phase) v Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0445
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	17.9

Secondary: Maintenance Phase: Percentage of Subjects with Clinical Remission at Week 66 Among Subjects Who Had Achieved Clinical Remission at Week 14, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Clinical Remission at Week 66 Among Subjects Who Had Achieved Clinical Remission at Week 14, as Determined by the MCS
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores \leq 1 and a rectal bleeding subscore of 0. Clinical Remission is MCS \leq 2 with individual subscores \leq 1.
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	42		
Units: Percentage of Subjects				
number (not applicable)	36.4	38.1		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9959
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.67
upper limit	19.88

Secondary: Maintenance Phase: Percentage of Subjects with Clinical Remission at Week 66, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Clinical Remission at Week 66, as Determined by the MCS
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores \leq 1 and a rectal bleeding subscore of 0. Clinical Remission is MCS \leq 2 with individual subscores \leq 1.
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	114	112		
Units: Percentage of Subjects				
number (not applicable)	21.1	25.0		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5014
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.26
upper limit	14.7

Secondary: Maintenance Phase: Percentage of Subjects with Remission at Week 66 Among Subjects Who Had Achieved Remission at Week 14, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Remission at Week 66 Among Subjects Who Had Achieved Remission at Week 14, as Determined by the MCS
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Remission was defined as MCS less than or equal to (\leq)2 with individual subscores \leq 1 and a rectal bleeding subscore of 0.
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	41		
Units: Percentage of Subjects				
number (not applicable)	34.1	36.6		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9538
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.08
upper limit	20.35

Secondary: Maintenance Phase: Percentage of Subjects with Improvement From Baseline in Endoscopic Appearance of the Mucosa at Week 66, as Determined by the MCS Endoscopic Subscore

End point title	Maintenance Phase: Percentage of Subjects with Improvement From Baseline in Endoscopic Appearance of the Mucosa at Week 66, as Determined by the MCS Endoscopic Subscore
End point description:	
The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Improvement in endoscopic appearance of the mucosa is Endoscopy subscore ≤ 1 .	
End point type	Secondary
End point timeframe:	
Baseline and Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	114	112		
Units: Percentage of Subjects				
number (not applicable)	21.1	35.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0153
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.66
upper limit	25.78

Secondary: Maintenance Phase: Percentage of Subjects with Histologic Remission at Week 66, as Determined by the Nancy Histological Index

End point title	Maintenance Phase: Percentage of Subjects with Histologic Remission at Week 66, as Determined by the Nancy Histological Index
End point description:	Nancy Histological Index (NHI) is a 5-level classification ranging from grade 0 (No histologically significant disease) to grade 4 (severely active disease). Histologic remission is defined as a Nancy Histological Index of 0 or 1.
End point type	Secondary
End point timeframe:	Week 66

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	92	91		
Units: Percentage of Subjects				
number (not applicable)	14.1	30.8		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0073
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	16.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.44
upper limit	28.41

Secondary: Maintenance Phase: Percentage of Subjects with Endoscopic Remission at Week 66, as Determined by the MCS Endoscopic Subscore

End point title	Maintenance Phase: Percentage of Subjects with Endoscopic Remission at Week 66, as Determined by the MCS Endoscopic Subscore
End point description:	The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Endoscopic Remission is Endoscopy subscore = 0.
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	114	112		
Units: Percentage of Subjects				
number (not applicable)	11.4	23.2		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0174
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.87
upper limit	21.71

Secondary: Maintenance Phase: Percentage of Subjects with Corticosteroid-Free Clinical Remission at Week 66 Among Subjects Who Were Receiving Corticosteroids at Baseline, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Corticosteroid-Free Clinical Remission at Week 66 Among Subjects Who Were Receiving Corticosteroids at Baseline, as Determined by the MCS
End point description:	
<p>The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Corticosteroid-Free analysis was conducted only on a subgroup of participants who were randomized into the maintenance phase and receiving Corticosteroids (CS) at baseline. Subjects were defined as being off CS if they had no record of taking CS on the date that was 24 weeks prior to Week 66.</p>	
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	54		
Units: Percentage of Subjects				
number (not applicable)	12.7	20.4		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3015
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.83
upper limit	21.6

Secondary: Maintenance Phase: Percentage of Subjects with Corticosteroid-Free Remission at Week 66 Among Subjects Who Were Receiving Corticosteroids at Baseline, as Determined by the MCS

End point title	Maintenance Phase: Percentage of Subjects with Corticosteroid-Free Remission at Week 66 Among Subjects Who Were Receiving Corticosteroids at Baseline, as Determined by the MCS
End point description:	
The MCS ranges from 0 to 12 and is a composite of 4 assessments (each rated from 0-3): stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores represent greater disease severity. Corticosteroid-Free analysis was conducted only on a subgroup of subjects who were randomized into the maintenance phase and receiving Corticosteroids (CS) at baseline. Subjects were defined as being off CS if they had no record of taking CS on the date that was 24 weeks prior to Week 66.	
End point type	Secondary
End point timeframe:	
Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	54		
Units: Percentage of Subjects				
number (not applicable)	10.9	18.5		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2787
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	21.17

Secondary: Maintenance Phase: Change From Baseline to Week 66 in UC Bowel Movement Signs and Symptoms, as Assessed by the UC-PRO/SS Questionnaire

End point title	Maintenance Phase: Change From Baseline to Week 66 in UC Bowel Movement Signs and Symptoms, as Assessed by the UC-PRO/SS Questionnaire
End point description:	The UC-PRO questionnaire is collected in the e-diary and completed by subjects for at least 9-12 consecutive days prior to a study visit. The UC-PRO is being reported in three domains; two domains are key endpoints and reported as UC-PRO Signs and Symptoms (UC-PRO/SS). The bowel domain score ranges from 0-27, with a higher score indicating a worse disease state.
End point type	Secondary
End point timeframe:	
Baseline and Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	83	83		
Units: Score on a Scale				
least squares mean (standard error)	-6.3 (± 0.6)	-7.8 (± 0.6)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0763
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.2

Secondary: Maintenance Phase: Change From Baseline to Week 66 in UC Functional Symptoms, as Assessed by the UC-PRO/SS Questionnaire

End point title	Maintenance Phase: Change From Baseline to Week 66 in UC Functional Symptoms, as Assessed by the UC-PRO/SS Questionnaire
End point description:	The UC-PRO questionnaire is collected in the e-diary and completed by subjects for at least 9-12 consecutive days prior to a study visit. The UC-PRO is being reported in three domains; two domains are key endpoints and reported as UC-PRO Signs and Symptoms (UC-PRO/SS). The functional (abdominal symptoms) domain score ranges from 0-12, with a higher score indicating a worse disease state.
End point type	Secondary
End point timeframe:	
Baseline and Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	83	83		
Units: Score on a Scale				
least squares mean (standard error)	-1.8 (± 0.3)	-2.0 (± 0.3)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5329
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5

Secondary: Maintenance Phase: Change From Baseline to Week 66 in Health-Related Quality of Life, as Assessed by the Overall Score of the IBDQ

End point title	Maintenance Phase: Change From Baseline to Week 66 in Health-Related Quality of Life, as Assessed by the Overall Score of the IBDQ
End point description:	The IBDQ is used to assess subject's health-related quality of life (QOL). The 32-item questionnaire contains four domains: bowel symptoms (10 items), systemic symptoms (5 items), emotional function (12 items), and social function (5 items). The items are scored on a 7-point Likert scale with a higher score indicating better health-related QOL.
End point type	Secondary
End point timeframe:	
Baseline and Week 66	

End point values	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99	99		
Units: Adjusted Mean				
number (not applicable)	57.2	52.3		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Placebo
Comparison groups	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT) v Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2228
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	3

Secondary: Number of Subjects with at Least One Adverse Event by Severity, According to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0 (NCI-CTCAE v4.0)

End point title	Number of Subjects with at Least One Adverse Event by Severity, According to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0 (NCI-CTCAE v4.0)
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End point description:

All Adverse Events (AEs) were graded for severity using the NCI-CTCAE v4.0. Any AE not specifically listed was assessed per the following 5 grades: Grade 1 = mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; or intervention not indicated. Grade 2 = moderate; minimal, local, or non-invasive intervention indicated; or limiting age-appropriate instrumental activities of daily living. Grade 3 = severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care activities of daily living. Grade 4 = life-threatening consequences or urgent intervention indicated. Grade 5 = death related to AE. Not all grades are appropriate for all AEs; some AEs have fewer than 5 options. The terms "severe" and "serious" are not synonymous and are independently assessed for each AE. Multiple occurrences of AEs were counted only once per subject at the highest (worst) grade.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 78

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects				
Grade 1	39	8	31	19
Grade 2	38	14	26	64
Grade 3	15	1	5	14
Grade 4	0	0	1	0
Grade 5	0	0	0	0

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects				
Grade 1	117	33		
Grade 2	97	45		
Grade 3	37	19		
Grade 4	2	1		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events Leading to Study Drug Discontinuation

End point title	Number of Subjects with Adverse Events Leading to Study Drug Discontinuation
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End point description:

End point type	Secondary
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End point timeframe:

From Baseline up to Week 78

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	2	4	1	9

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects	12	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Serious Infection-Related Adverse Events

End point title	Number of Subjects with Serious Infection-Related Adverse Events
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 78	

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	2	0	1	3

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
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Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Infection-Related Adverse Events

End point title	Number of Subjects with Infection-Related Adverse Events
End point description:	
All Adverse Events (AEs) were graded for severity using the NCI-CTCAE v4.0. Any AE not specifically listed was assessed per the following 5 grades: Grade 1 = mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; or intervention not indicated. Grade 2 = moderate; minimal, local, or non-invasive intervention indicated; or limiting age-appropriate instrumental activities of daily living. Grade 3 = severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care activities of daily living. Grade 4 = life-threatening consequences or urgent intervention indicated. Not all grades are appropriate for all AEs; some AEs have fewer than 5 options. The terms "severe" and "serious" are not synonymous and are independently assessed for each AE. Multiple occurrences of AEs were counted only once per subject at the highest (worst) grade.	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 78	

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	38	13	29	44

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects	100	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Injection-Site Reaction-Related Adverse Events

End point title	Number of Subjects with Injection-Site Reaction-Related Adverse Events
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 78	

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	7	2	5	2

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects	4	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Hypersensitivity Reaction-Related Adverse Events

End point title	Number of Subjects with Hypersensitivity Reaction-Related Adverse Events
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 78	

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	0	0	0	0

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Malignancies

End point title	Number of Subjects with Malignancies
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 78	

End point values	Cohort 1: Etrolizumab (Open-Label Induction (OLI) Phase)	Placebo Responders: Placebo (Maintenance Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	27	95	114
Units: Subjects	0	0	0	0

End point values	Cohort 2: Etrolizumab (Double-Blind Induction Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	112		

Units: Subjects	2	2		
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-Therapeutic Antibodies to Etrolizumab at Baseline and During the Study

End point title	Number of Subjects with Anti-Therapeutic Antibodies to Etrolizumab at Baseline and During the Study
End point description: A tiered strategy was used to detect and characterize etrolizumab antibodies within this clinical study. When determining post baseline incidence, subjects were considered to be ADA positive if they were ADA negative or had missing data at baseline but developed an ADA response following etrolizumab drug exposure (treatment-induced ADA response), or if they were ADA positive at baseline and the titer of one or more post baseline samples was at least 0.60 titer unit greater than the titer of the baseline sample (treatment-enhanced ADA response). Subjects were considered to be ADA negative if they were ADA negative or had missing data at baseline and all post baseline samples were negative, or if they were ADA positive at baseline but did not have any post baseline samples with a titer that was at least 0.60 titer unit greater than the titer of the baseline sample (treatment unaffected). (n=X; n=X; n=X) refers to Number of Subjects analysed at each timepoint.	
End point type	Secondary
End point timeframe: Pre-dose at Baseline, Weeks 4, 14, 24, 44, and 66, and Early Termination/End of Safety Follow-Up (up to Week 78)	

End point values	Cohort 1: Etro (OLI Phase) + Cohort 2: Etro (DB Ind Phase)	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	286	114	112	
Units: Participants				
Baseline (n=286; n=114; n=110)	9	2	6	
Post-Baseline (n=284; n=114; n=112)	68	35	28	

Statistical analyses

No statistical analyses for this end point

Secondary: Etrolizumab Serum Trough Concentration

End point title	Etrolizumab Serum Trough Concentration
End point description: The Serum Pharmacokinetics of Etrolizumab was summarized with a mean serum concentration at steady state (trough) and at the two primary endpoint times (Weeks 14 and 66). Mean and Standard deviation values are presented below. (n=X; n=X; n=X) refers to Number of Subjects analysed at each	

timepoint. 999 = Not Estimable as more than a third of the samples were below the lower limit of quantification (LLOQ).

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour) at Baseline and Weeks 14, 24, 44 and 66

End point values	Cohort 1: Etro (OLI Phase) + Cohort 2: Etro (DB Ind Phase)	Etrolizumab Responders: Placebo (Maintenance Phase) (mITT)	Etrolizumab Responders: Etrolizumab (Maintenance Phase) (mITT)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	251	113	110	
Units: micrograms per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Week 14 (n=251; n=113; n=110)	11.0 (± 4.66)	12.7 (± 5.50)	14.0 (± 6.12)	
Week 24 (n=0; n=93; n=92)	0 (± 0)	0.474 (± 0.742)	9.55 (± 5.24)	
Week 44 (n=0; n=54; n=71)	0 (± 0)	999 (± 999)	10.7 (± 5.72)	
Week 66 (n=0; n=40; n=59)	0 (± 0)	999 (± 999)	16.2 (± 7.75)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up until a maximum of 78 weeks.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Cohort 1: Etrolizumab (OLI Induction Phase)
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Reporting group description:

Participants assigned to this arm will receive treatment with open-label etrolizumab 105 milligrams (mg) subcutaneous (SC) injection once every 4 weeks (Q4W) for 14 weeks during the induction phase.

Reporting group title	Cohort 2: Placebo (Double-Blind Induction Phase)
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Reporting group description:

Participants randomized to this arm will receive treatment with double-blind placebo SC injection Q4W for 14 weeks during the induction phase.

Reporting group title	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
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Reporting group description:

Participants randomized to this arm will receive treatment with double-blind etrolizumab 105 mg SC injection Q4W for 14 weeks during the induction phase.

Reporting group title	Placebo Responders: Placebo (Maintenance Phase)
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Reporting group description:

Participants who received placebo during the induction phase, Cohort 2: Placebo (Double-Blind Induction Phase), and achieve a clinical response with placebo at Week 14 will continue to receive blinded placebo from Week 16 up to Week 66 during the maintenance phase.

Reporting group title	Etrolizumab Responders: Placebo (Maintenance Phase)
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Reporting group description:

Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive placebo SC injection Q4W from Week 16 up to Week 66.

Reporting group title	Etrolizumab Responders: Etrolizumab (Maintenance Phase)
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Reporting group description:

Participants who received etrolizumab during the induction phase, Cohort 1: Etrolizumab (Open-Label Induction Phase) and Cohort 2: Etrolizumab (Double-Blind Induction Phase), and achieved a clinical response at Week 14 will be re-randomized by Week 16 for the double-blind maintenance phase. Clinical responders re-randomized to this arm will receive etrolizumab 105 mg SC injection Q4W from Week 16 up to Week 66.

Serious adverse events	Cohort 1: Etrolizumab (OLI Induction Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 130 (8.46%)	5 / 95 (5.26%)	20 / 384 (5.21%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleomorphic adenoma			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uteric cancer			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 130 (0.00%)	2 / 95 (2.11%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Cheilitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	6 / 130 (4.62%)	2 / 95 (2.11%)	10 / 384 (2.60%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 130 (0.00%)	1 / 95 (1.05%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal necrosis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pouchitis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 95 (1.05%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilic pneumonia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affect liability			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 130 (0.00%)	1 / 95 (1.05%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			

subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	1 / 130 (0.77%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	1 / 384 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 95 (0.00%)	0 / 384 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 27 (7.41%)	7 / 114 (6.14%)	11 / 112 (9.82%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleomorphic adenoma			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uteric cancer			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	2 / 114 (1.75%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 27 (0.00%)	1 / 114 (0.88%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Cheilitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 27 (0.00%)	2 / 114 (1.75%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 27 (3.70%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal necrosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pouchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilic pneumonia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affect liability			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			

subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	2 / 112 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 114 (0.88%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 114 (0.88%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 114 (0.88%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 27 (0.00%)	1 / 114 (0.88%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: Etrolizumab (OLI Induction Phase)	Cohort 2: Placebo (Double-Blind Induction Phase)	Cohort 2: Etrolizumab (Double-Blind Induction Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 130 (29.23%)	31 / 95 (32.63%)	115 / 384 (29.95%)
Nervous system disorders			
Dizziness			

subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	10 / 130 (7.69%) 11	6 / 95 (6.32%) 8	22 / 384 (5.73%) 26
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	8 / 130 (6.15%) 11	1 / 95 (1.05%) 1	10 / 384 (2.60%) 13
Injection site erythema subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	5 / 130 (3.85%) 7	6 / 95 (6.32%) 8	3 / 384 (0.78%) 3
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Colitis ulcerative subjects affected / exposed occurrences (all)	9 / 130 (6.92%) 9	10 / 95 (10.53%) 10	36 / 384 (9.38%) 37
Diarrhoea subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Rash			

subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 130 (3.85%) 6	7 / 95 (7.37%) 7	33 / 384 (8.59%) 38
Infections and infestations Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 130 (9.23%) 12	7 / 95 (7.37%) 8	33 / 384 (8.59%) 35
Oral herpes subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 95 (0.00%) 0	0 / 384 (0.00%) 0

Non-serious adverse events	Placebo Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Placebo (Maintenance Phase)	Etrolizumab Responders: Etrolizumab (Maintenance Phase)
Total subjects affected by non-serious adverse events subjects affected / exposed	20 / 27 (74.07%)	78 / 114 (68.42%)	78 / 112 (69.64%)
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	1 / 114 (0.88%) 1	2 / 112 (1.79%) 2
Headache			

subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3	10 / 114 (8.77%) 12	10 / 112 (8.93%) 10
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 27 (7.41%)	3 / 114 (2.63%)	5 / 112 (4.46%)
occurrences (all)	3	3	6
Fatigue			
subjects affected / exposed	1 / 27 (3.70%)	4 / 114 (3.51%)	12 / 112 (10.71%)
occurrences (all)	1	4	13
Injection site erythema			
subjects affected / exposed	2 / 27 (7.41%)	2 / 114 (1.75%)	5 / 112 (4.46%)
occurrences (all)	2	3	9
Pyrexia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 114 (0.00%)	0 / 112 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 27 (3.70%)	7 / 114 (6.14%)	10 / 112 (8.93%)
occurrences (all)	1	7	11
Colitis ulcerative			
subjects affected / exposed	11 / 27 (40.74%)	46 / 114 (40.35%)	31 / 112 (27.68%)
occurrences (all)	11	52	32
Diarrhoea			
subjects affected / exposed	1 / 27 (3.70%)	5 / 114 (4.39%)	6 / 112 (5.36%)
occurrences (all)	1	5	6
Nausea			
subjects affected / exposed	2 / 27 (7.41%)	4 / 114 (3.51%)	7 / 112 (6.25%)
occurrences (all)	2	7	7
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 27 (0.00%)	6 / 114 (5.26%)	4 / 112 (3.57%)
occurrences (all)	0	7	4
Rash			
subjects affected / exposed	1 / 27 (3.70%)	2 / 114 (1.75%)	8 / 112 (7.14%)
occurrences (all)	1	2	12
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	2 / 114 (1.75%) 2	6 / 112 (5.36%) 8
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 6	8 / 114 (7.02%) 11	19 / 112 (16.96%) 26
Infections and infestations Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 114 (0.88%) 1	6 / 112 (5.36%) 6
Influenza subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	9 / 114 (7.89%) 9	5 / 112 (4.46%) 5
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 5	17 / 114 (14.91%) 22	23 / 112 (20.54%) 33
Oral herpes subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	1 / 114 (0.88%) 1	5 / 112 (4.46%) 6
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 5	5 / 114 (4.39%) 8	5 / 112 (4.46%) 7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2014	Following updates were made: [1] The listed dose for each etrolizumab subcutaneous (SC) administration was changed from 100 mg to 105 mg. The change was made to more accurately list the actual dose of 105 mg in each prefilled syringe, rather than the nominal dose of 100 mg and [2] The study design section was modified to clarify that any U.S. subjects receiving immunosuppressants after Week 10 were not to receive further study treatment or open-label treatment and after completion of the Week 14 visit, were to be entered into the 12-week safety follow-up phase.
11 March 2014	Following updates were made: [1] The definition of moderately to severely active Ulcerative Colitis (UC) was updated to include stool frequency sub-score of ≥ 1 . Further, for Mayo Clinic Score (MCS)/partial Mayo Clinic Score (pMCS) calculation, the worst rectal bleeding score from the most recent 3 days prior to clinical visit was to be used and [2] Progressive Multifocal Leukoencephalopathy (PML) assessment was modified to include the PML Subjective Checklist (symptom assessment) and the PML Objective Checklist (neurologic evaluation). The algorithm for evaluation of PML was updated.
29 May 2014	Following updates were made: [1] The study assessments were updated to reflect that all subjects would be queried and closely monitored for any Adverse Event (AE) at all study assessment timepoints (every 4 weeks) during both clinic visits and study assessments made over the telephone.
27 September 2015	Following updates were made: [1] The protocol was amended to reflect FDA's agreement regarding continued use of a stable, baseline dose of immunosuppressant through the full duration of the study, with dose adjustment or discontinuation if a subject experienced related toxicity. These changes aligned instructions of immunosuppressant use in the U.S. with instructions already present for the rest of the world.
16 November 2016	Following updates were made: [1] Guidelines for managing specific AEs were updated to include hepatic effects as a potential risk for etrolizumab, to be in line with the safety profile of other anti-integrins, including vedolizumab, for which hepatic AEs have been reported.
02 September 2017	Following updates were made: [1] The inclusion criteria were revised to include subjects with previous exposure to at least one induction regimen with the following α TNF (tumor necrosis factor- α) therapies: infliximab, adalimumab, and/or golimumab. Subjects were categorized as TNF inhibitor refractory, TNF inhibitor intolerant, or neither refractory nor intolerant to α TNF therapies at screening; [2] The window for performing the endoscopy prior to Day 1 was extended from 10 to 16 days. The requirement for Medical Monitor approval for endoscopies conducted during this window was eliminated; [3] The time qualification for derivation of Mayo Clinic Score (MCS) baseline stool frequency and rectal bleeding subscores was redefined to include subscores obtained within 22 days prior to Day 1 and [4] The requirement to communicate John Cunningham virus (JCV) antibody status to a subject prior to Day 1 was removed, given the high prevalence of JCV antibody positivity in the general population and risk of false-negative tests. Aside from a plasma sample collected during screening for storage, serum and plasma samples collected during the study for potential JCV testing have been removed. All subjects will be counseled on JCV prevalence and risk of progressive multifocal leukoencephalopathy.

11 July 2018	<p>Following updates were made: [1] The primary efficacy endpoint for the maintenance phase was changed to remission at Week 66 for subjects who achieved clinical response (rather than remission) at Week 14, to align with clinical practice standards; [2] To assess the onset of action of etrolizumab, a secondary efficacy endpoint of change in MCS rectal bleeding and stool frequency subscores from baseline to Week 6 was added; [3] Histologic remission, defined as a Nancy histological index of ≤ 1, was added as a secondary efficacy outcome measure. The definition is based on consensus guidelines recommending that histologic remission should be defined by the absence of neutrophils in the crypts and lamina propria; [4] The study sample size was reduced from 800 to 605 subjects as a result of the change in the maintenance phase primary efficacy endpoint, which would be powered at $>90\%$. The induction phase primary efficacy endpoint definition (proportion of subjects in remission at Week 14) remained unchanged, but the reduction in sample size would lead to a drop in power from $>90\%$ to 80%. For the purpose of statistical analyses and sample size calculations, the induction and maintenance phases would be treated as two independent studies, and as such, no adjustment to alpha was required and [5] Derivation of the MCS endoscopic subscore at post-baseline timepoints was amended to be consistent with emerging normative standards of endoscopic assessment in clinical trials (Sandborn et al. 2017). The sigmoid colon MCS endoscopic subscore will be used (rather than the score from the worst affected segment, i.e., rectum, sigmoid colon, or descending colon) if the baseline sigmoid colon MCS endoscopic subscore was 2-3. The sigmoid colon MCS endoscopic subscore is considered to be more reliable in assessing earlier treatment response.</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported