Clinical trial results:
Phase III, Randomized, Multicenter Double-Blind, Double Dummy Study to Evaluate the Efficacy and Safety of Etrolizumab Compared With Infliximab in Patients With Moderate to Severe Active Ulcerative Colitis Who Are Naive to TNF Inhibitors

Summary

EudraCT number	2013-004282-14
Trial protocol	GB DE CZ AT PT NL NO ES BE IT HU FR
Global end of trial date	23 June 2020

Results information

Result version number	v1 (current)
This version publication date	04 July 2021
First version publication date	04 July 2021

Trial information

Trial identification

Sponsor protocol code	GA29103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02136069
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F.Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
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	23 June 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of etrolizumab subcutaneously [SC] every 4 weeks (Q4W) compared with infliximab in achieving both clinical response at Week 10 and clinical remission at Week 54 in patients with ulcerative colitis (UC).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	Czechia: 70
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	Hungary: 39
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 57
Country: Number of subjects enrolled	Korea, Republic of: 58
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Romania: 14
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	South Africa: 5

Worldwide total number of subjects	397
EEA total number of subjects	256

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)	370
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 397 patients were randomized in a 1:1 ratio into the study and received treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Etrolizumab + Placebo (IV)

Arm description:

Participants will receive ertolizumab (SC) Q4W until Week 52 along with placebo matched to infliximab as IV infusion until Week 46.

Arm type	Experimental
Investigational medicinal product name	Etrolizumab
Investigational medicinal product code	
Other name	PRO145223, RO5490261 and RG7413
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

105 mg administered by subcutaneous (SC) injection once every 4 weeks (Q4W)

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:

Etrolizumab matching placebo

Arm title	Infliximab + Placebo (Injection)

Arm description:

Participants will receive IV infusion of infliximab at Weeks 0,2, and 6, then every 8 weeks until Week 46 partnered with placebo matched to etrolizumab by SC injection Q4W until Week 52.

Arm type	Active comparator
Investigational medicinal product name	Infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg administered by intravenous (IV) infusion

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Infliximab matching placebo

Number of subjects in period 1	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)
Started	199	198
Completed	165	170
Not completed	34	28
Adverse event, serious fatal	-	1
Non-Compliance	1	-
Physician decision	5	4
Consent withdrawn by subject	10	11
Adverse event, non-fatal	6	8
UC flare-up	1	-
Lost to follow-up	1	-
Lack of efficacy	10	4

Baseline characteristics

Reporting groups	
Reporting group title	Etrolizumab + Placebo (IV)
Reporting group description:	
Participants will receive ertolizumab (SC) Q4W until Week 52 along with placebo matched to infliximab as IV infusion until Week 46.	
Reporting group title	Infliximab + Placebo (Injection)
Reporting group description:	
Participants will receive IV infusion of infliximab at Weeks 0,2, and 6, then every 8 weeks until Week 46 partnered with placebo matched to etrolizumab by SC injection Q4W until Week 52.	

Reporting group values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)	Total
Number of subjects	199	198	397
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)	181	189	370
From 65-84 years	18	9	27
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	40.0	39.5	
standard deviation	± 15.2	± 13.4	-
Sex: Female, Male Units:			
Female	81	66	147
Male	118	132	250
Race/Ethnicity, Customized Units: Subjects			
Asian	39	30	69
Black or African American	1	0	1
White	150	158	308
Other	9	10	19
Mayo Clinic Score (MCS) ≤9 or ≥10 at Baseline			
Measure Description: Participants were stratified by concomitant treatment with corticosteroids (yes/no) at randomization, concomitant treatment with immunosuppressants (yes/no) at randomization, and disease activity measured during screening (MCS ≤9/MCS ≥10). The MCS ranges from 0 to 12 and is a composite of the four following assessments of disease activity: stool frequency subscore, rectal bleeding subscore, endoscopy subscore, and physician's global assessment (PGA) subscore. Each of the four assessments was rated with a score from 0 to 3, with higher scores indicating more severe disease.			
Units: Subjects			
MCS ≤9	139	147	286

MCS ≥10	60	50	110
Unknown	0	1	1
Baseline Treatment: None, Corticosteroids (CS) or Immunosuppressants (IS) Alone, or Both CS and IS			
Participants were stratified by concomitant treatment with corticosteroids (yes/no) at randomization, concomitant treatment with immunosuppressants (yes/no) at randomization, and disease activity measured during screening (MCS ≤9/MCS ≥10).			
Units: Subjects			
Corticosteroids (CS) Alone	59	56	115
Immunosuppressants (IS) Alone	40	36	76
Both CS and IS	25	30	55
None	75	76	151

End points

End points reporting groups

Reporting group title	Etrolizumab + Placebo (IV)
Reporting group description:	
Participants will receive ertolizumab (SC) Q4W until Week 52 along with placebo matched to infliximab as IV infusion until Week 46.	
Reporting group title	Infliximab + Placebo (Injection)
Reporting group description:	
Participants will receive IV infusion of infliximab at Weeks 0,2, and 6, then every 8 weeks until Week 46 partnered with placebo matched to etrolizumab by SC injection Q4W until Week 52.	

Primary: Percentage of Participants with Both Clinical Response at Week 10 and Clinical Remission at Week 54, as determined by the Mayo Clinic Score (MCS)

End point title	Percentage of Participants with Both Clinical Response at Week 10 and Clinical Remission at Week 54, as determined by the Mayo Clinic Score (MCS)
End point description:	
Mayo Clinic Score (MCS) is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. 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. Clinical Remission is MCS ≤2 with individual subscores ≤1.	
End point type	Primary
End point timeframe:	
Week 10, Week 54	

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	18.6	19.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8114
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	6.83

Secondary: Percentage of Participants Achieving Clinical Remission at Week 10, Defined as MCS ≤2 with Individual Subscores ≤1

End point title	Percentage of Participants Achieving Clinical Remission at Week 10, Defined as MCS ≤2 with Individual Subscores ≤1

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease.

End point type	Secondary

End point timeframe:

Week 10

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	20.6	32.8		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1293 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.5
upper limit	-3.26

Notes:

[1] - p-values are not multiplicity adjusted

Secondary: Percentage of Participants Achieving Clinical Remission at Week 54, as

determined by the MCS

End point title	Percentage of Participants Achieving Clinical Remission at Week 54, as determined by the MCS

End point description:

Mayo Clinic Score (MCS) is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Clinical Remission is MCS ≤2 with individual subscores ≤1.

End point type	Secondary

End point timeframe:

Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	20.1	23.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4056 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.53
upper limit	4.74

Notes:

[2] - p-values are not multiplicity adjusted

Secondary: Percentage of Participants Achieving Clinical Remission at Both Week 10 and Week 54, as determined by the MCS

End point title	Percentage of Participants Achieving Clinical Remission at Both Week 10 and Week 54, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Clinical Remission is MCS ≤2 with individual subscores ≤1.

End point type	Secondary

End point timeframe:

Week 10 and Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	10.6	13.1		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4591 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.88
upper limit	4.14

Notes:

[3] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants Achieving Clinical Remission at Week 54 Among Those with a Clinical Response at Week 10, as determined by the MCS

End point title	Percentage of Participants Achieving Clinical Remission at Week 54 Among Those with a Clinical Response at Week 10, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician’s global assessment. Higher scores indicate more severe disease. Clinical Remission is MCS ≤2 with individual subscores ≤1. 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 10 and Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	37.8	33.3		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4196 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.54
upper limit	18.13

Notes:

[4] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants with Endoscopic Remission at Week 54, as determined by the MCS

End point title	Percentage of Participants with Endoscopic Remission at Week 54, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician’s global assessment. Higher scores indicate more severe disease. Endoscopic Remission is Endoscopy subscore = 0.

End point type	Secondary

End point timeframe:

Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	17.6	22.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2168 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.84
upper limit	2.94

Notes:

[5] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants Achieving Clinical Response at Week 10, as determined by the MCS

End point title	Percentage of Participants Achieving Clinical Response at Week 10, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. 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 10

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	49.2	59.1		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0564 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	-9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.06
upper limit	0.29

Notes:

[6] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants Achieving Clinical Response at Both Weeks 10 and 54, as determined by the MCS

End point title	Percentage of Participants Achieving Clinical Response at Both Weeks 10 and 54, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. 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 10, Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	23.1	29.3		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)

Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1729 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.51
upper limit	2.7

Notes:

[7] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants that Achieve Clinical Remission Corticosteroid-Free at Week 54 (off Corticosteroid for at Least 24 Weeks Prior to Week 54) Among Those Who Were Receiving Corticosteroids at Baseline, as determined by the MCS

End point title	Percentage of Participants that Achieve Clinical Remission Corticosteroid-Free at Week 54 (off Corticosteroid for at Least 24 Weeks Prior to Week 54) Among Those Who Were Receiving Corticosteroids at Baseline, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Clinical Remission is MCS ≤2 with individual subscores ≤1.

End point type	Secondary

End point timeframe:

Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	86		
Units: percentage of participants				
number (not applicable)	15.5	17.4		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)

Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8941 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Remission Rates
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.01
upper limit	10.68

Notes:

[8] - p-value has not been adjusted for multiplicity

Secondary: Number of Participants with Adverse Events, Severity Determined According to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0 (NCI CTCAE v4.0)

End point title	Number of Participants with Adverse Events, Severity Determined According to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0 (NCI CTCAE v4.0)

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 participant at the highest (worst) grade.

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants				
Grade 1	42	48		
Grade 2	72	74		
Grade 3	35	23		
Grade 4	5	5		
Grade 5	0	1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants with Adverse Events Leading to Study Drug Discontinuation

End point description:

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants	29	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Infection-Related Adverse Events, Severity Determined According to the NCI CTCAE v4.0

End point title	Number of Participants with Infection-Related Adverse Events, Severity Determined According to the NCI CTCAE v4.0

End point description:

All 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 participant at the highest (worst) grade.

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants				
Grade 1	28	27		
Grade 2	31	29		
Grade 3	8	4		
Grade 4	2	1		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants with Serious Infection-Related Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants	11	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Malignancies

End point title	Number of Participants with Malignancies

End point description:

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Injection-Site Reactions, Severity Determined According to the NCI CTCAE v4.0

End point title	Number of Participants with Injection-Site Reactions, Severity Determined According to the NCI CTCAE v4.0

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 participant at the highest (worst) grade.

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants				
Grade 1	7	5		
Grade 2	0	2		
Grade 3	0	0		
Grade 4	0	0		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hypersensitivity Reaction Events, Severity Determined According to the NCI CTCAE v4.0

End point title	Number of Participants with Hypersensitivity Reaction Events, Severity Determined According to the NCI CTCAE v4.0

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 participant at the highest (worst) grade.

End point type	Secondary

End point timeframe:

Baseline until the end of study (up to 66 weeks)

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: participants				
Grade 1	0	2		
Grade 2	0	7		
Grade 3	0	1		
Grade 4	0	2		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Etrolizumab Serum Concentration

End point title	Pharmacokinetics: Etrolizumab Serum Concentration[9]

End point description:

End point type	Secondary

End point timeframe:

Weeks 2, 10, 12, 30, and 54

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: Etrolizumab concentrations are provided only for the arm that received treatment with etrolizumab.

End point values	Etrolizumab + Placebo (IV)			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: microgram/milliliter				
arithmetic mean (standard deviation)				
Week 2	7.64 (± 2.75)			
Week 10	12.0 (± 4.63)			
Week 12	6.92 (± 3.18)			
Week 32	13.9 (± 5.96)			
Week 54	13.2 (± 5.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Overall Score at Weeks 10, 30, and 54

End point title	Change from Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Overall Score at Weeks 10, 30, and 54

End point description:

The IBDQ is used to assess participant'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:

Weeks 10, 30, and 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	156		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Week 10	43.2 (± 36.6)	45.1 (± 39.4)		
Week 30	53.5 (± 40.8)	59.6 (± 34.4)		
Week 54	58.2 (± 32.9)	63.2 (± 38.5)		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)

Number of subjects included in analysis	321
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4106 [10]
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	4.3

Notes:

[10] - p-value has not been adjusted for multiplicity

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	321
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1434 [11]
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	1.9

Notes:

[11] - p-value has not been adjusted for multiplicity

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	321
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1103 [12]
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	1.4

Notes:

[12] - p-value has not been adjusted for multiplicity

Secondary: Number of Participants with Anti-Therapeutic Antibodies (ATAs) to

Etrolizumab

End point title	Number of Participants with Anti-Therapeutic Antibodies (ATAs) to Etrolizumab[13]

End point description:

End point type	Secondary

End point timeframe:

Weeks 0, 4, 10, 12, 30, and 54

Notes:

[13] - 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: ATAs to Etrolizumab were provided only for the arm that received treatment with etrolizumab.

End point values	Etrolizumab + Placebo (IV)			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: participants	69			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Week 10, determined by the MCS

End point title	Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Week 10, determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Improvement in endoscopic appearance of the mucosa is Endoscopy subscore ≤1.

End point type	Secondary

End point timeframe:

Baseline to Week 10

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	36.7	49.5		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0118 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	-12.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.84
upper limit	-2.66

Notes:

[14] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Week 54, as determined by the MCS

End point title	Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Week 54, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Improvement in endoscopic appearance of the mucosa is Endoscopy subscore ≤1.

End point type	Secondary

End point timeframe:

Baseline to Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	27.1	32.3		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)

Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2845 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.76
upper limit	4.12

Notes:

[15] - p-value has not been adjusted for multiplicity

Secondary: Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Both Week 10 and Week 54, as determined by the MCS

End point title	Percentage of Participants with Improvement in Endoscopic Appearance of the Mucosa at Both Week 10 and Week 54, as determined by the MCS

End point description:

MCS is a composite of 4 assessments, each rated from 0-3: stool frequency, rectal bleeding, endoscopy, and physician's global assessment. Higher scores indicate more severe disease. Improvement in endoscopic appearance of the mucosa is Endoscopy subscore ≤1.

End point type	Secondary

End point timeframe:

Baseline to Week 10, Week 54

End point values	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	198		
Units: percentage of participants				
number (not applicable)	18.1	24.7		

Statistical analyses

Statistical analysis title	Etrolizumab vs. Infliximab
Comparison groups	Etrolizumab + Placebo (IV) v Infliximab + Placebo (Injection)
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1234 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference in Response Rates
Point estimate	-6.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	1.84

Notes:

[16] - p-value has not been adjusted for multiplicity

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline until the end of study (up to 66 weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Etrolizumab + Placebo (IV)
Reporting group description:	
Participants will receive ertolizumab (SC) Q4W until Week 52 along with placebo matched to infliximab as IV infusion until Week 46.	
Reporting group title	Infliximab + Placebo (Injection)
Reporting group description:	
Participants will receive IV infusion of infliximab at Weeks 0,2, and 6, then every 8 weeks until Week 46 partnered with placebo matched to etrolizumab by SC injection Q4W until Week 52.	

Serious adverse events	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)	
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 199 (16.08%)	20 / 198 (10.10%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Investigations			
Haemoglobin decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system vasculitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vein occlusion			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 199 (1.01%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 199 (6.03%)	11 / 198 (5.56%)	
occurrences causally related to treatment / all	0 / 12	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 199 (1.01%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 199 (1.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 199 (1.01%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis listeria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 199 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stitch abscess			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 199 (0.50%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Etrolizumab + Placebo (IV)	Infliximab + Placebo (Injection)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 199 (47.24%)	80 / 198 (40.40%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 199 (11.06%)	19 / 198 (9.60%)	
occurrences (all)	30	28	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 199 (5.03%)	5 / 198 (2.53%)	
occurrences (all)	11	6	
Colitis ulcerative			
alternative assessment type: Systematic			

subjects affected / exposed	45 / 199 (22.61%)	33 / 198 (16.67%)	
occurrences (all)	47	36	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 199 (5.53%)	4 / 198 (2.02%)	
occurrences (all)	12	4	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 199 (5.03%)	4 / 198 (2.02%)	
occurrences (all)	10	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 199 (10.55%)	15 / 198 (7.58%)	
occurrences (all)	24	16	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 199 (11.06%)	23 / 198 (11.62%)	
occurrences (all)	30	30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2014	1) The definition of moderately to severely ulcerative colitis (UC) was updated to include stool frequency subscore of ≥1; and 2) UC Disease Activity Assessments section was modified to include that: 1) given the potential for increased rectal bleeding following endoscopic procedures, rectal bleeding Mayo Clinic Score (MCS) would be derived prior to endoscopy, 2) postbaseline endoscopy could be performed on the same day as the study visit instead of 4 days prior to the visit, 3) each segment, instead of the worst affected segment, of the colon up to the splenic flexure (rectum, sigmoid, and descending colon) would be assigned an endoscopic subscore and the score from the worst affected segment up to the splenic flexure was to be used for the MCS calculation, 4) any discrepancy between the endoscopic subscore obtained by the local versus central readers would require a third adjudication read by a different central reader.
09 July 2014	1) The primary endpoint was updated to sustained remission (including a rectal bleeding score of 0) and sustained clinical remission was changed to a secondary endpoint; and 2) Updates were made to clarify the risk mitigation strategy, including the potential risks associated with etrolizumab treatment and the risks associated with disease worsening.
07 December 2015	The protocol was amended to allow extensions of the screening and endoscopy windows when this was required to ensure enrollment of eligible patients and following approval from the Medical Monitor.
02 November 2016	The protocol was amended to update and align the safety section with information regarding potential risks for etrolizumab in the current Etrolizumab Investigator's Brochure.
25 January 2018	1) The primary efficacy endpoint was changed from sustained remission (at Weeks 10, 30 and 54) to achievement of both clinical response at Week 10 and clinical remission at Week 54; 2) Secondary and exploratory efficacy endpoints were amended to align with the revision of the primary efficacy endpoint; 3) 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. 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 is 2−3. The sigmoid colon MCS endoscopic subscore is considered to be more reliable in assessing earlier treatment response; 4) 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; and 5) The time qualification for derivation of MCS baseline stool frequency and rectal bleeding subscores was redefined to include subscores obtained within 22 days prior to randomization (Day 1).
22 October 2018	1) The difference in treatment effect between etrolizumab and infliximab was considered to be higher than previously assumed. As a result, the estimated sample size for this study was reduced from 600 to 390 patients. Patients were continued to be randomized in the same 1:1 ratio; and 2) A secondary efficacy endpoint, to evaluate clinical remission at Week 54 among patients with a clinical response at Week 10, was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported