



Clinical trial results:

A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study, with a Vedolizumab IV Reference Arm, to Evaluate the Efficacy and Safety of Vedolizumab Subcutaneous as Maintenance Therapy in Subjects With Moderately to Severely Active Ulcerative Colitis Who Achieved Clinical Response Following Open-Label Vedolizumab Intravenous Therapy Summary

EudraCT number	2015-000480-14
Trial protocol	NL SK CZ BG GB DE BE SE DK LT ES HU RO HR IT
Global end of trial date	21 August 2018

Results information

Result version number	v1 (current)
This version publication date	14 June 2019
First version publication date	14 June 2019

Trial information

Trial identification

Sponsor protocol code	MLN0002SC-3027
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02611830
WHO universal trial number (UTN)	U1111-1168-0813

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	40 Landsdowne Street, Cambridge, MA, United States, 02139
Public contact	Medical Director, Takeda, +1877 8253327, trialdisclosures@takeda.com
Scientific contact	Medical Director, Takeda, +1877 8253327, trialdisclosures@takeda.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the trial is to assess the effect of vedolizumab subcutaneous (vedolizumab SC) maintenance treatment on clinical remission at Week 52 in participants with moderately to severely active ulcerative colitis (UC) who achieved clinical response following administration of vedolizumab intravenous (vedolizumab IV) induction therapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Poland: 95
Country: Number of subjects enrolled	Serbia: 3
Country: Number of subjects enrolled	Slovakia: 10
Country: Number of subjects enrolled	Bosnia and Herzegovina: 2
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Croatia: 10
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	Ukraine: 23
Country: Number of subjects enrolled	Canada: 11

Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	383
EEA total number of subjects	190

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)	355
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at one hundred forty-one investigative sites in North America, South America, Western/Northern Europe, Central Europe, Eastern Europe and Africa/Asia/Australia from 18-Dec-2015 to 21-Aug-2018.

Pre-assignment

Screening details:

A total of 383 participants were enrolled in open-label (OL) induction phase, 353 participants completed. 216 participants achieved clinical response at Week 6 were randomized into maintenance phase and participants who did not achieve clinical response at Week 6, received 3rd dose of open label vedolizumab IV 300 mg and completed Week 14 visit.

Period 1

Period 1 title	OL Induction Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Open-Label Induction Phase: Vedolizumab 300 mg IV
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Arm description:

Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 in the open-label induction phase.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab 300 mg IV infusion once at Weeks 0, 2 in the open-label induction phase.

Number of subjects in period 1	Open-Label Induction Phase: Vedolizumab 300 mg IV
Started	383
Completed	216
Not completed	167
Pretreatment Event/Adverse Event	10
Voluntary Withdrawal	7
Significant Protocol Deviation	4
Did not achieve clinical response	122
Lost to follow-up	2
Reason not specified	5
Lack of efficacy	17

Period 2

Period 2 title	Overall Study
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Maintenance Phase: Induction IV + Placebo

Arm description:

Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase. Placebo-matching subcutaneous (SC) injections, once every 2 weeks (Q2W) and placebo-matching IV infusions, once every 8 weeks (Q8W) starting at Week 6 up to approximately Week 50.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Matching placebo SC injections, once every 2 weeks (Q2W) and placebo-matching IV infusions, once every 8 weeks (Q8W) starting at Week 6 up to approximately Week 70.

Arm title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
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Arm description:

Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab SC in maintenance phase. Vedolizumab SC, 108 mg, injection, Q2W and placebo-matching IV infusions, Q8W, starting at Week 6 up to approximately Week 50.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab 108 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Vedolizumab subcutaneous (SC), 108 mg, injection Q2W and placebo-matching IV infusions, Q8W starting at Week 6 up to approximately Week 77.

Arm title	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
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Arm description:

Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab IV in maintenance phase. Vedolizumab

300 mg, IV infusion, Q8W and placebo-matching SC injection, Q2W starting at Week 6 up to approximately Week 50.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab 300 mg IV infusion Q8W and placebo-matching SC injection, Q2W starting at Week 6 up to approximately Week 71.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline characteristics were reported per arm groups of the maintenance phase, therefore it is selected as the baseline period and participants who were not randomized in the maintenance phase are reported as subject analysis set.

Number of subjects in period 2 ^[2]	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Started	56	106	54
Completed	20	75	39
Not completed	36	31	15
Pretreatment Event/Adverse Event	5	5	2
Voluntary Withdrawal	1	2	5
Significant Protocol Deviation	-	1	1
Pregnancy	-	1	-
Reason not specified	1	4	-
Lost to follow-up	-	-	1
Lack of efficacy	29	18	6

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics were reported per arm groups of the maintenance phase and participants who were not randomized in the maintenance phase are reported as subject analysis set.

Baseline characteristics

Reporting groups

Reporting group title	Maintenance Phase: Induction IV + Placebo
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase. Placebo-matching subcutaneous (SC) injections, once every 2 weeks (Q2W) and placebo-matching IV infusions, once every 8 weeks (Q8W) starting at Week 6 up to approximately Week 50.	
Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab SC in maintenance phase. Vedolizumab SC, 108 mg, injection, Q2W and placebo-matching IV infusions, Q8W, starting at Week 6 up to approximately Week 50.	
Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab IV in maintenance phase. Vedolizumab 300 mg, IV infusion, Q8W and placebo-matching SC injection, Q2W starting at Week 6 up to approximately Week 50.	

Reporting group values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects	56	106	54
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean full range (min-max)	39.4 21 to 66	38.1 18 to 69	41.6 18 to 68
Sex: Female, Male Units: Subjects			
Female	22	41	23
Male	34	65	31
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	0	0
Non-Hispanic and Latino	6	7	8
Not Collected	49	99	46
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	13	14	5
Black or African American	0	0	2
White	42	92	47
Female Reproductive Status Units: Subjects			
Postmenopausal	4	3	8

Surgically Sterile	1	2	3
Female of Childbearing Potential	17	36	12
Participant is a male	34	65	31
Smoking Classification			
Units: Subjects			
Has never smoked	38	70	33
Is a current smoker	0	11	10
is an ex-smoker	18	25	11
Region of Enrollment			
Units: Subjects			
Australia	0	2	1
Japan	10	10	2
Korea, Republic Of	3	4	3
Czech Republic	3	10	4
Hungary	2	2	6
Poland	13	35	10
Serbia	1	0	1
Slovakia	0	4	3
Bosnia	0	2	0
Bulgaria	1	1	1
Croatia	1	0	1
Estonia	0	0	0
Israel	0	0	0
Romania	0	3	0
Russia	0	5	3
Turkey	2	0	0
Ukraine	4	6	2
Canada	3	2	2
United States	6	7	8
Brazil	0	3	1
Mexico	1	0	0
Belgium	2	0	0
Denmark	1	0	0
Germany	3	3	1
Italy	0	2	3
Lithuania	0	4	1
Netherlands	0	0	0
Spain	0	0	0
United Kingdom	0	1	1
Height			
Units: cm			
arithmetic mean	172.4	171.9	171.2
full range (min-max)	147 to 194	151 to 197	152 to 196
Weight			
Units: kg			
arithmetic mean	73.96	71.58	76.95
full range (min-max)	40.6 to 160.0	44.0 to 131.0	50.6 to 124.8
Body Mass Index (BMI)			
Body Mass Index = weight/height.			
Units: kg/m^2			
arithmetic mean	24.66	24.07	26.21

full range (min-max)	14.1 to 51.1	17.0 to 41.0	16.3 to 35.3
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Reporting group values	Total		
Number of subjects	216		
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean			
full range (min-max)	-		
Sex: Female, Male			
Units: Subjects			
Female	86		
Male	130		
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	1		
Non-Hispanic and Latino	21		
Not Collected	194		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	32		
Black or African American	2		
White	181		
Female Reproductive Status			
Units: Subjects			
Postmenopausal	15		
Surgically Sterile	6		
Female of Childbearing Potential	65		
Participant is a male	130		
Smoking Classification			
Units: Subjects			
Has never smoked	141		
Is a current smoker	21		
is an ex-smoker	54		
Region of Enrollment			
Units: Subjects			
Australia	3		
Japan	22		
Korea, Republic Of	10		
Czech Republic	17		
Hungary	10		
Poland	58		
Serbia	2		
Slovakia	7		
Bosnia	2		
Bulgaria	3		

Croatia	2		
Estonia	0		
Israel	0		
Romania	3		
Russia	8		
Turkey	2		
Ukraine	12		
Canada	7		
United States	21		
Brazil	4		
Mexico	1		
Belgium	2		
Denmark	1		
Germany	7		
Italy	5		
Lithuania	5		
Netherlands	0		
Spain	0		
United Kingdom	2		
Height			
Units: cm			
arithmetic mean			
full range (min-max)	-		
Weight			
Units: kg			
arithmetic mean			
full range (min-max)	-		
Body Mass Index (BMI)			
Body Mass Index = weight/height.			
Units: kg/m^2			
arithmetic mean			
full range (min-max)	-		

Subject analysis sets

Subject analysis set title	Vedolizumab 300 mg IV
Subject analysis set type	Safety analysis

Subject analysis set description:

Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 in the open-label induction phase. Participants who did not achieve clinical response at Week 6 were not randomized into the maintenance phase and received a 3rd dose of vedolizumab 300 mg IV infusion at Week 6.

Reporting group values	Vedolizumab 300 mg IV		
Number of subjects	167		
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	42.7		
full range (min-max)	18 to 79		

Sex: Female, Male			
Units: Subjects			
Female	79		
Male	88		
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	0		
Non-Hispanic and Latino	24		
Not Collected	143		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	2		
Asian	39		
Black or African American	1		
White	125		
Female Reproductive Status			
Units: Subjects			
Postmenopausal	17		
Surgically Sterile	8		
Female of Childbearing Potential	54		
Participant is a male	88		
Smoking Classification			
Units: Subjects			
Has never smoked	107		
Is a current smoker	7		
is an ex-smoker	53		
Region of Enrollment			
Units: Subjects			
Australia	1		
Japan	27		
Korea, Republic Of	10		
Czech Republic	2		
Hungary	2		
Poland	37		
Serbia	1		
Slovakia	3		
Bosnia	0		
Bulgaria	3		
Croatia	8		
Estonia	2		
Israel	2		
Romania	4		
Russia	12		
Turkey	1		
Ukraine	11		
Canada	4		
United States	24		
Brazil	4		
Mexico	2		
Belgium	0		
Denmark	0		

Germany	0		
Italy	4		
Lithuania	0		
Netherlands	1		
Spain	1		
United Kingdom	1		
Height			
Units: cm			
arithmetic mean	169.3		
full range (min-max)	145 to 193		
Weight			
Units: kg			
arithmetic mean	68.20		
full range (min-max)	37.0 to 150.2		
Body Mass Index (BMI)			
Body Mass Index = weight/height.			
Units: kg/m ²			
arithmetic mean	23.65		
full range (min-max)	15.1 to 40.3		

End points

End points reporting groups

Reporting group title	Open-Label Induction Phase: Vedolizumab 300 mg IV
Reporting group description: Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 in the open-label induction phase.	
Reporting group title	Maintenance Phase: Induction IV + Placebo
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase. Placebo-matching subcutaneous (SC) injections, once every 2 weeks (Q2W) and placebo-matching IV infusions, once every 8 weeks (Q8W) starting at Week 6 up to approximately Week 50.	
Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab SC in maintenance phase. Vedolizumab SC, 108 mg, injection, Q2W and placebo-matching IV infusions, Q8W, starting at Week 6 up to approximately Week 50.	
Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Reporting group description: Participants received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab IV in maintenance phase. Vedolizumab 300 mg, IV infusion, Q8W and placebo-matching SC injection, Q2W starting at Week 6 up to approximately Week 50.	
Subject analysis set title	Vedolizumab 300 mg IV
Subject analysis set type	Safety analysis
Subject analysis set description: Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 in the open-label induction phase. Participants who did not achieve clinical response at Week 6 were not randomized into the maintenance phase and received a 3rd dose of vedolizumab 300 mg IV infusion at Week 6.	

Primary: Percentage of Participants Achieving Clinical Remission at Week 52

End point title	Percentage of Participants Achieving Clinical Remission at Week 52
End point description: Clinical remission is defined as a complete Mayo score ≤ 2 points and no individual subscore > 1 point. The Mayo score is a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consists of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore is scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). The Full Analysis Set (FAS) included all randomized participants who received at least 1 dose of study drug. Participants who only received induction IV therapy and were not randomized into the maintenance phase were not included in the FAS; participants were analyzed according to the randomized treatment assignment.	
End point type	Primary
End point timeframe: Week 52	

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	106	54	
Units: percentage of participants				
number (confidence interval 95%)	14.3 (6.4 to 26.2)	46.2 (36.5 to 56.2)	42.6 (29.2 to 56.8)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC v Maintenance Phase: Induction IV + Placebo
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	32.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.7
upper limit	45

Notes:

[1] - P-value was calculated by Cochran-Mantel-Haenszel (CMH) test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF- α antagonist failure/concomitant immunomodulator.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	27.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.3
upper limit	43.5

Notes:

[2] - P-value was calculated by CMH test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF- α antagonist failure/concomitant immunomodulator.

Secondary: Percentage of Participants Achieving Mucosal Healing at Week 52

End point title	Percentage of Participants Achieving Mucosal Healing at Week 52
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End point description:

Mucosal healing is defined as Mayo endoscopic subscore ≤ 1 point. The Mayo score is a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consists of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. The findings on endoscopy scale ranges from 0 to 3, where 0=normal or inactive disease 1=mild disease (erythema, decreased vascular pattern, mild friability) 2=moderate disease (marked erythema, lack of vascular pattern, friability, erosions) 3=severe disease (spontaneous bleeding, ulceration). The FAS included all randomized participants who received at least 1 dose of study drug. Participants who only received induction IV therapy and were not randomized into the maintenance phase were not included in the FAS; participants were analyzed according to the randomized treatment assignment.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	106	54	
Units: percentage of participants				
number (confidence interval 95%)	21.4 (11.6 to 34.4)	56.6 (46.6 to 66.2)	53.7 (39.6 to 67.4)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	35.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.1
upper limit	49.3

Notes:

[3] - P-value was calculated by CMH test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF- α antagonist failure/concomitant immunomodulator.

Statistical analysis title	Statistical Analysis 2
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Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	32.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.7
upper limit	48.7

Notes:

[4] - P-value was calculated by CMH test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-α antagonist failure/concomitant immunomodulator.

Secondary: Percentage of Participants Achieving Durable Clinical Response at Week 6 and Week 52

End point title	Percentage of Participants Achieving Durable Clinical Response at Week 6 and Week 52
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End point description:

Durable clinical response is defined as clinical response at both Weeks 6 and 52, where clinical response is defined as a reduction in complete Mayo score of ≥ 3 points and $\geq 30\%$ from Baseline (Week 0) with an accompanying decrease in rectal bleeding subscore of ≥ 1 point or absolute rectal bleeding subscore of ≤ 1 point. The Mayo score is a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. Index consists of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore is scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). FAS included all randomized participants who received at least 1 dose of study drug. Participants who only received induction IV therapy and were not randomized into the maintenance phase were not included in the FAS; participants were analyzed according to the randomized treatment assignment.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 6 and 52

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	106	54	
Units: percentage of participants				
number (confidence interval 95%)	28.6 (17.3 to 42.2)	64.2 (54.3 to 73.2)	72.2 (58.4 to 83.5)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	36.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.2
upper limit	50.9

Notes:

[5] - P-value was calculated by CMH test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF- α antagonist failure/concomitant immunomodulator.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	44.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.3
upper limit	60.6

Notes:

[6] - P-value was calculated by CMH test stratified by randomization strata according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF- α antagonist failure/concomitant immunomodulator.

Secondary: Percentage of Participants Achieving Durable Clinical Remission at Week 6 and Week 52

End point title	Percentage of Participants Achieving Durable Clinical Remission at Week 6 and Week 52
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End point description:

Durable clinical remission is defined as clinical remission at both Weeks 6 and 52. Clinical remission is defined as a complete Mayo score of less than or equal to (\leq) 2 points and no individual subscore greater than ($>$) 1 point. The Mayo score is a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consists of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore is scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). The FAS included all randomized participants who received at least 1 dose of study drug. Participants who only received induction IV therapy and were not randomized into the maintenance phase were not included in the FAS; participants were analyzed according to the randomized treatment assignment.

End point type	Secondary
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End point timeframe:

Weeks 6 and 52

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	106	54	
Units: percentage of participants				
number (confidence interval 95%)	5.4 (1.1 to 14.9)	15.1 (8.9 to 23.4)	16.7 (7.9 to 29.3)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.076 ^[7]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	25.7

Notes:

[7] - P-value was calculated by Fisher's Exact Test.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.071 ^[8]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	11.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	29.9

Notes:

[8] - P-value was calculated by Fisher's Exact Test.

Secondary: Percentage of Participants Achieving Corticosteroid-free Remission at Week 52

End point title	Percentage of Participants Achieving Corticosteroid-free Remission at Week 52
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End point description:

Corticosteroid-free remission is defined as participants using oral corticosteroids at Baseline(Week 0)who have discontinued oral corticosteroids and are in clinical remission at Week 52. Clinical remission is defined as complete Mayo score of ≤ 2 points and no individual subscore > 1 point. Mayo score is standard assessment tool to measure ulcerative colitis disease activity in clinical trials. Index consists of 4 subscores:rectal bleeding,stool frequency,findings on endoscopy,and physician's global assessment. Each subscore is scored on a scale from 0 to 3 and complete Mayo score ranges from 0 to 12(higher scores indicate greater disease activity). Participants from FAS, who used concomitant oral corticosteroid at Baseline. FAS included all randomized participants who received at least 1 dose of study drug and who only received induction IV therapy, were not randomized into maintenance phase were not included in FAS;participants analyzed according to randomized treatment assignment.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	45	21	
Units: percentage of participants				
number (confidence interval 95%)	8.3 (1.0 to 27.0)	28.9 (16.4 to 44.3)	28.6 (11.3 to 52.2)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.067 ^[9]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	20.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	43.7

Notes:

[9] - P-value was calculated by Fisher's Exact Test.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121 ^[10]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	20.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	47.8

Notes:

[10] - P-value was calculated by Fisher's Exact Test.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 18 weeks after the last dose of study drug (Up to approximately 68 weeks)

Adverse event reporting additional description:

At each visit the investigator had to assess any occurrence of adverse events. Participants may report AEs occurring at any other time during the study. Any adverse event reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Open-Label Induction Phase: Vedolizumab 300 mg IV
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Reporting group description:

Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 in the open-label induction phase.

Reporting group title	Maintenance Phase: Induction IV + Placebo
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Reporting group description:

Placebo-matching subcutaneous (SC) injections, once every 2 weeks (Q2W) and placebo-matching IV infusions, once every 8 weeks (Q8W) starting at Week 6 up to approximately Week 70. Participants received vedolizumab in open-label induction phase and achieved clinical response at Week 6 and were randomized to receive placebo in maintenance phase.

Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
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Reporting group description:

Vedolizumab SC, 108 mg, injection, Q2W and placebo-matching IV infusions, Q8W, starting at Week 6 up to approximately Week 77. Participants received vedolizumab in open-label induction phase and achieved clinical response at Week 6 and were randomized to receive vedolizumab SC in maintenance phase.

Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV
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Reporting group description:

Vedolizumab 300 mg, IV infusion, Q8W and placebo-matching SC injection, Q2W starting at Week 6 up to approximately Week 71. Participants received vedolizumab in open-label induction phase and achieved clinical response at Week 6 and were randomized to receive vedolizumab IV in maintenance phase.

Serious adverse events	Open-Label Induction Phase: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 167 (10.18%)	6 / 56 (10.71%)	10 / 106 (9.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 167 (0.00%)	1 / 56 (1.79%)	0 / 106 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Clavicle fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Scapula fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Ligament rupture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Road traffic accident			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Facial bones fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Jaw fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Rib fracture			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
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	2 / 167 (1.20%)	1 / 56 (1.79%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drug resistance			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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
Pyrexia			

subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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 disorders			
Colitis ulcerative			
subjects affected / exposed	12 / 167 (7.19%)	5 / 56 (8.93%)	3 / 106 (2.83%)
occurrences causally related to treatment / all	0 / 12	0 / 5	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute abdomen			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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
Colitis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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			
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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

Pneumothorax			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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			
Major depression			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	0 / 106 (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			
Anal abscess			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 167 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 167 (0.60%)	0 / 56 (0.00%)	0 / 106 (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

Serious adverse events	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 54 (12.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Scapula fracture			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial bones fracture			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Jaw fracture			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drug resistance			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute abdomen			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary sarcoidosis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumothorax			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Open-Label Induction Phase: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 167 (20.36%)	31 / 56 (55.36%)	42 / 106 (39.62%)
Investigations			

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1	0 / 56 (0.00%) 0	1 / 106 (0.94%) 2
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 167 (0.00%) 0	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	5 / 167 (2.99%) 8	6 / 56 (10.71%) 6	9 / 106 (8.49%) 12
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	9 / 167 (5.39%) 10	2 / 56 (3.57%) 2	5 / 106 (4.72%) 5
Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences (all)	7 / 167 (4.19%) 8	14 / 56 (25.00%) 14	12 / 106 (11.32%) 12
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 167 (0.00%) 0	1 / 56 (1.79%) 1	1 / 106 (0.94%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 167 (0.00%) 0	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 167 (2.40%) 4	1 / 56 (1.79%) 1	6 / 106 (5.66%) 7
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 167 (2.40%) 4	11 / 56 (19.64%) 13	11 / 106 (10.38%) 15
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 167 (1.80%) 4	1 / 56 (1.79%) 2	10 / 106 (9.43%) 13

Sinusitis			
subjects affected / exposed	0 / 167 (0.00%)	3 / 56 (5.36%)	1 / 106 (0.94%)
occurrences (all)	0	4	1
Urinary tract infection			
subjects affected / exposed	5 / 167 (2.99%)	2 / 56 (3.57%)	0 / 106 (0.00%)
occurrences (all)	5	3	0

Non-serious adverse events	Maintenance Phase: Induction IV + Vedolizumab 300 mg IV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 54 (57.41%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 54 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 54 (9.26%)		
occurrences (all)	5		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	5 / 54 (9.26%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Psychiatric disorders			
Insomnia			

subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 5		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	10 / 54 (18.52%) 14 2 / 54 (3.70%) 3 0 / 54 (0.00%) 0 4 / 54 (7.41%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2015	The following changes were made in the amendment: a. Additional exploratory objectives and endpoints were added to the protocol to gather alternative clinical data. b. Updates were made in the clinical pharmacology background and PK endpoints which reflect the updated dosing simulation modeling. c. Correction of inconsistencies within the original protocol.
10 February 2016	The following changes were made in the amendment: a. Benefit:Risk assessment was included in new section 4.3 b. Exploratory endpoints were added to section 5.2.4: Proportion of subjects with clinical response at $\geq 80\%$ study visits, including the final visit and Proportion of subjects with clinical remission at $\geq 80\%$ study visits, including the final visit.
12 May 2016	The following changes were made in the amendment: a. Correctly assigned the definition of clinical remission. b. Addition of exploratory endpoints. c. Correction to Exclusion Criterion #24, Exclusion Criterion #26 removed as this is a repeat of Exclusion Criterion #4 d. Updated and additional text added to Section 7.3.1 Permitted Medications and Treatments. e. Updates made to schedule of assessments.
26 July 2016	The following changes were made in the amendment: a. Administrative change made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported