Clinical trial results:
Phase III, Multicenter, Randomized, Double-blinded, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Intravenous MLN0002 (300 mg) Infusion in Induction and Maintenance Therapy in Japanese Subjects with Moderate or Severe Crohn's Disease

Summary

EudraCT number	2019-001199-12
Trial protocol	Outside EU/EEA
Global end of trial date	21 May 2019

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	MLN0002/CCT-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02038920
WHO universal trial number (UTN)	U1111-1150-2688
Other trial identifiers	Japan Ministry of Health, Labour and Welfare: JapicCTI-142402

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	Takeda Pharmaceutical Company Limited, 1-1, Doshomachi 4-chome, Chuo-ku, Osaka-shi, Osaka, Japan,
Public contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.com
Scientific contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is a phase 3, multicenter, randomised, double-blinded, placebo-controlled, parallel-group study to examine the efficacy, safety, and pharmacokinetics of vedolizumab (MLN0002) in induction and maintenance therapy in Japanese participants with moderately or severely active Crohn's disease.

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	28 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 157
Worldwide total number of subjects	157
EEA total number of subjects	0

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)	6
Adults (18-64 years)	149
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 77 investigative sites in Japan from 28 Jan 2014 to 21 May 2019.

Pre-assignment

Screening details:

Participants with moderate to severe Crohn’s disease were enrolled. 157 participants enrolled in induction phase, 41 participants entered maintenance phase and 134 participants entered open-label cohort and received placebo or vedolizumab 300 mg. Open-label cohort occurred between Week 10 and 154 through study with maximum of 94 weeks of treatment.

Period 1

Period 1 title	Induction Phase (Week 0 to 14)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Induction Phase: Vedolizumab, 300 mg

Arm description:

Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 and 6 in the induction phase.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab
Investigational medicinal product code	
Other name	MLN0002
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab IV injection

Arm title	Induction Phase: Placebo

Arm description:

Vedolizumab placebo-matching IV infusion once at Weeks 0, 2 and 6 in the induction phase.

Arm type	Placebo
Investigational medicinal product name	Vedolizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab placebo-matching IV infusion

Number of subjects in period 1	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo
Started	79	78
Completed	73	66
Not completed	6	12
Pretreatment Event/Adverse Event	3	11
Voluntary Withdrawal	2	-
Lack of efficacy	1	1

Period 2

Period 2 title	Maintenance Phase (Week 14 to 60)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Maintenance Phase: Vedolizumab 300 mg

Arm description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved Crohn's Disease Activity Index (CDAI)-70 response at Week 10 and were randomized to receive vedolizumab in maintenance phase.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab
Investigational medicinal product code	
Other name	MLN0002
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab IV injection

Arm title	Maintenance Phase: Placebo

Arm description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved CDAI-70 response at Week 10 and were randomized to receive placebo in maintenance phase.

Arm type	Placebo
Investigational medicinal product name	Vedolizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab placebo-matching IV infusion

Arm title	Maintenance Phase: Placebo Continuation

Arm description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab placebo-matching in induction phase and achieved CDAI-70 response at Week 10 received placebo in maintenance phase without randomization.

Arm type	Placebo
Investigational medicinal product name	Vedolizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab placebo-matching IV infusion

Number of subjects in period 2[1]	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo	Maintenance Phase: Placebo Continuation
Started	12	12	17
Completed	7	4	5
Not completed	5	8	12
Pretreatment Event/Adverse Event	2	4	2
Lost to follow-up	1	-	-
Lack of efficacy	2	4	10

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants from the Induction Phase entered the Maintenance Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Induction Phase: Vedolizumab, 300 mg
Reporting group description:	
Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 and 6 in the induction phase.	
Reporting group title	Induction Phase: Placebo
Reporting group description:	
Vedolizumab placebo-matching IV infusion once at Weeks 0, 2 and 6 in the induction phase.	

Reporting group values	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo	Total
Number of subjects	79	78	157
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	33.9	32.6	
standard deviation	± 12.25	± 10.93	-
Sex: Female, Male Units: Subjects			
Female	28	26	54
Male	51	52	103
Disease Localization Units: Subjects			
Small Intestine Type	13	9	22
Large Intestine Type	11	19	30
Small/large Intestine Type	55	50	105
Smoking Classification Units: Subjects			
Never Smoked	46	42	88
Current Smoker	13	11	24
Ex-smoker	20	25	45
Extraintestinal Manifestations (Based on CDAI subscore)			
CDAI is scoring system for the Assessment of Crohn's Disease Activity. The total CDAI score ranges from 0 to approximately 600, where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease.			
Units: Subjects			
Had No Extraintestinal Manifestations	24	22	46
Had Extraintestinal Manifestations	55	56	111
Extraintestinal Manifestations (Based on Case Report Form) Units: Subjects			
Had No Extraintestinal Manifestations	42	52	94
Had Extraintestinal Manifestations	37	26	63
History of Prior Surgery for Crohn's Disease (CD)			

Units: Subjects			
Had No Surgical History	55	48	103
Had Surgical History	24	30	54
Current Medical Condition Related to Fistula Units: Subjects			
Had No Current Medical Condition	72	66	138
Had Current Medical Condition	7	12	19
Region of Enrollment Units: Subjects			
Japan	79	78	157
Height Units: cm			
arithmetic mean	166.3	166.4	
standard deviation	± 8.73	± 7.97	-
Weight Units: kg			
arithmetic mean	58.53	55.03	
standard deviation	± 14.095	± 8.928	-
Body Mass Index (BMI)			
Body Mass Index = weight(kg)/[height(m)^2]			
Units: kg/m^2			
arithmetic mean	21.15	19.81	
standard deviation	± 4.942	± 2.567	-
Duration of Crohn's Disease			
Duration between the first diagnosis of Crohn's disease and the start of the study was reported.			
Units: years			
median	7.20	8.35	
full range (min-max)	0.3 to 27.8	0.3 to 32.0	-
C-Reactive Protein (CRP) Units: mg/dL			
arithmetic mean	2.234	2.848	
standard deviation	± 2.1763	± 3.2303	-
CDAI Score at Week 0			
CDAI is scoring system for the Assessment of Crohn's Disease Activity. The total CDAI score ranges from 0 to approximately 600 , where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease.			
Units: score on a scale			
arithmetic mean	303.9	295.0	
standard deviation	± 63.19	± 64.81	-

End points

End points reporting groups

Reporting group title	Induction Phase: Vedolizumab, 300 mg
Reporting group description:	
Vedolizumab 300 mg, intravenous (IV) infusion, once at Weeks 0, 2 and 6 in the induction phase.	
Reporting group title	Induction Phase: Placebo
Reporting group description:	
Vedolizumab placebo-matching IV infusion once at Weeks 0, 2 and 6 in the induction phase.	
Reporting group title	Maintenance Phase: Vedolizumab 300 mg
Reporting group description:	
Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved Crohn's Disease Activity Index (CDAI)-70 response at Week 10 and were randomized to receive vedolizumab in maintenance phase.	
Reporting group title	Maintenance Phase: Placebo
Reporting group description:	
Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved CDAI-70 response at Week 10 and were randomized to receive placebo in maintenance phase.	
Reporting group title	Maintenance Phase: Placebo Continuation
Reporting group description:	
Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab placebo-matching in induction phase and achieved CDAI-70 response at Week 10 received placebo in maintenance phase without randomization.	
Subject analysis set title	Open-Label: Vedolizumab 300 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vedolizumab 300 mg, IV infusion, once at Weeks 0, 2 and 6 and then every 8 weeks thereafter up to Week 94 as a maximum duration in open-label phase.	

Primary: Induction phase: Percentage of Participants with Crohn's Disease Activity Index (CDAI)-100 Response

End point title	Induction phase: Percentage of Participants with Crohn's Disease Activity Index (CDAI)-100 Response
End point description:	
A response to therapy is considered a decrease from baseline of at least 100 points in the CDAI score at Week 10. CDAI is scoring system for the assessment of Crohn's disease activity. The total CDAI score ranges from 0 to approximately 600, where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. Full analysis set (FAS) in the induction phase included participants who were randomised and received at least one dose of the study drug in induction phase.	
End point type	Primary
End point timeframe:	
Week 10	

End point values	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	78		
Units: percentage of participants				

number (confidence interval 95%)	26.6 (17.268 to 37.720)	16.7 (9.184 to 26.813)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MLN0002 group/placebo group. Cochran-Mantel-Haenszel (CMH) test was used for analysis. Prior tumor necrosis factor alpha (TNFα) antagonist use (yes/no) was used as stratification factor.

Comparison groups	Induction Phase: Vedolizumab, 300 mg v Induction Phase: Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1448
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.816
upper limit	3.958

Primary: Maintenance Phase: Percentage of Participants with Clinical Remission

End point title	Maintenance Phase: Percentage of Participants with Clinical Remission

End point description:

Clinical remission is defined as the CDAI score ≤150. CDAI is scoring system for the assessment of Crohn's disease activity. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. FAS in the maintenance phase included participants who were randomised and received at least one dose of the study drug in the maintenance phase. The FAS in the maintenance phase does not include participants who received placebo in the induction phase and were enrolled into the maintenance phase.

End point type	Primary

End point timeframe:

Week 60

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percentage of participants				
number (confidence interval 95%)	41.7 (15.165	16.7 (2.086 to		

to 72.333)	48.414)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: MLN0002 group/placebo group	
Comparison groups	Maintenance Phase: Vedolizumab 300 mg v Maintenance Phase: Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1779
Method	Pearson's Chi-square Test
Parameter estimate	Odds ratio (OR)
Point estimate	3.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.532
upper limit	23.953

Primary: Number of Participants Who Experienced at Least One or More Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants Who Experienced at Least One or More Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

An Adverse event (AE) is defined as any untoward medical occurrence in a study participant who received a drug (including a study drug); it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (e.g., a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug whether or not it is considered related to the drug. A TEAE is defined as an adverse event with an onset that occurs after receiving study drug. Safety analysis set included participants who received at least one dose of the study drug in either the induction phase, the maintenance phase or the open-label cohort.

End point type	Primary

End point timeframe:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses are reported for this end point.

End point values	Induction Phase: Vedolizumab, 300 mg	Maintenance Phase: Vedolizumab 300 mg	Induction Phase: Placebo	Maintenance Phase: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	12	78	12
Units: participants	49	9	42	10

End point values	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	134		
Units: participants	12	130		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with TEAE Related to Body Weight (Weight Decreased)

End point title	Number of Participants with TEAE Related to Body Weight (Weight Decreased)[2]

End point description:

Reported events on this outcome measure were "Weight Decreased". Safety analysis set included participants who received at least one dose of the study drug in either the induction phase, the maintenance phase or the open-label cohort.

End point type	Primary

End point timeframe:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses are reported for this end point.

End point values	Induction Phase: Vedolizumab, 300 mg	Maintenance Phase: Vedolizumab 300 mg	Induction Phase: Placebo	Maintenance Phase: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	12	78	12
Units: participants	0	0	0	0

End point values	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	134		

Units: participants	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with TEAE Related to Vital Signs

End point title	Number of Participants with TEAE Related to Vital Signs[3]

End point description:

Vital signs included body temperature (axilla), sitting blood pressure (after the participant has rested for at least 5 minutes), and pulse (bpm). Reported events on this outcome measure were "Pyrexia", "Body temperature increased", "Hypertension", and "Orthostatic hypotension". Safety analysis set included participants who received at least one dose of the study drug in either the induction phase, the maintenance phase or the open-label cohort.

End point type	Primary

End point timeframe:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses are reported for this end point.

End point values	Induction Phase: Vedolizumab, 300 mg	Maintenance Phase: Vedolizumab 300 mg	Induction Phase: Placebo	Maintenance Phase: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	12	78	12
Units: participants				
Pyrexia	3	0	1	1
Body Temperature Increased	1	0	0	0
Hypertension	0	1	0	0
Orthostatic Hypotension	0	0	0	0

End point values	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	134		
Units: participants				
Pyrexia	1	19		
Body Temperature Increased	0	0		
Hypertension	0	1		
Orthostatic Hypotension	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with TEAE Related to Electrocardiogram (ECG) [Bundle Branch Block Right]

End point title	Number of Participants with TEAE Related to Electrocardiogram (ECG) [Bundle Branch Block Right][4]

End point description:

Reported events on this outcome measure were "Bundle Branch Block Right". Safety analysis set included participants who received at least one dose of the study drug in either the induction phase, the maintenance phase or the open-label cohort.

End point type	Primary

End point timeframe:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses are reported for this end point.

End point values	Induction Phase: Vedolizumab, 300 mg	Maintenance Phase: Vedolizumab 300 mg	Induction Phase: Placebo	Maintenance Phase: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	12	78	12
Units: participants	0	0	0	0

End point values	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	134		
Units: participants	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Markedly Abnormal Values of Laboratory Parameters Values

End point title	Number of Participants with Markedly Abnormal Values of Laboratory Parameters Values[5]

End point description:

The laboratory values outside the range (Hemoglobin <=7 g/dL, Lymphocytes <500 /microL, White Blood Cell (WBC) <2000 /microL, Platelets <7.5 10^4/microL, Neutrophils <1000 /microL, Alanine Aminotransferase (ALT) (Glutamic Pyruvic Transaminase; GPT) >3.0 U/L x upper limit of normal (ULN), Aspartate Aminotransferase (AST) (Glutamic Oxaloacetic Transaminase; GOT) >3.0 U/L x ULN, Total Bilirubin >2.0 mg/dL x ULN, Amylase >2.0 (U/L) x ULN are considered markedly abnormal. Safety analysis set included participants who received at least one dose of the study drug in either the induction phase, the maintenance phase or the open-label cohort.

End point type	Primary

End point timeframe:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses are reported for this end point.

End point values	Induction Phase: Vedolizumab, 300 mg	Maintenance Phase: Vedolizumab 300 mg	Induction Phase: Placebo	Maintenance Phase: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	11	78	12
Units: participants				
Hemoglobin (g/dL) <=7	0	0	1	0
Lymphocytes (/uL) <500	7	1	6	2
WBC (/uL) <2000	0	0	0	0
Platelets (10^4/uL) <7.5	0	0	0	0
Neutrophils (/uL) <1000	0	0	0	0
ALT (GPT) (U/L) >3.0 x ULN	1	0	1	0
AST (GOT) (U/L) >3.0 x ULN	1	0	0	0
Total Bilirubin (mg/dL) >2.0 x ULN	0	0	0	0
Amylase (U/L) >2.0 x ULN	1	0	0	0

End point values	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	134		
Units: participants				
Hemoglobin (g/dL) <=7	0	4		
Lymphocytes (/uL) <500	1	18		
WBC (/uL) <2000	0	1		
Platelets (10^4/uL) <7.5	0	1		
Neutrophils (/uL) <1000	0	1		
ALT (GPT) (U/L) >3.0 x ULN	0	1		
AST (GOT) (U/L) >3.0 x ULN	0	1		
Total Bilirubin (mg/dL) >2.0 x ULN	0	4		
Amylase (U/L) >2.0 x ULN	0	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Induction phase: Percentage of Participants with Clinical Remission

End point title	Induction phase: Percentage of Participants with Clinical Remission

End point description:

Clinical remission is defined as the CDAI score ≤150. CDAI is scoring system for the assessment of

Crohn's disease activity. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. FAS in the induction phase included participants who were randomised and received at least one dose of the study drug in induction phase.

End point type	Secondary

End point timeframe:

Week 10

End point values	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	78		
Units: percentage of participants				
number (confidence interval 95%)	17.7 (10.041 to 27.942)	10.3 (4.533 to 19.213)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MLN0002 group/placebo group. Cochran-Mantel-Haenszel (CMH) test was used for analysis. Prior tumor necrosis factor alpha (TNFα) antagonist use (yes/no) was used as stratification factor.

Comparison groups	Induction Phase: Vedolizumab, 300 mg v Induction Phase: Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1963
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	4.673

Secondary: Induction phase: Change from Baseline in C-reactive Protein (CRP) Values

End point title	Induction phase: Change from Baseline in C-reactive Protein (CRP) Values

End point description:

Participants from 'FAS in the induction phase' with CRP value exceeding 0.30 mg/dL at Baseline were analysed at given time point. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Baseline to Week 10

End point values	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	78		
Units: mg/dL				
arithmetic mean (standard deviation)				
Change from Baseline at Week 2 (n=64, 70)	0.022 (± 2.1421)	-0.125 (± 2.8417)		
Change from Baseline at Week 6 (n=61, 65)	-0.089 (± 2.0266)	0.130 (± 2.1674)		
Change from Baseline at Week 10 (n=60, 59)	-0.164 (± 2.2729)	0.077 (± 2.8690)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maintenance Phase: Percentage of Participants with Crohn's Disease Activity Index (CDAI)-100 Response

End point title	Maintenance Phase: Percentage of Participants with Crohn's Disease Activity Index (CDAI)-100 Response

End point description:

A response to therapy is considered a decrease from baseline of at least 100 points in the CDAI score at Week 10. CDAI is scoring system for the assessment of Crohn's disease activity. The total CDAI score ranges from 0 to approximately 600, where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. FAS in the maintenance phase included participants who were randomised and received at least one dose of the study drug in the maintenance phase. The FAS in the maintenance phase does not include participants who received placebo in the induction phase and were enrolled into the maintenance phase.

End point type	Secondary

End point timeframe:

Week 60

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percentage of participants				
number (confidence interval 95%)	58.3 (27.667 to 84.835)	8.3 (0.211 to 38.480)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Vedolizumab 300 mg v Maintenance Phase: Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0094
Method	Pearson's Chi-square Test
Parameter estimate	Odds ratio (OR)
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.473
upper limit	160.972

Secondary: Maintenance Phase: Percentage of Participants with Durable Clinical Remission

End point title	Maintenance Phase: Percentage of Participants with Durable Clinical Remission

End point description:

Durable clinical remission is defined as participants with CDAI score ≤ 150 at both Weeks 14 and 60. CDAI is scoring system for the assessment of Crohn's disease activity. The total CDAI score ranges from 0 to approximately 600, where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. FAS in the maintenance phase included participants who were randomised and received at least one dose of the study drug in the maintenance phase. The FAS in the maintenance phase does not include participants who received placebo in the induction phase and were enrolled into the maintenance phase.

End point type	Secondary

End point timeframe:

From Week 14 and Week 60

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percentage of participants				
number (confidence interval 95%)	33.3 (9.925 to 65.112)	25.0 (5.486 to 57.186)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: MLN0002 group/placebo group	
Comparison groups	Maintenance Phase: Vedolizumab 300 mg v Maintenance Phase: Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6534
Method	Pearson's Chi-square Test
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.254
upper limit	8.844

Secondary: Maintenance Phase: Percentage of Participants with Corticosteroid-free Clinical Remission

End point title	Maintenance Phase: Percentage of Participants with Corticosteroid-free Clinical Remission

End point description:

Corticosteroid-free clinical remission is defined as participants using oral corticosteroids at baseline (Week 0) who discontinued corticosteroids and were in clinical remission (CDAI score ≤ 150) at Week 60. CDAI is scoring system for the assessment of Crohn's disease activity. The total CDAI score ranges from 0 to approximately 600, where higher scores indicate more severe disease. Index values of 150 and below are associated with quiescent disease; values above that indicate active disease. Participants from FAS in maintenance phase included participants who were randomised and received at least one dose of the study drug in the maintenance phase and administered oral corticosteroids concomitantly at Week 0, were analsed at the given timepoint.

End point type	Secondary

End point timeframe:

Week 60

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: percentage of participants				
number (confidence interval 95%)	40.0 (5.274 to 85.337)	0.0 (0.000 to 70.760)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maintenance Phase: Vedolizumab 300 mg v Maintenance Phase: Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2059
Method	Pearson's Chi-square Test

Secondary: Serum Vedolizumab Concentration in Induction Phase

End point title	Serum Vedolizumab Concentration in Induction Phase[6]

End point description:

Participants from 'FAS in Induction Phase', who were randomised and received at least one dose of the study drug in the induction phase and for whom samples were available for pharmacokinetic (PK) analysis. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 2, 6, 10 and 14

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all participants from the Baseline Period are applicable for this endpoint.

End point values	Induction Phase: Vedolizumab, 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: ug/mL				
arithmetic mean (standard deviation)				
Week 2 (n=57)	28.23 (± 11.018)			
Week 6 (n=50)	21.01 (± 14.076)			
Week 10 (n=60)	22.31 (± 14.049)			
Week 14 (n=17)	12.24 (± 10.350)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Vedolizumab Concentration in Maintenance Phase

End point title	Serum Vedolizumab Concentration in Maintenance Phase

End point description:

Participants from 'FAS in Maintenance Phase', who were randomised and received at least one dose of the study drug in the maintenance phase and for whom samples were available for PK analysis. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 2, 6, 10, 14, 22, 30 and 60

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: ug/mL				
arithmetic mean (standard deviation)				
Week 2 (n=10, 9)	29.32 (± 13.880)	30.54 (± 9.7495)		
Week 6 (n=10, 9)	25.19 (± 17.054)	24.90 (± 14.490)		
Week 10 (n=11, 9)	26.24 (± 15.464)	26.60 (± 15.642)		
Week 14 (n=10, 7)	11.20 (± 8.5793)	13.72 (± 13.072)		
Week 22 (n=9, 7)	9.102 (± 6.1809)	1.502 (± 2.8285)		
Week 30 (n=8, 4)	9.013 (± 6.8774)	0.000 (± 0.0000)		
Week 60 (n=6, 3)	13.68 (± 4.2659)	0.000 (± 0.0000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-vedolizumab Antibodies (AVA) in Induction Phase

End point title	Number of Participants with Anti-vedolizumab Antibodies (AVA)

	in Induction Phase[7]

End point description:

Participants who underwent proper AVA test out of 'the FAS in the induction phase' were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10 and 16 weeks after the last dose of study drug in induction phase

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all participants from the Baseline Period are applicable for this endpoint.

End point values	Induction Phase: Vedolizumab, 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: participants				
Week 0 (n=63)	1			
Week 10 (n=63)	1			
16 Weeks After Last Administration (n=4)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-vedolizumab Antibodies (AVA) in Maintenance Phase

End point title	Number of Participants with Anti-vedolizumab Antibodies (AVA) in Maintenance Phase

End point description:

Participants who underwent proper AVA test out of the 'FAS in Maintenance Phase', the participants who received at least one dose of study drug in the maintenance phase were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10, 30, 60 and 16 weeks after the last dose of study drug in maintenance phase

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: participants				
Week 0 (n=11, 9)	0	0		
Week 10 (n=11, 9)	0	0		

Week 30 (n=10, 9)	0	2		
Week 60 (n=9, 4)	0	1		
16 Weeks After Last Administration (n=1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-vedolizumab Antibodies (AVA) in Open Label Cohort

End point title	Number of Participants with Anti-vedolizumab Antibodies (AVA) in Open Label Cohort

End point description:

Participants who underwent proper AVA test out of the 'FAS in Open Label Cohort', the participants who received at least one dose of study drug in the open label cohort were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10, 30, 62, 94 and 16 weeks after the last dose of study drug in open-label cohort

End point values	Open-Label: Vedolizumab 300 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: participants				
Week 0 (n=57)	2			
Week 10 (n=108)	2			
Week 30 (n=94)	2			
Week 62 (n=66)	0			
Week 94 (n=49)	0			
16 Weeks After Last Administration (n=98)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Induction Phase

End point title	Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Induction Phase[8]

End point description:

Participants who underwent proper AVA test out of 'the FAS in the induction phase' were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10 and 16 weeks after the last dose of study drug in induction phase

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all participants from the Baseline Period are applicable for this endpoint.

End point values	Induction Phase: Vedolizumab, 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: participants				
Week 0 (n=63)	0			
Week 10 (n=63)	1			
16 Weeks After Last Administration (n=4)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Maintenance Phase

End point title	Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Maintenance Phase

End point description:

Participants who underwent proper AVA test out of the 'FAS in Maintenance Phase', the participants who received at least one dose of study drug in the maintenance phase were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10, 30, 60 and 16 weeks after the last dose of study drug in maintenance phase

End point values	Maintenance Phase: Vedolizumab 300 mg	Maintenance Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: participants				
Week 0 (n=11, 9)	0	0		
Week 10 (n=11, 9)	0	0		
Week 30 (n=10, 9)	0	2		
Week 60 (n=9, 4)	0	1		
16 Weeks After Last Administration (n=1, 1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Open Label Cohort

End point title	Number of Participants with Neutralizing Anti-vedolizumab Antibodies (AVA) in Open Label Cohort

End point description:

Participants who underwent proper AVA test out of the 'FAS in Open Label Cohort', the participants who received at least one dose of study drug in the open label cohort were analysed in this outcome measure. Number analysed is the number of participants with evaluable data at the given time-point.

End point type	Secondary

End point timeframe:

Weeks 0, 10, 30, 62, 94 and 16 weeks after the last dose of study drug in open-label cohort

End point values	Open-Label: Vedolizumab 300 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: participants				
Week 0 (n=57)	2			
Week 10 (n=108)	2			
Week 30 (n=94)	1			
Week 62 (n=66)	0			
Week 94 (n=49)	0			
16 Weeks After Last Administration (n=98)	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 16 weeks after the last dose of study drug (Up to approximately 170 weeks)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Induction Phase: Vedolizumab, 300 mg

Reporting group description:

Vedolizumab 300 mg, IV infusion, once at Weeks 0, 2 and 6 in the induction phase.

Reporting group title	Induction Phase: Placebo

Reporting group description:

Vedolizumab placebo-matching IV infusion once at Weeks 0, 2 and 6 in the induction phase.

Reporting group title	Maintenance Phase: Vedolizumab 300 mg

Reporting group description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved CDAI -70 response at Week 10 and were randomized to receive vedolizumab in maintenance phase.

Reporting group title	Maintenance Phase: Placebo

Reporting group description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab in induction phase and achieved CDAI-70 response at Week 10 and were randomized to receive placebo in maintenance phase.

Reporting group title	Maintenance Phase: Placebo Continuation

Reporting group description:

Vedolizumab placebo-matching, IV infusion, once at Weeks 14, 22, 30, 38, 46 and 54 in maintenance phase. Participants received vedolizumab placebo-matching in induction phase and achieved CDAI-70 response at Week 10 received placebo in maintenance phase without randomization.

Reporting group title	Open-Label: Vedolizumab 300 mg

Reporting group description:

Vedolizumab 300 mg, IV infusion, once at Weeks 0, 2 and 6 and then every 8 weeks thereafter up to Week 94 as a maximum duration in open-label phase.

Serious adverse events	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo	Maintenance Phase: Vedolizumab 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 79 (10.13%)	10 / 78 (12.82%)	2 / 12 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Thyroid adenoma			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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 lumbar puncture syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Dyslalia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Intracranial hypotension			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Immune system disorders			
Anaphylactoid reaction			

subjects affected / exposed	0 / 79 (0.00%)	1 / 78 (1.28%)	0 / 12 (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
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 79 (2.53%)	10 / 78 (12.82%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 2	3 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 79 (0.00%)	1 / 78 (1.28%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Intestinal obstruction			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Subileus			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Abdominal adhesions			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal stenosis			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Abdominal pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Enterovesical fistula			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Ileal stenosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Large intestine perforation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Melaena			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 79 (0.00%)	1 / 78 (1.28%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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			
Pleurisy			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Gastroenteritis viral			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Cellulitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Abdominal abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Enteritis infectious			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Device related infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Escherichia sepsis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Mesenteric abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Mycotic endophthalmitis			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Otitis media			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Perirectal abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Periumbilical abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Rectal abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Sepsis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Septic shock			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Mediastinitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 79 (1.27%)	0 / 78 (0.00%)	0 / 12 (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
Hypocalcaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Hypokalaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Hypomagnesaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (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
Malnutrition			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Maintenance Phase: Placebo	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	2 / 17 (11.76%)	70 / 134 (52.24%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid adenoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (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
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyslalia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactoid reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 12 (16.67%)	1 / 17 (5.88%)	35 / 134 (26.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1	3 / 39
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	2 / 134 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	4 / 134 (2.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	3 / 134 (2.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal stenosis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	3 / 134 (2.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal stenosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
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 intestinal stenosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (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
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	4 / 134 (2.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (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
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (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
Abdominal abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	2 / 134 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	2 / 134 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycotic endophthalmitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periumbilical abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Induction Phase: Vedolizumab, 300 mg	Induction Phase: Placebo	Maintenance Phase: Vedolizumab 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 79 (21.52%)	19 / 78 (24.36%)	9 / 12 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ocular neoplasm			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin papilloma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Immune system disorders			
Allergy to metals			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Seasonal allergy			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood urine present			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Heat illness			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 79 (1.27%)	4 / 78 (5.13%)	0 / 12 (0.00%)
occurrences (all)	1	4	0
Hypoaesthesia			
subjects affected / exposed	4 / 79 (5.06%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Cervicobrachial syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Crohn's disease			
subjects affected / exposed	0 / 79 (0.00%)	5 / 78 (6.41%)	0 / 12 (0.00%)
occurrences (all)	0	5	0
Diarrhoea			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 79 (13.92%)	11 / 78 (14.10%)	4 / 12 (33.33%)
occurrences (all)	12	13	6
Enteritis infectious			
subjects affected / exposed	4 / 79 (5.06%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anal abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatophytosis of nail			

subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 78 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Maintenance Phase: Placebo	Maintenance Phase: Placebo Continuation	Open-Label: Vedolizumab 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	12 / 17 (70.59%)	113 / 134 (84.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ocular neoplasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	19 / 134 (14.18%)
occurrences (all)	1	1	30
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to metals			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	9 / 134 (6.72%)
occurrences (all)	0	0	13
Investigations			
Blood urine present			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Glucose urine present			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Heat illness			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	9 / 134 (6.72%)
occurrences (all)	0	0	9
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Cervicobrachial syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	13 / 134 (9.70%)
occurrences (all)	0	0	16
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	27 / 134 (20.15%)
occurrences (all)	0	2	28
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	9 / 134 (6.72%)
occurrences (all)	1	0	10
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	1	0	0
Dental caries			

subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	15 / 134 (11.19%)
occurrences (all)	0	2	17
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	11 / 134 (8.21%)
occurrences (all)	0	0	11
Stomatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	10 / 134 (7.46%)
occurrences (all)	0	0	11
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	1	0	0
Ingrowing nail			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	8 / 134 (5.97%)
occurrences (all)	0	0	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 12 (33.33%)	4 / 17 (23.53%)	55 / 134 (41.04%)
occurrences (all)	6	6	90
Enteritis infectious			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	10 / 134 (7.46%)
occurrences (all)	1	1	19
Anal abscess			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 134 (0.00%)
occurrences (all)	0	2	0
Dermatophytosis of nail			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 134 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 134 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	16 / 134 (11.94%)
occurrences (all)	0	0	18
Gastroenteritis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	8 / 134 (5.97%)
occurrences (all)	0	0	9
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	7 / 134 (5.22%)
occurrences (all)	0	0	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported