Clinical trial results:
An Open-Label Phase 3b Study to Assess Mucosal Healing in Subjects With Moderately to Severely Active Crohn's Disease Treated With Vedolizumab IV

Summary

EudraCT number	2014-003509-13
Trial protocol	HU CZ PL BE IT
Global end of trial date	21 February 2018

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	MLN0002-3028

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02425111
WHO universal trial number (UTN)	U1111-1159-5806

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	40 Landsdowne Street, Cambridge, MA, United States, 02139
Public contact	Medical Director, Takeda, +1 8778253327, clinicaltrialregistry@tpna.com
Scientific contact	Medical Director, Takeda, +1 8778253327, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate endoscopic remission at Week 26 as assessed by ileocolonoscopy.

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	30 March 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?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	101
EEA total number of subjects	54

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	96
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 42 investigative sites in Belgium, Canada, Czech Republic, France, Hungary, Italy, Poland and the United States from 30 March 2015 to 21 February 2018.

Pre-assignment

Screening details:

Participants with a diagnosis of Crohn’s Disease were enrolled to receive vedolizumab IV.

Period 1

Period 1 title	Part A: Treatment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Vedolizumab 300 mg

Arm description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Blood fraction modifier, Injection
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab 300 mg IV injection

Number of subjects in period 1	Vedolizumab 300 mg
Started	101
Completed	74
Not completed	27
Pretreatment Event/Adverse Event (s)	5
Voluntary Withdrawal	4
Lost to follow-up	2
Lack of efficacy	16

Period 2

Period 2 title	Part B: Treatment Extension Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Vedolizumab 300 mg

Arm description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

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

Dosage and administration details:

Vedolizumab 300 mg IV injection

Number of subjects in period 2[1]	Vedolizumab 300 mg
Started	56
Completed	46
Not completed	10
Pretreatment Event/Adverse Event (s)	3
Lack of efficacy	7

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: A total of 56 participants were consented under Amendment 4 and were thus eligible for Part B.

Baseline characteristics

Reporting groups	
Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.	

Reporting group values	Vedolizumab 300 mg	Total	
Number of subjects	101	101	
Age categorical Units: Subjects			
Adults (18-64 years)	96	96	
From 65-84 years	5	5	
Age Continuous Units: years			
arithmetic mean	38.0		
standard deviation	± 14.00	-	
Sex: Female, Male Units: Subjects			
Female	49	49	
Male	52	52	
Race/Ethnicity, Customized			
Ethnicity was collected only in the United States.			
Units: Subjects			
Hispanic or Latino	1	1	
Non-Hispanic and Latino	32	32	
Not Collected	68	68	
Race/Ethnicity, Customized Units: Subjects			
Asian	2	2	
Black or African American	1	1	
White	98	98	
Smoking Classification Units: Subjects			
Participant has never smoked	46	46	
Participant is a current smoker	33	33	
Participant is an ex-smoker	22	22	
Female Reproductive Status Units: Subjects			
Postmenopausal	6	6	
Surgically Sterile	9	9	
Female of Childbearing Potential	34	34	
N/A (Participant is a Male)	52	52	
Region of Enrollment Units: Subjects			
Belgium	8	8	
Canada	14	14	
Czech Republic	14	14	

France	2	2	
Hungary	14	14	
Italy	9	9	
Poland	7	7	
United States	33	33	
Number of Participants with Endoscopic Remission			
Endoscopic remission is defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of ≤4. FAS included all enrolled participants who received at least 1 dose of study drug.			
Units: Subjects			
Endoscopic Remission - Yes	3	3	
Endoscopic Remission - No	98	98	
Height			
Units: cm			
arithmetic mean	172.5		
standard deviation	± 9.81	-	
Weight			
Units: kg			
arithmetic mean	73.94		
standard deviation	± 18.807	-	
Body Mass Index (BMI)			
Body Mass Index = weight (kg)/[height (m)^2]			
Units: kg/m^2			
arithmetic mean	24.71		
standard deviation	± 5.370	-	

End points

End points reporting groups

Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.	
Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22, followed by Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.	

Primary: Part A: Percentage of Participants Achieving Endoscopic Remission at Week 26

End point title	Part A: Percentage of Participants Achieving Endoscopic Remission at Week 26[1]
End point description:	
Endoscopic remission is defined as a simple endoscopic score for Crohn's Disease (SES-CD) score of ≤4. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Week 26	

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: Statistical analyses were not planned for this endpoint.

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	11.9 (6.3 to 19.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Complete Mucosal Healing at Week 26

End point title	Part A: Percentage of Participants Achieving Complete Mucosal Healing at Week 26
End point description:	
Complete mucosal healing is defined as absence of ulceration. FAS included all enrolled participants who	

received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	14.9 (8.6 to 23.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Complete Mucosal Healing at Week 52

End point title	Part B: Percentage of Participants Achieving Complete Mucosal Healing at Week 52

End point description:

Complete mucosal healing is defined as absence of ulceration. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	17.9 (8.9 to 30.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Endoscopic Remission at Week 14

End point title	Part A: Percentage of Participants Achieving Endoscopic

	Remission at Week 14

End point description:

Endoscopic remission is defined as a SES-CD score of ≤4. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 14

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	16.8 (10.1 to 25.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Endoscopic Remission at Week 52

End point title	Part B: Percentage of Participants Achieving Endoscopic Remission at Week 52

End point description:

Endoscopic remission is defined as a SES-CD score of ≤4. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	17.9 (8.9 to 30.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants with Endoscopic Response at Week 14

End point title	Part A: Percentage of Participants with Endoscopic Response at Week 14

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by ≥50%. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 14

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	33.7 (24.6 to 43.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants with Endoscopic Response at Week 26

End point title	Part A: Percentage of Participants with Endoscopic Response at Week 26

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by ≥50%. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS included all enrolled participants who

received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	24.8 (16.7 to 34.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants with Endoscopic Response at Week 52

End point title	Part B: Percentage of Participants with Endoscopic Response at Week 52

End point description:

Endoscopic response is defined as a reduction in SES-CD from Baseline by ≥50%. The SES-CD evaluates 4 endoscopic variables (ulcer size, proportion of the surface area that is ulcerated, proportion of the surface area affected, and stenosis in 5 segments evaluated during ileocolonoscopy (ileum, right colon, transverse colon, left colon, and rectum). The score for each endoscopic variable is the sum of values obtained for each segment. The SES-CD total is the sum of the 4 endoscopic variable scores from 0 to 56, where higher scores indicate more severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	53.6 (39.7 to 67.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Clinical Response at Week 10

End point title	Part A: Percentage of Participants Achieving Clinical Response at Week 10

End point description:

Clinical response is defined as Crohn's Disease Activity Index (CDAI) decrease from Baseline of ≥100 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 10

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	54.5 (44.2 to 64.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Clinical Response at Week 26

End point title	Part A: Percentage of Participants Achieving Clinical Response at Week 26

End point description:

Clinical response is defined as CDAI decrease from Baseline of ≥100 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	60.4 (50.2 to 70.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Clinical Response at Week 52

End point title	Part B: Percentage of Participants Achieving Clinical Response at Week 52

End point description:

Clinical response is defined as CDAI decrease from Baseline of ≥100 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	58.9 (45.0 to 71.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Clinical Remission at Week 10

End point title	Part A: Percentage of Participants Achieving Clinical Remission at Week 10

End point description:

Clinical remission is defined as CDAI score of ≤150 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 10

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	35.6 (26.4 to 45.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Achieving Clinical Remission at Week 26

End point title	Part A: Percentage of Participants Achieving Clinical Remission at Week 26

End point description:

Clinical remission is defined as CDAI score of ≤150 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. FAS included all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: percentage of participants				
number (confidence interval 95%)	41.6 (31.9 to 51.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Clinical Remission at Week 52

End point title	Part B: Percentage of Participants Achieving Clinical Remission at Week 52

End point description:

Clinical remission is defined as CDAI score of ≤150 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. PPS (Per Protocol Set)-Extension is the subset of participants in the PPS who continue into Part B. PPS is a subset of the FAS and consists of all participants who do not deviate the terms of the protocol in a way that would impact the study outcome significantly.

End point type	Secondary

End point timeframe:

Week 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	50.0 (36.3 to 63.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants with Durable Clinical Remission

End point title	Part B: Percentage of Participants with Durable Clinical Remission

End point description:

Durable clinical remission is defined as clinical remission at both Week 26 and Week 52. Clinical remission is defined as CDAI score of ≤150 points. CDAI is a 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 and values above 450 are seen with extremely severe disease. The percentage of participants assessed at Week 52 who had clinical remission at Week 26 of Part A and also had clinical remission at Week 52 is reported. FAS-Extension is the subset of participants in the FAS who were able to be consented for Part B, based on the timing of Amendment 4. FAS included all enrolled participants who received at least 1 dose of study drug. Participants with missing durable clinical remission status are considered as No durable clinical remission.

End point type	Secondary

End point timeframe:

Weeks 26 and 52

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (confidence interval 95%)	37.5 (24.9 to 51.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug and up to the last dose or early termination plus 18-week follow-up if applicable (Up to 44 Weeks for Part A Treatment and Up to 70 Weeks for Part B Extension)

Adverse event reporting additional description:

At each visit adverse events (AEs) and abnormal laboratory findings reported by participant or observed by the investigator were recorded, irrespective of relation to study treatment. Due to the design of the study, the most common (≥ 3%) non-serious AEs were determined separately for each period of the study, Part A and Part B.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Vedolizumab 300 mg Part B

Reporting group description:

Following Part A, Part B: Vedolizumab 300 mg, intravenously (IV), once at Weeks 30, 38, and 46.

Reporting group title	Vedolizumab 300 mg Part A

Reporting group description:

Part A: Vedolizumab 300 mg, intravenously (IV), once on Day 1 and Weeks 2, 6, 14 and 22.

Serious adverse events	Vedolizumab 300 mg Part B	Vedolizumab 300 mg Part A	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 56 (10.71%)	12 / 101 (11.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Postoperative ileus			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 56 (1.79%)	6 / 101 (5.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Vedolizumab 300 mg Part B	Vedolizumab 300 mg Part A	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 56 (30.36%)	40 / 101 (39.60%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 56 (3.57%)	5 / 101 (4.95%)	
occurrences (all)	3	8	
Sciatica			
subjects affected / exposed	0 / 56 (0.00%)	3 / 101 (2.97%)	
occurrences (all)	0	3	
Paraesthesia			
subjects affected / exposed	2 / 56 (3.57%)	0 / 101 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 56 (0.00%)	4 / 101 (3.96%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	0 / 56 (0.00%)	4 / 101 (3.96%)	
occurrences (all)	0	5	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	5 / 56 (8.93%)	12 / 101 (11.88%)	
occurrences (all)	5	12	
Abdominal pain			
subjects affected / exposed	3 / 56 (5.36%)	5 / 101 (4.95%)	
occurrences (all)	5	5	
Nausea			
subjects affected / exposed	0 / 56 (0.00%)	5 / 101 (4.95%)	
occurrences (all)	0	6	
Vomiting			
subjects affected / exposed	0 / 56 (0.00%)	4 / 101 (3.96%)	
occurrences (all)	0	4	
Anal fistula			
subjects affected / exposed	2 / 56 (3.57%)	0 / 101 (0.00%)	
occurrences (all)	2	0	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 56 (0.00%)	3 / 101 (2.97%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 56 (0.00%)	4 / 101 (3.96%)	
occurrences (all)	0	4	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)	6 / 101 (5.94%)	
occurrences (all)	3	7	
Bronchitis			
subjects affected / exposed	0 / 56 (0.00%)	3 / 101 (2.97%)	
occurrences (all)	0	3	
Influenza			
subjects affected / exposed	0 / 56 (0.00%)	3 / 101 (2.97%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	3 / 101 (2.97%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	2 / 56 (3.57%)	0 / 101 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2015	Amendment No. 1: The duration of the long term follow up (LTFU) safety questionnaire has been reduced from 24 months from the last dose of study drug to 6 months from the last dose of study drug. Clarification on the collection and reporting of SAEs was added.
28 April 2016	Amendment No. 4: Updated the protocol on the duration of the treatment period from 26 weeks to 52 weeks. The study design was split into two parts, Part A for treatment up to 26 weeks and Part B for treatment from 26 weeks to 52 weeks. Updated the protocol regarding the required duration of observation following infusion and to include an overall risk/benefit assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported