Clinical trial results:
A Randomized, Double-Blind, Double-Dummy, Multicenter, Active-Controlled Study to Evaluate the Efficacy and Safety of Vedolizumab IV Compared to Adalimumab SC in Subjects with Ulcerative Colitis

Summary

EudraCT number	2015-000939-33
Trial protocol	CZ SK NL BG GB DE HU BE ES LV EE LT PL DK PT HR IT
Global end of trial date	18 January 2019

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	MLN0002-3026

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02497469
WHO universal trial number (UTN)	U1111-1168-6713

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2019
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 the efficacy and safety of vedolizumab intravenous (IV) treatment compared to adalimumab subcutaneous (SC) treatment over a 52-week treatment period.

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	29 June 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	Australia: 8
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Korea, Republic of: 35
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Czech Republic: 21
Country: Number of subjects enrolled	Hungary: 32
Country: Number of subjects enrolled	Poland: 163
Country: Number of subjects enrolled	Serbia: 29
Country: Number of subjects enrolled	Slovakia: 13
Country: Number of subjects enrolled	Bosnia and Herzegovina: 3
Country: Number of subjects enrolled	Bulgaria: 16
Country: Number of subjects enrolled	Croatia: 16
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	Russian Federation: 85
Country: Number of subjects enrolled	Turkey: 14
Country: Number of subjects enrolled	Ukraine: 65
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Argentina: 4

Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	Mexico: 12
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Lithuania: 14
Country: Number of subjects enrolled	Portugal: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	771
EEA total number of subjects	371

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	737
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 205 investigative sites worldwide from 29 June 2015 up to 18 January 2019.

Pre-assignment

Screening details:

Participants with a diagnosis of moderately to severely active ulcerative colitis (UC) were enrolled in a 1:1 ratio to receive vedolizumab or adalimumab or matching placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adalimumab SC, 160/80/40 mg

Arm description:

Adalimumab 160 mg, injection, subcutaneously on Day 1, adalimumab 80 mg, injection, subcutaneously at Week 2, then adalimumab 40 mg, injection, subcutaneously every 2 weeks thereafter up to Week 50. Vedolizumab placebo-matching infusion, intravenously on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	HUMIRA
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab 160 mg, injection, subcutaneously on Day 1, adalimumab 80 mg, injection, subcutaneously at Week 2, then adalimumab 40 mg, injection, subcutaneously every 2 weeks thereafter up to Week 50. Vedolizumab placebo-matching infusion, intravenously on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.

Arm title	Vedolizumab IV 300 mg

Arm description:

Vedolizumab 300 mg, infusion, intravenously over 30 minutes on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46. Adalimumab placebo-matching injection, subcutaneously on Day 1, Week 2, and every 2 weeks thereafter up to Week 50.

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 300 mg, infusion, intravenously over 30 minutes on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46. Adalimumab placebo-matching injection, subcutaneously on Day 1, Week 2, and every 2 weeks thereafter up to Week 50.

Number of subjects in period 1	Adalimumab SC, 160/80/40 mg	Vedolizumab IV 300 mg
Started	386	385
Safety Analysis Set	386	383
Completed	217	270
Not completed	169	115
Pretreatment Event/Adverse Event	18	16
Voluntary Withdrawal	39	41
Significant Protocol Deviation	4	5
Leukopenia or Lymphopenia	1	-
Pregnancy	1	1
Randomized but not Treated	-	2
Lost to follow-up	14	4
Reason not Specified	6	6
Lack of efficacy	86	40

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab SC, 160/80/40 mg
Reporting group description:	
Adalimumab 160 mg, injection, subcutaneously on Day 1, adalimumab 80 mg, injection, subcutaneously at Week 2, then adalimumab 40 mg, injection, subcutaneously every 2 weeks thereafter up to Week 50. Vedolizumab placebo-matching infusion, intravenously on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.	
Reporting group title	Vedolizumab IV 300 mg
Reporting group description:	
Vedolizumab 300 mg, infusion, intravenously over 30 minutes on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46. Adalimumab placebo-matching injection, subcutaneously on Day 1, Week 2, and every 2 weeks thereafter up to Week 50.	

Reporting group values	Adalimumab SC, 160/80/40 mg	Vedolizumab IV 300 mg	Total
Number of subjects	386	385	771
Age categorical Units: Subjects			
Adults (18-64 years)	371	366	737
From 65-85 years	15	19	34
Age Continuous Units: years			
arithmetic mean	40.5	40.8	
standard deviation	± 13.44	± 13.74	-
Sex: Female, Male Units: Subjects			
Female	170	151	321
Male	216	234	450
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	8	14
Not Hispanic or Latino	39	23	62
Unknown or Not Reported	341	354	695
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	11	4	15
Asian	30	32	62
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	3	2	5
White	341	345	686
More than one race	0	2	2
Unknown or Not Reported	0	0	0
Smoking Classification Units: Subjects			
Has Never Smoked	259	280	539
Is a Current Smoker	23	19	42
Is an Ex-smoker	104	84	188
Missing	0	2	2

Region of Enrollment Units: Subjects			
Australia	3	5	8
Hong Kong	1	4	5
Korea, Republic Of	19	16	35
Taiwan, Province Of China	4	1	5
Czech Republic	13	8	21
Hungary	16	16	32
Poland	78	85	163
Serbia	11	18	29
Slovakia	5	8	13
Bosnia	2	1	3
Bulgaria	10	6	16
Croatia	11	5	16
Israel	9	13	22
Romania	6	6	12
Russia	41	44	85
Turkey	9	5	14
Ukraine	26	39	65
Canada	18	20	38
United States	42	29	71
Argentina	1	3	4
Colombia	2	2	4
Mexico	9	3	12
France	4	6	10
Germany	3	6	9
Italy	9	11	20
Latvia	6	7	13
Lithuania	7	7	14
Portugal	9	4	13
United Kingdom	2	3	5
Denmark	8	3	11
Belgium	0	1	1
Netherlands	1	0	1
Spain	1	0	1
Height Units: cm			
arithmetic mean	170.5	172.0	
standard deviation	± 9.65	± 9.90	-
Weight Units: kg			
arithmetic mean	73.43	72.67	
standard deviation	± 18.374	± 16.952	-
Body Mass Index (BMI)			
BMI is calculated from the weight taken prior to the first dose of study drug and height taken at Screening using formula, Body Mass Index = weight/[height]^2.			
Units: kg/m^2			
arithmetic mean	25.17	24.46	
standard deviation	± 5.646	± 4.786	-

End points

End points reporting groups

Reporting group title	Adalimumab SC, 160/80/40 mg
Reporting group description:	
Adalimumab 160 mg, injection, subcutaneously on Day 1, adalimumab 80 mg, injection, subcutaneously at Week 2, then adalimumab 40 mg, injection, subcutaneously every 2 weeks thereafter up to Week 50. Vedolizumab placebo-matching infusion, intravenously on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.	
Reporting group title	Vedolizumab IV 300 mg
Reporting group description:	
Vedolizumab 300 mg, infusion, intravenously over 30 minutes on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46. Adalimumab placebo-matching injection, subcutaneously on Day 1, Week 2, and every 2 weeks thereafter up to Week 50.	

Primary: Percentage of Participants who Achieved Clinical Remission

End point title	Percentage of Participants who Achieved Clinical Remission
End point description:	
Clinical remission was defined as a complete Mayo score of ≤2 points and no individual subscore >1 point. The Mayo score was a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consisted of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore was scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). Full Analysis Set (FAS) included all randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Week 52	

End point values	Adalimumab SC, 160/80/40 mg	Vedolizumab IV 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	383		
Units: percentage of participants				
number (confidence interval 95%)	22.5 (18.5 to 27.0)	31.3 (26.7 to 36.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Adalimumab SC, 160/80/40 mg v Vedolizumab IV 300 mg

Number of subjects included in analysis	769
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0061 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	15

Notes:

[1] - P-value of the adjusted difference was based on the Cochran-Mantel-Haenszel method, stratified by concomitant use of oral corticosteroids (Yes/No) and prior use of TNF-alpha antagonist (Yes/No) or the Fisher's exact method if the numerator was <=5.

Secondary: Percentage of Participants who Achieved Mucosal Healing

End point title	Percentage of Participants who Achieved Mucosal Healing

End point description:

Mucosal healing was defined as a Mayo score endoscopic subscore of <= 1 point. The Mayo score was a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consisted of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore was scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). FAS included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 52

End point values	Adalimumab SC, 160/80/40 mg	Vedolizumab IV 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	383		
Units: percentage of participants				
number (confidence interval 95%)	27.7 (23.3 to 32.5)	39.7 (34.8 to 44.8)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Adalimumab SC, 160/80/40 mg v Vedolizumab IV 300 mg
Number of subjects included in analysis	769
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	11.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	18.5

Notes:

[2] - P-value of the adjusted difference was based on the Cochran-Mantel-Haenszel method, stratified by concomitant use of oral corticosteroids (Yes/No) and prior use of TNF-alpha antagonist (Yes/No) or the Fisher's exact method if the numerator was <=5.

Secondary: Percentage of Participants who Used Oral Corticosteroids at Baseline who Discontinued Corticosteroids and were in Clinical Remission

End point title	Percentage of Participants who Used Oral Corticosteroids at Baseline who Discontinued Corticosteroids and were in Clinical Remission

End point description:

Corticosteroid-free remission was defined as participants using oral corticosteroids at Baseline (Week 0) who had discontinued oral corticosteroids and were in clinical remission at Week 52. Clinical remission was defined as a complete Mayo score of ≤ 2 points and no individual subscore > 1 point. The Mayo score was a standard assessment tool to measure ulcerative colitis disease activity in clinical trials. The index consisted of 4 subscores: rectal bleeding, stool frequency, findings on endoscopy, and physician's global assessment. Each subscore was scored on a scale from 0 to 3 and the complete Mayo score ranges from 0 to 12 (higher scores indicate greater disease activity). FAS, included all randomized participants who received at least 1 dose of study drug who used who used oral corticosteroids at Baseline.

End point type	Secondary

End point timeframe:

Week 52

End point values	Adalimumab SC, 160/80/40 mg	Vedolizumab IV 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	111		
Units: percentage of participants				
number (confidence interval 95%)	21.8 (14.8 to 30.4)	12.6 (7.1 to 20.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Adalimumab SC, 160/80/40 mg v Vedolizumab IV 300 mg
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0641 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted Difference
Point estimate	-9.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.9
upper limit	0.4

Notes:

[3] - P-value of the adjusted difference was based on the Cochran-Mantel-Haenszel method, stratified by prior use of TNF-alpha antagonist (Yes/No) or the Fisher's exact method if the numerator was <=5.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug and up to 126 days after the last dose (Up to 68 weeks)

Adverse event reporting additional description:

At each visit investigator document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by participant or observed by investigator was recorded, irrespective of relation to study treatment. Safety analysis set: Participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Vedolizumab IV 300 mg

Reporting group description:

Vedolizumab 300 mg, infusion, intravenously over 30 minutes on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46. Adalimumab placebo-matching injection, subcutaneously on Day 1, Week 2, and every 2 weeks thereafter up to Week 50.

Reporting group title	Adalimumab SC, 160/80/40 mg

Reporting group description:

Adalimumab 160 mg, injection, subcutaneously on Day 1, adalimumab 80 mg, injection, subcutaneously at Week 2, then adalimumab 40 mg, injection, subcutaneously every 2 weeks thereafter up to Week 50. Vedolizumab placebo-matching infusion, intravenously on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.

Serious adverse events	Vedolizumab IV 300 mg	Adalimumab SC, 160/80/40 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 383 (10.97%)	53 / 386 (13.73%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			

subjects affected / exposed	1 / 383 (0.26%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Therapeutic response decreased			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 383 (0.26%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			

subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Traumatic haemothorax			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain stem haemorrhage			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysgraphia			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve root compression			
subjects affected / exposed	2 / 383 (0.52%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 383 (0.26%)	4 / 386 (1.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative	Additional description: One treatment-emergent death occurred during treatment with Vedolizumab IV 300 mg and was not related.		
subjects affected / exposed	19 / 383 (4.96%)	25 / 386 (6.48%)	
occurrences causally related to treatment / all	3 / 20	5 / 27	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colitis			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 383 (0.52%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	3 / 383 (0.78%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 383 (0.26%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			

subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	2 / 383 (0.52%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 383 (0.26%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Clostridium difficile colitis			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	3 / 383 (0.78%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
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 / 383 (0.00%)	2 / 386 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 383 (0.26%)	0 / 386 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	0 / 383 (0.00%)	1 / 386 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Vedolizumab IV 300 mg	Adalimumab SC, 160/80/40 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	103 / 383 (26.89%)	114 / 386 (29.53%)	
Nervous system disorders			
Headache			
subjects affected / exposed	27 / 383 (7.05%)	21 / 386 (5.44%)	
occurrences (all)	32	25	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 383 (4.96%)	23 / 386 (5.96%)	
occurrences (all)	20	26	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	26 / 383 (6.79%)	42 / 386 (10.88%)	
occurrences (all)	30	46	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	27 / 383 (7.05%)	30 / 386 (7.77%)	
occurrences (all)	41	43	
Upper respiratory tract infection			
subjects affected / exposed	20 / 383 (5.22%)	17 / 386 (4.40%)	
occurrences (all)	22	20	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2015	Amendment 3: -Main changes in the protocol include inclusion of information from the adalimumab label to guide investigators as well as specific changes such as a change of period for use of contraception to align with adalimumab label - Exclusion of participants with moderate heart failure; exclusion of additional medication that could interact with adalimumab and addition of information on the risk:benefit profile of the study.
16 July 2016	Amendment 5: -Change in Takeda Signatory from Nigel Brayshaw to Jing Xu, Claudia Lopez to Vilhelm Tetens -Screening Period increased to 4-weeks to allow sufficient time to complete all assessments -Update to inclusion criteria increase the age range for eligible participants -Clarification to the main exclusion criteria -Additional objectives and endpoints added for vedolizumab concentration and immunogenicity assessment -Clarification added to Study Design -Excluded Medications for the exclusion of all live vaccines -Rescreening added to provide details on rescreening of participants -Update to Post Study Care -Information included on the Week 52 interim analysis -Updates to Appendix A for clarification purposes.
08 March 2017	Amendment 7: -Administrative change to the Responsible Medical Officer -Additional interim analysis included - Inclusion of a Data Monitoring Committee -Update to sample size determination -Update to the tumor necrosis factor-alpha naïve versus failure ratio.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported