



## Clinical trial results:

### A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Vedolizumab Subcutaneous as Maintenance Therapy in Subjects With Moderately to Severely Active Crohn's Disease Who Achieved Clinical Response Following Open-Label Vedolizumab Intravenous Therapy

#### Summary

EudraCT number	2015-000481-58
Trial protocol	SK CZ NL BG GB DE BE SE DK LT HU ES IT
Global end of trial date	06 August 2019

#### Results information

Result version number	v1 (current)
This version publication date	23 May 2020
First version publication date	23 May 2020

#### Trial information

##### Trial identification

Sponsor protocol code	MLN0002SC-3031
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02611817
WHO universal trial number (UTN)	U1111-1168-0845

Notes:

#### Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	40 Landsdowne Street, Cambridge, MA, United States, 02139
Public contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, <a href="mailto:trialdisclosure@takeda.com">trialdisclosure@takeda.com</a>
Scientific contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, <a href="mailto:trialdisclosure@takeda.com">trialdisclosure@takeda.com</a>

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	06 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 August 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 assess the effect of vedolizumab subcutaneous (SC) as maintenance treatment in subjects with moderately to severely active Crohn's disease (CD) who achieved clinical response following administration of vedolizumab intravenous (IV) induction therapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	Czech Republic: 32
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	Poland: 122
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Serbia: 14
Country: Number of subjects enrolled	Slovakia: 10
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	Israel: 33
Country: Number of subjects enrolled	Russian Federation: 49
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	Ukraine: 38
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	United States: 133

Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 7
Worldwide total number of subjects	644
EEA total number of subjects	265

Notes:

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### 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)	621
From 65 to 84 years	23
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects with moderate to severe CD took part in the study at 169 investigative sites in North America, South America, Western/Northern Europe, Central Europe, Eastern Europe, East Asia, and Africa/Australia from 04 Jan 2016 to 06 Aug 2019.

### Pre-assignment

Screening details:

Subjects were enrolled in open-label (OL) induction phase to receive vedolizumab IV. Subjects with CR at Week 6 were randomized into double-blind maintenance phase to receive vedolizumab subcutaneous/placebo, and who did not achieve CR at Week 6 received 3rd infusion of OL vedolizumab IV and completed Week 14 visit.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Open-label Induction Phase: Vedolizumab 300 mg IV

Arm description:

Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab 300 mg IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab 300 mg, infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

<b>Arm title</b>	Maintenance Phase: Induction IV + Placebo
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Arm description:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

<b>Arm title</b>	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
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Arm description:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab 108 mg SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

Number of subjects in period 1	Open-label Induction Phase: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Started	235	134	275
Completed	235	72	168
Not completed	0	62	107
Consent withdrawn by subject	-	5	14
Adverse event, non-fatal	-	12	11
Other	-	1	2
Pregnancy	-	-	1
Randomized but not Treated	-	1	-
Lost to follow-up	-	-	1
Lack of efficacy	-	43	78

## Baseline characteristics

### Reporting groups

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

Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

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

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

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

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

Reporting group values	Open-label Induction Phase: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects	235	134	275
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	228	131	262
From 65-84 years	7	3	13
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	37.4	36.1	38.2
standard deviation	± 12.79	± 12.93	± 13.85
Sex: Female, Male Units: participants			
Female	119	68	118
Male	116	66	157
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	2
Not Hispanic or Latino	50	20	60
Unknown or Not Reported	185	113	213
Race (NIH/OMB) Units: Subjects			

American Indian or Alaska Native	0	2	0
Asian	23	6	17
Native Hawaiian or Other Pacific Islander	2	1	0
Black or African American	3	1	7
White	207	124	250
More than one race	0	0	1
Unknown or Not Reported	0	0	0
Smoking Classification			
Units: Subjects			
Never smoked	140	85	148
Current smoker	49	26	54
Ex-smoker	46	23	73
Weight			
Units: kilogram (kg)			
arithmetic mean	69.94	69.79	74.08
standard deviation	± 18.403	± 18.103	± 18.994
Body Mass Index			
Units: kilogram per square meter (kg/m^2)			
arithmetic mean	24.20	23.93	25.06
standard deviation	± 6.073	± 5.541	± 5.915

<b>Reporting group values</b>	Total		
Number of subjects	644		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	621		
From 65-84 years	23		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	305		
Male	339		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	130		
Unknown or Not Reported	511		
Race (NIH/OMB)			
Units: Subjects			

American Indian or Alaska Native	2		
Asian	46		
Native Hawaiian or Other Pacific Islander	3		
Black or African American	11		
White	581		
More than one race	1		
Unknown or Not Reported	0		
Smoking Classification			
Units: Subjects			
Never smoked	373		
Current smoker	129		
Ex-smoker	142		
Weight			
Units: kilogram (kg)			
arithmetic mean			
standard deviation	-		
Body Mass Index			
Units: kilogram per square meter (kg/m^2)			
arithmetic mean			
standard deviation	-		

## End points

### End points reporting groups

Reporting group title	Open-label Induction Phase: Vedolizumab 300 mg IV
Reporting group description: Vedolizumab 300 milligram (mg), infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.	
Reporting group title	Maintenance Phase: Induction IV + Placebo
Reporting group description: Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.	
Reporting group title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Reporting group description: Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.	
Subject analysis set title	Maintenance Phase: Induction IV + Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.	
Subject analysis set title	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Subject analysis set type	Full analysis
Subject analysis set description: Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.	

### Primary: Percentage of Subjects Achieving Clinical Remission at Week 52

End point title	Percentage of Subjects Achieving Clinical Remission at Week
End point description: Clinical remission: Crohn's Disease Activity Index (CDAI) score less than or equal to ( $\leq$ ) 150 at Week 52. CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days includes subject reported symptoms, physician-assessed signs/laboratory markers. CDAI score is equal to (=) sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approx. from 0 to 600, higher scores indicating greater disease activity. Full analysis set (FAS): All randomized subjects who received at least 1 dose of study SC drug (placebo/VDZ). Subjects who only received induction IV therapy and not randomized into the maintenance phase were not included in FAS. Subjects in this set were analyzed according to treatment they were randomized to receive.	
End point type	Primary
End point timeframe: Week 52	
Notes: [1] - 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: Descriptive data was planned to be analyzed for the reported arms.	

<b>End point values</b>	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	275		
Units: percentage of subjects				
number (confidence interval 95%)	34.3 (26.3 to 43.0)	48.0 (42.0 to 54.1)		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Statistical analysis description:	
P-value was calculated by Cochran-Mantel-Haenszel (CMH) test stratified by electronic data capture (EDC) stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.	
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Cochran-Mantel-Haenszel
Parameter estimate	Clopper-Pearson method
Point estimate	13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	23.7

## Secondary: Percentage of Subjects Achieving Enhanced Clinical Response at Week 52

End point title	Percentage of Subjects Achieving Enhanced Clinical Response at Week 52 <sup>[2]</sup>
End point description:	
Enhanced clinical response: A decrease from Baseline of greater than or equal to(>=)100 points in the CDAI score at Week 52.CDAI is a multi-item instrument which measures severity of active CD monitored over 7 days includes subject reported symptoms, physician-assessed signs, and laboratory markers.CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approx from 0 to 600, higher scores indicating greater disease activity. FAS included all randomized subjects who received at least 1 dose of study SC drug (placebo/VDZ). Subjects who only received induction IV therapy and not randomized into the maintenance phase were not included in FAS. Subjects in this set were analyzed according to the treatment they were randomized to receive.	
End point type	Secondary
End point timeframe:	
Week 52	

Notes:

[2] - 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: Descriptive data was planned to be analyzed for the reported arms.

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	275		
Units: percentage of subjects				
number (confidence interval 95%)	44.8 (36.2 to 53.6)	52.0 (45.9 to 58.0)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.	
Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.167
Method	Cochran-Mantel-Haenszel
Parameter estimate	Clopper-Pearson method
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	17.5

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

End point title	Percentage of Subjects Achieving Corticosteroid-free Remission at Week 52 <sup>[3]</sup>
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End point description:

Corticosteroid-free remission is defined as subjects using oral corticosteroids at Baseline (Week 0) who have discontinued oral corticosteroids and are in clinical remission at Week 52. Clinical remission is defined as a CDAI score  $\leq 150$  at Week 52. CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestations, body weight). CDAI scores range approximately from 0 to 600, higher scores indicating greater disease activity. Subjects from FAS, who used concomitant oral corticosteroid at Baseline. FAS had all subjects who received at least 1 dose of SC drug. Subjects who only received induction IV therapy and were not randomized into maintenance phase were not included in FAS. Subjects were analyzed according to

randomized treatment assignment.

End point type	Secondary
End point timeframe:	
Week 52	
Notes:	

[3] - 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: Descriptive data was planned to be analyzed for the reported arms.

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	95		
Units: percentage of subjects				
number (confidence interval 95%)	18.2 (8.2 to 32.7)	45.3 (35.0 to 55.8)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Clopper-Pearson method
Point estimate	27.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.9
upper limit	42.3

## Secondary: Percentage of TNF-alpha Antagonist Naive Subjects Achieving Clinical Remission at Week 52

End point title	Percentage of TNF-alpha Antagonist Naive Subjects Achieving Clinical Remission at Week 52 <sup>[4]</sup>
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End point description:

Clinical remission is defined as CDAI score  $\leq 150$  at Week 52. CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (use of anti-diarrhoeal medication, abdominal mass, haematocrit, presence of extraintestinal manifestation, body weight). CDAI scores range approximately from 0 to 600, higher

scores indicating greater disease activity. Subjects from FAS, who were TNF-alpha antagonist naïve and had clinical remission. FAS had all subjects who received at least 1 dose of SC drug. Subjects who only received induction IV therapy and were not randomized in maintenance phase were not included in FAS. Subjects were analyzed according to randomized treatment assignment.

End point type	Secondary
End point timeframe:	
Week 52	

Notes:

[4] - 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: Descriptive data was planned to be analyzed for the reported arms.

End point values	Maintenance Phase: Induction IV + Placebo	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	107		
Units: percentage of subjects				
number (confidence interval 95%)	42.9 (30.5 to 56.0)	48.6 (38.8 to 58.5)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-value was calculated by CMH test stratified by EDC stratum according to concomitant use of corticosteroids, clinical remission status at Week 6, and previous TNF-alpha antagonist failure/exposed or concomitant immunomodulator use.

Comparison groups	Maintenance Phase: Induction IV + Placebo v Maintenance Phase: Induction IV + Vedolizumab 108 mg SC
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.591
Method	Cochran-Mantel-Haenszel
Parameter estimate	Clopper-Pearson method
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	20.3

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are adverse events that started after the first dose of study drug up to 18 weeks after the last dose of study drug (up to Week 68)

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 subject or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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### Reporting groups

Reporting group title	Induction Phase Only: Vedolizumab 300 mg IV
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Reporting group description:

Vedolizumab 300 mg, infusion, intravenously, once at Weeks 0, 2 in the open-label induction phase. Subjects who did not achieve clinical response at Week 6 received third infusion of vedolizumab 300 mg IV on Week 6.

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

Vedolizumab 108 mg, injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive vedolizumab injection subcutaneously in maintenance phase.

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

Vedolizumab placebo-matching injection, subcutaneously, once every 2 weeks from Week 6 up to Week 50. Subjects who received vedolizumab 300 mg IV infusion in open-label induction phase and achieved clinical response at Week 6 were randomized to receive placebo in maintenance phase.

<b>Serious adverse events</b>	Induction Phase Only: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 235 (16.60%)	23 / 275 (8.36%)	14 / 134 (10.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal papilloma of breast			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
General disorders and administration site conditions			

General physical health deterioration subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Immune system disorders			
Anaphylactic reaction subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (0.00%)	0 / 134 (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
Psychiatric disorders			
Alcoholism subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Suicidal ideation subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Investigations			
White blood cell count increased subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Injury, poisoning and procedural complications			
Gastrointestinal anastomotic complication subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Incisional hernia subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Gastrointestinal anastomotic stenosis			

subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Infusion related reaction			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (0.00%)	0 / 134 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Atrial fibrillation			
subjects affected / exposed	0 / 235 (0.00%)	2 / 275 (0.73%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhagic stroke			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Intraventricular haemorrhage			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Hemiparesis			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Hemiplegia			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Blood and lymphatic system disorders			

Anaemias			
subjects affected / exposed	1 / 235 (0.43%)	1 / 275 (0.36%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Febrile neutropenia			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Crohn's disease			
subjects affected / exposed	14 / 235 (5.96%)	6 / 275 (2.18%)	5 / 134 (3.73%)
occurrences causally related to treatment / all	3 / 14	1 / 7	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 235 (0.43%)	1 / 275 (0.36%)	2 / 134 (1.49%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal stenosis			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	0 / 134 (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
Anal fistula			
subjects affected / exposed	1 / 235 (0.43%)	1 / 275 (0.36%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			

subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Intestinal obstruction			
subjects affected / exposed	1 / 235 (0.43%)	2 / 275 (0.73%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 235 (0.43%)	1 / 275 (0.36%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 235 (0.85%)	0 / 275 (0.00%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocutaneous fistula			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (0.00%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jejunal perforation			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Large intestinal ulcer			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Large intestine perforation			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Nausea			

subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Vomiting			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Hepatobiliary disorders			
Hepatitis cholestatic			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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	1 / 235 (0.43%)	0 / 275 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Infections and infestations			
Anal abscess			
subjects affected / exposed	2 / 235 (0.85%)	1 / 275 (0.36%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess intestinal			

subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	0 / 134 (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
Appendicitis			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Gastroenteritis			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (0.00%)	1 / 134 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 235 (0.00%)	1 / 275 (0.36%)	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
Dengue fever			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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
Bronchitis			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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	1 / 235 (0.43%)	1 / 275 (0.36%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	4 / 235 (1.70%)	0 / 275 (0.00%)	0 / 134 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Colonic abscess			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Perirectal abscess			
subjects affected / exposed	1 / 235 (0.43%)	0 / 275 (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
Metabolism and nutrition disorders			
Weight gain poor			
subjects affected / exposed	0 / 235 (0.00%)	0 / 275 (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 %

<b>Non-serious adverse events</b>	Induction Phase Only: Vedolizumab 300 mg IV	Maintenance Phase: Induction IV + Vedolizumab 108 mg SC	Maintenance Phase: Induction IV + Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 235 (17.02%)	102 / 275 (37.09%)	54 / 134 (40.30%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 235 (4.26%)	15 / 275 (5.45%)	5 / 134 (3.73%)
occurrences (all)	10	19	9
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	7 / 235 (2.98%)	36 / 275 (13.09%)	23 / 134 (17.16%)
occurrences (all)	7	36	25
Abdominal pain			
subjects affected / exposed	9 / 235 (3.83%)	21 / 275 (7.64%)	11 / 134 (8.21%)
occurrences (all)	11	25	14
Nausea			

subjects affected / exposed occurrences (all)	9 / 235 (3.83%) 10	11 / 275 (4.00%) 14	7 / 134 (5.22%) 7
Vomiting subjects affected / exposed occurrences (all)	4 / 235 (1.70%) 5	6 / 275 (2.18%) 7	7 / 134 (5.22%) 8
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	8 / 235 (3.40%) 8	17 / 275 (6.18%) 21	9 / 134 (6.72%) 10
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 235 (2.98%) 8	25 / 275 (9.09%) 26	6 / 134 (4.48%) 8
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 235 (0.85%) 2	17 / 275 (6.18%) 23	5 / 134 (3.73%) 6

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2015	The primary purpose of this amendment was to update the protocol regarding inclusion of additional exploratory objectives and endpoints to gather alternative clinical data.
10 February 2016	The primary purpose of this amendment was to update the protocol regarding inclusion of a benefit-risk assessment.
12 May 2016	The primary purpose of this amendment was to update the protocol to include additional information for clarification.
28 July 2016	The primary purpose of this amendment was to clarify the inclusion/exclusion criteria and to provide additional information regarding the voluntary ileocolonoscopies.
28 September 2016	The primary purpose of this amendment was to extend the visit window for Week 6a from 3 days to 5 days to adjust for clinical practice in Japan.
24 August 2017	The primary purpose of this amendment was to include a pre-Week 14 visit and to clarify the Week 14 procedures for subjects who enroll or do not enroll into the OLE study (SC-3030).

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported