Clinical trial results:
Entyvio (Vedolizumab IV) Extended Access Program in Ulcerative Colitis and Crohn's Disease

Summary

EudraCT number	2016-000678-40
Trial protocol	LV CZ HU EE BG IT
Global end of trial date	03 January 2023

Results information

Result version number	v1 (current)
This version publication date	17 November 2023
First version publication date	17 November 2023

Trial information

Trial identification

Sponsor protocol code	Vedolizumab-4013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02743806
WHO universal trial number (UTN)	U1111-1180-9339

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, 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	03 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to monitor ongoing safety in participants with ulcerative colitis (UC) and Crohn's disease (CD) and to provide access to vedolizumab for qualifying participants who, in the opinion of the investigator, continued to derive benefit from vedolizumab and for whom continued treatment with vedolizumab was desired because there was no other comparable product available, or the participant may have been expected to develop worsening of disease if they were to modify treatment.

Protection of trial subjects:

Each participant signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Czechia: 115
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Hungary: 46
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Ukraine: 5
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	India: 13
Country: Number of subjects enrolled	Korea, Republic of: 21
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	Serbia: 1
Country: Number of subjects enrolled	South Africa: 12
Country: Number of subjects enrolled	Turkey: 5

Worldwide total number of subjects	331
EEA total number of subjects	219

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)	310
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 78 investigative sites in Australia, Bulgaria, the Czech Republic, Estonia, Hungary, India, Italy, Republic of Korea, Latvia, Malaysia, New Zealand, Poland, Romania, Russian Federation, Serbia, South Africa, Turkey, and Ukraine from 01 August 2016 to 03 January 2023.

Pre-assignment

Screening details:

A total of 331 participants with a diagnosis of ulcerative colitis (UC) or Crohn's disease (CD) who have successfully completed the participation in qualifying vedolizumab clinical studies (C13008 [NCT00790933] and MLN0002-3028 [NCT02425111]) were enrolled in this extended access program (XAP) study to receive vedolizumab 300 mg.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Vedolizumab 300 mg

Arm description:

Vedolizumab 300 mg, intravenous (IV) infusion, once every 8 weeks (Q8W) that maybe reduced to once every 4 weeks (Q4W) based on the investigator's judgment of participant's clinical status and acknowledged by the medical monitor for up to 6 years.

Arm type	Experimental
Investigational medicinal product name	Vedolizumab
Investigational medicinal product code	
Other name	MLN0002, Entyvio, Kynteles
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab 300 mg, intravenous (IV) infusion, Q8W or Q4W for up to 6 years.

Number of subjects in period 1	Vedolizumab 300 mg
Started	331
Completed	150
Not completed	181
Study Termination	65
Adverse event, non-fatal	9
Voluntary Withdrawal	54
Reason Not Specified	12
Pregnancy	6
No Longer Clinically Benefiting	27
Lost to follow-up	8

Baseline characteristics

Reporting groups	
Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Vedolizumab 300 mg, intravenous (IV) infusion, once every 8 weeks (Q8W) that maybe reduced to once every 4 weeks (Q4W) based on the investigator's judgment of participant's clinical status and acknowledged by the medical monitor for up to 6 years.	

Reporting group values	Vedolizumab 300 mg	Total	
Number of subjects	331	331	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	44.5		
standard deviation	± 12.29	-	
Gender categorical Units: Subjects			
Female	147	147	
Male	184	184	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	36	36	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	292	292	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
Australia	13	13	
Bulgaria	4	4	
Czech Republic	115	115	
Estonia	4	4	
Hungary	46	46	
India	13	13	
Italy	5	5	
Korea, Republic of	21	21	
Latvia	1	1	
Malaysia	1	1	
New Zealand	6	6	
Poland	41	41	
Romania	3	3	
Russian Federation	35	35	
Serbia	1	1	

Turkey	5	5	
Ukraine	5	5	
South Africa	12	12	
Weight			
Units: kilograms (kg)			
arithmetic mean			
standard deviation	±	-	
Height			
Units: centimeters (cm)			
arithmetic mean			
standard deviation	±	-	
Body Mass Index (BMI)			
BMI = weight (kg) / [height (m^2)]			
Units: kilograms per meter square (kg/m^2)			
arithmetic mean			
standard deviation	±	-	

Subject analysis sets

Subject analysis set title	Vedolizumab 300 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set includes participants with data available for weight, height, and body mass index (BMI) at Baseline.

Reporting group values	Vedolizumab 300 mg		
Number of subjects	330		
Age Categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Region of Enrollment			
Units: Subjects			

Australia Bulgaria Czech Republic Estonia Hungary India Italy Korea, Republic of Latvia Malaysia New Zealand Poland Romania Russian Federation Serbia Turkey Ukraine South Africa			
Weight Units: kilograms (kg) arithmetic mean standard deviation	 76.91 ± 16.988		
Height Units: centimeters (cm) arithmetic mean standard deviation	 171.4 ± 11.06		
Body Mass Index (BMI)			
BMI = weight (kg) / [height (m^2)]			
Units: kilograms per meter square (kg/m^2) arithmetic mean standard deviation	 26.16 ± 5.667		

End points

End points reporting groups

Reporting group title	Vedolizumab 300 mg

Reporting group description:

Vedolizumab 300 mg, intravenous (IV) infusion, once every 8 weeks (Q8W) that maybe reduced to once every 4 weeks (Q4W) based on the investigator's judgment of participant's clinical status and acknowledged by the medical monitor for up to 6 years.

Subject analysis set title	Vedolizumab 300 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set includes participants with data available for weight, height, and body mass index (BMI) at Baseline.

Primary: Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug whether or not it is considered related to the study drug. A SAE is defined as any untoward medical occurrence that at any dose results in death, is life-threatening, requires participant hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, leads to a congenital anomaly/birth defect or is an important medical event. Percentages are rounded off to the nearest decimal point. FAS consisted of all participants enrolled in the XAP study, who received at least 1 dose of study drug (i.e., vedolizumab IV treatment), including the dose given at T0 (last vedolizumab dose in the qualifying study).

End point type	Primary

End point timeframe:

From first dose of study drug in this XAP study through 18 weeks after the last dose of study drug (up to 6.3 years)

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: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	331			
Units: percentage of participants				
number (not applicable)				
AEs	61.9			
SAEs	15.1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Adverse Events of Special Interest (AESIs)

End point title	Percentage of Participants With Adverse Events of Special

	Interest (AESIs)[2]

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug whether or not it is considered related to the study drug. AESIs included serious infections (opportunistic infections, such as progressive multifocal leukoencephalopathy [PML]), malignancies, liver injury, infusion-related hypersensitivity reactions, and injection site reactions. Percentages are rounded off to the nearest decimal point. FAS consisted of all participants enrolled in the XAP study, who received at least 1 dose of study drug (i.e., vedolizumab IV treatment), including the dose given at T0 (last vedolizumab dose in the qualifying study).

End point type	Primary

End point timeframe:

From first dose of study drug in this XAP study through 18 weeks after the last dose of study drug (up to 6.3 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned to be analysed for this endpoint.

End point values	Vedolizumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	331			
Units: percentage of participants				
number (not applicable)	3.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug in this XAP study through 18 weeks after the last dose of study drug (up to 6.3 years)

Adverse event reporting additional description:

FAS consisted of all participants enrolled in the XAP study, who received at least 1 dose of study drug (i.e., vedolizumab IV treatment), including the dose given at T0 (last vedolizumab dose in the qualifying study).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Vedolizumab 300 mg

Reporting group description: -

Serious adverse events	Vedolizumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 331 (15.11%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine benign neoplasm			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			

subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous aneurysm			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery dissection			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Device dislocation			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Amylase increased			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fracture displacement			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hand fracture			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			

subjects affected / exposed	2 / 331 (0.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Goitre			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	2 / 331 (0.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intracranial aneurysm			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Eye disorders			
Cataract			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileal stenosis			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestinal obstruction			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Anal fistula				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed[1]	4 / 142 (2.82%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed[2]	5 / 189 (2.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestinal stenosis				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 331 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				

subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudopolyposis			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	2 / 331 (0.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 331 (0.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

COVID-19			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal viral infection			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 331 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The number of subjects exposed to this adverse event are those with preferred disease condition of ulcerative colitis.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The number of subjects exposed to this adverse event are those with preferred disease condition of Crohn's disease.

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

Non-serious adverse events	Vedolizumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 331 (30.21%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 331 (6.34%)		
occurrences (all)	22		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed[3]	20 / 142 (14.08%)		
occurrences (all)	28		
Crohn's disease			

subjects affected / exposed[4]	35 / 189 (18.52%)		
occurrences (all)	50		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 331 (6.65%)		
occurrences (all)	30		
COVID-19			
subjects affected / exposed	17 / 331 (5.14%)		
occurrences (all)	17		

Notes:

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to this adverse event are those with preferred disease condition of ulcerative colitis.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to this adverse event are those with preferred disease condition of Crohn's disease.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2016	The following major changes were implemented based on Amendment 2: 1. Included Takeda sponsor companies in the European and Asian regions. 2. Included language per Declaration of Helsinki requirement. 3. Included details related to study design, objectives, participants, endpoints, and statistical considerations about extended access program-pharmacokinetic (XAP-PK) substudy. 4. Added references to the "assent form" for use if applicable, e.g., mentally incapacitated persons or participants deemed otherwise incapable of providing informed consent.
19 October 2021	The following major changes were implemented based on Amendment 7: 1. Excluded European Union (EU) Takeda sponsor company. 2. Included countries for XAP and XAP-PK studies. 3. Included text related to risk and mitigation approach due to interruption from coronavirus disease 2019 (COVID-19). 4. Date updated as per the details in the latest investigator's brochure (IB). 5. Deleted text related to sperm donation period for male participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 January 2023	Terminated (Early Completed - Alternative Source of Drug Available)	-

Notes:

Limitations and caveats

None reported