



Clinical trial results:

A Multicenter, Single Arm, Open-label Study to Investigate the Efficacy and Safety of Ravagalimab (ABBV-323) in Subjects With Moderate to Severe Ulcerative Colitis Who Failed Prior Therapy

Summary

EudraCT number	2018-000930-37
Trial protocol	NL DE GB FR ES HU IT
Global end of trial date	10 January 2022

Results information

Result version number	v1
This version publication date	25 January 2023
First version publication date	25 January 2023

Trial information

Trial identification

Sponsor protocol code	M15-722
-----------------------	---------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03695185
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United States, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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	10 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to investigate the efficacy, safety, and tolerability of ravagalimab (ABBV-323) in subjects with moderate to severe ulcerative colitis (UC) who failed prior 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	26 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	42
EEA total number of subjects	27

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)	40
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 42 subjects were enrolled in Induction Period to receive ravagalimab 600 mg intravenously(IV) followed by ravagalimab 300 mg subcutaneously(SC) up to Week 12. Those who completed Induction Period and achieved clinical response per partial adapted Mayo score at Week 12 entered Maintenance Period to receive ravagalimab 300 mg SC up to Week 102.

Period 1

Period 1 title	Induction Period (Week 0 to Week 12)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ravagalimab 600 mg/ 300 mg
-----------	----------------------------

Arm description:

Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from double-blind (DB) placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period. Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC every other week (EOW) from Week 12 through Week 102.

Arm type	Experimental
Investigational medicinal product name	Ravagalimab 600 mg
Investigational medicinal product code	
Other name	ABBV-323
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ravagalimab 600 mg administered by IV infusion.

Investigational medicinal product name	Ravagalimab 300 mg
Investigational medicinal product code	
Other name	ABBV-323
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ravagalimab 300 mg administered by SC injection.

Number of subjects in period 1	Ravagalimab 600 mg/ 300 mg
Started	42
Completed	29
Not completed	13
Adverse event	1
Withdrew consent	2

Lack of efficacy	10
------------------	----

Period 2

Period 2 title	Maintenance Period (Week 12 to Week 102)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ravagalimab 600 mg/ 300 mg
------------------	----------------------------

Arm description:

Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from DB placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period. Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC every other week (EOW) from Week 12 through Week 102.

Arm type	Experimental
Investigational medicinal product name	Ravagalimab 600 mg
Investigational medicinal product code	
Other name	ABBV-323
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ravagalimab 600 mg administered by IV infusion.

Investigational medicinal product name	Ravagalimab 300 mg
Investigational medicinal product code	
Other name	ABBV-323
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Ravagalimab 300 mg administered by SC injection.

Number of subjects in period 2	Ravagalimab 600 mg/ 300 mg
Started	29
Completed	1
Not completed	28
Withdrew consent	3
Reason not specified	23
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Ravagalimab 600 mg/ 300 mg
-----------------------	----------------------------

Reporting group description:

Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from double-blind (DB) placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period. Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC every other week (EOW) from Week 12 through Week 102.

Reporting group values	Ravagalimab 600 mg/ 300 mg	Total	
Number of subjects	42	42	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	42.3 ± 14.41	-	
Gender categorical Units: Subjects			
Female	17	17	
Male	25	25	
Ethnicity Units: Subjects			
Hispanic or Latino	5	5	
Not Hispanic or Latino	37	37	
Unknown or Not Reported	0	0	
Race Units: Subjects			
White	39	39	
Non-White	3	3	

End points

End points reporting groups

Reporting group title	Ravagalimab 600 mg/ 300 mg
Reporting group description: Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from double-blind (DB) placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period. Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC every other week (EOW) from Week 12 through Week 102.	
Reporting group title	Ravagalimab 600 mg/ 300 mg
Reporting group description: Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from DB placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period. Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC every other week (EOW) from Week 12 through Week 102.	

Primary: Percentage of Subjects with Endoscopic Improvement During Induction Period

End point title	Percentage of Subjects with Endoscopic Improvement During Induction Period ^[1]
End point description: Endoscopic Improvement is defined as Mayo endoscopic subscore of 0 or 1. Mayo endoscopic score is classified as 0=Normal or inactive disease; 1=Mild disease (erythema, decreased vascular pattern); 2=Moderate disease (marked erythema, absent vascular pattern, friability, erosions); 3=Severe disease (spontaneous bleeding, ulceration). Higher score indicates worsening of the disease. Full Analysis Set (FAS) included all enrolled subjects who received at least 1 dose of ravagalimab. The number of responders is calculated based on the total number of subjects and estimated response rate, rounding to a nearest whole integer. Data was reported only for the Induction Period.	
End point type	Primary
End point timeframe: At Week 8	
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: Descriptive data are summarized for this end point per protocol	

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	18.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Remission per Adapted Mayo Score During Induction Period

End point title	Percentage of Subjects with Clinical Remission per Adapted Mayo Score During Induction Period
End point description: Clinical remission per Adapted Mayo score is defined as stool frequency subscore (SFS) ≤ 1 , and not greater than baseline, rectal bleeding subscore (RBS) = 0, and endoscopic subscore ≤ 1 . Adapted Mayo Score is composite score of UC disease activity based on the following 3 subscores: Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal), Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed), Endoscopic subscore confirmed by central reader, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). Overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. FAS included all enrolled subjects who received at least 1 dose of ravagalimab. Number of responders is calculated based on the total number of subjects and estimated response rate, rounding to nearest whole integer. Data was reported only for the Induction Period.	
End point type	Secondary
End point timeframe: At Week 8	

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	9.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Response Per Adapted Mayo Score During Induction Period

End point title	Percentage of Subjects With Clinical Response Per Adapted Mayo Score During Induction Period
End point description: Clinical response per Adapted Mayo score is defined as the decrease from Baseline ≥ 2 points and $\geq 30\%$, PLUS a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 . The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores: SFS, scored from 0 (normal number of stools) to 3 (5 or more stools more than normal); RBS, scored from 0 (no blood seen) to 3 (blood alone passed), Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). The overall Adapted Mayo score ranges from 0 to 9 with higher scores representing more severe disease. FAS included all enrolled subjects who received at least 1 dose of ravagalimab. The number of responders is calculated based on the total number of subjects and estimated response rate, rounding to a nearest whole integer. Data was reported only for the Induction Period.	
End point type	Secondary
End point timeframe: At Week 8	

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	40.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Response Per Partial Adapted Mayo Score During Induction Period

End point title	Percentage of Subjects With Clinical Response Per Partial Adapted Mayo Score During Induction Period
End point description:	
Clinical response per Partial Adapted Mayo Score is defined as a decrease in Partial Adapted Mayo score ≥ 1 point and $\geq 30\%$ from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1 . The Partial Adapted Mayo Score is a composite score of UC disease activity based on the following 2 subscores: SFS, scored from 0 (normal number of stools) to 3 (5 or more stools more than normal); RBS, scored from 0 (no blood seen) to 3 (blood alone passed). The overall Partial Adapted Mayo score ranges from 0 to 6 with higher scores representing more severe disease. FAS included all enrolled subjects who received at least 1 dose of ravagalimab. The number of responders is calculated based on the total number of subjects and estimated response rate, rounding to a nearest whole integer. Data was reported only for the Induction Period.	
End point type	Secondary
End point timeframe:	
Up to Week 8	

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	57.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Remission per Full Mayo Score During Induction Period in Subjects With a Full Mayo Score of 6 to 12 at Baseline

End point title	Percentage of Subjects With Clinical Remission per Full Mayo Score During Induction Period in Subjects With a Full Mayo Score of 6 to 12 at Baseline			
-----------------	--	--	--	--

End point description:

Clinical Remission per full Mayo score (FMS) is defined as Full Mayo score ≤ 2 with no subscore >1 . The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The FMS ranges from 0 (normal or inactive disease) to 12 (severe disease) and is calculated as the sum of 4 subscores (stool frequency, rectal bleeding, endoscopy [confirmed by a central reader], and physician's global assessment), each of which ranges from 0 (normal) to 3 (severe disease). Negative changes indicate improvement. The number of responders is calculated based on the total number of participants and estimated response rate, rounding to the nearest whole integer. FAS included all enrolled subjects who received at least 1 dose of ravagalimab. Subjects analysed are the number of subjects available for analyses. Data was reported only for the Induction Period.

End point type	Secondary
----------------	-----------

End point timeframe:

At Week 8

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of subjects				
number (not applicable)	7.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Endoscopic Remission During Induction Period

End point title	Percentage of Subjects with Endoscopic Remission During Induction Period
-----------------	--

End point description:

Endoscopic remission is defined as Mayo endoscopic subscore = 0. Mayo endoscopic subscore is classified as 0=Normal or inactive disease; 1=Mild disease (erythema, decreased vascular pattern, mild friability); 2=Moderate disease (marked erythema, absent vascular pattern, friability, erosions); 3=Severe disease (spontaneous bleeding, ulceration). Higher score indicates worsening of the disease. The number of responders is calculated based on the total number of participants and estimated response rate, rounding to the nearest whole integer. FAS included all enrolled subjects who received at least 1 dose of ravagalimab. Data was reported only for the Induction Period.

End point type	Secondary
----------------	-----------

End point timeframe:

At Week 8

End point values	Ravagalimab 600 mg/ 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	0.0			

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 up to safety follow up visit (up to approximately 116 weeks)

Adverse event reporting additional description:

Safety Analysis Set included all subjects who received at least 1 dose of study drug.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.1
--------------------	------

Reporting groups

Reporting group title	Maintenance Period: Ravagalimab 300 mg
-----------------------	--

Reporting group description:

Subjects who achieved clinical response per partial adapted Mayo score at Week 12 of the Induction Period entered the Maintenance Period to receive ravagalimab 300 mg SC EOW from Week 12 through Week 102.

Reporting group title	Induction Period: Ravagalimab 600 mg/ 300 mg
-----------------------	--

Reporting group description:

Subjects received ravagalimab 600 mg IV at Week 0 followed by ravagalimab 300 mg SC at Weeks 2, 4, 6, 8, and 10 in a 12-week Induction Period. Subjects from DB placebo-controlled (prior to protocol version 4.0 of this study) continued their treatment as randomized in the Induction Period.

Serious adverse events	Maintenance Period: Ravagalimab 300 mg	Induction Period: Ravagalimab 600 mg/ 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 29 (6.90%)	2 / 42 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 29 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 29 (3.45%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
PERIRECTAL ABSCESS			

subjects affected / exposed	0 / 29 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINE INFECTION			
subjects affected / exposed	1 / 29 (3.45%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Maintenance Period: Ravagalimab 300 mg	Induction Period: Ravagalimab 600 mg/ 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 29 (65.52%)	15 / 42 (35.71%)	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 29 (13.79%)	2 / 42 (4.76%)	
occurrences (all)	4	2	
PARAESTHESIA			
subjects affected / exposed	3 / 29 (10.34%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	3 / 29 (10.34%)	2 / 42 (4.76%)	
occurrences (all)	3	7	
PYREXIA			
subjects affected / exposed	4 / 29 (13.79%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	2 / 29 (6.90%)	1 / 42 (2.38%)	
occurrences (all)	2	1	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 29 (6.90%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
HAEMORRHOIDS			

subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1 1 / 29 (3.45%) 1	3 / 42 (7.14%) 3 3 / 42 (7.14%) 3	
Skin and subcutaneous tissue disorders ECZEMA subjects affected / exposed occurrences (all) RASH subjects affected / exposed occurrences (all) PRURITUS subjects affected / exposed occurrences (all) SKIN LESION subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2 1 / 29 (3.45%) 1 3 / 29 (10.34%) 3 2 / 29 (6.90%) 2	0 / 42 (0.00%) 0 3 / 42 (7.14%) 3 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0	
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all)	6 / 29 (20.69%) 7 3 / 29 (10.34%) 3	0 / 42 (0.00%) 0 1 / 42 (2.38%) 1	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) TOOTH ABSCESS subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 3 2 / 29 (6.90%) 2	0 / 42 (0.00%) 0 0 / 42 (0.00%) 0	
Metabolism and nutrition disorders IRON DEFICIENCY subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 42 (2.38%) 1	

VITAMIN D DEFICIENCY			
subjects affected / exposed	2 / 29 (6.90%)	0 / 42 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2018	The following changes were implemented with Amendment 1: -Clarified where dose and duration requirements was specified in the body text. -Highlighted key secondary endpoints and moved the rest to exploratory endpoints. -Rescreening was added. -"Systemic hypersensitivity reactions" was changed to "anaphylaxis," and text was added in regards to the types of tests to be carried out in the event of a suspected anaphylaxis. -Revised text to remove the requirement of additional consent for the use of biopsy samples for biomarker research. -Specified the only samples that are optional are blood samples and where the biopsies are taken from. -Added text to clarify that the initiation and/or increase of oral aminosalicylates, immunomodulators, IV or oral corticosteroids, and/or UC-related antibiotics is prohibited through Week 12 specifically, and that the initiation and/or increase of the aforementioned drugs is permissible after discussion with the AbbVie TA MD starting at Week 12. -Provided more detailed text around timing of Day 1 and subsequent serum ABBV-323 and anti-drug antibody (ADA)/ neutralizing antibody (nAb) collection.
13 February 2019	The following changes were implemented with Amendment 2: -Deleted secondary objectives and updated the overall objective. -Clarified that primary and secondary endpoints are efficacy endpoints and changed the terminology of "safety assessments" to "safety endpoints". -Updated language regarding optional continuation from the induction period into the maintenance period. -Included text regarding the provision of a separate study drug administration guideline. - Updated Primary Analysis text for clarification. -Revised wording to clarify that the subject must understand all aspects of the study and personally sign the informed consent. -Revised wording to further clarify that sites should avoid administration of two consecutive doses of ABBV-323 sooner than 7 days apart. -Updated text regarding golimumab induction regimen. -Updated the footnote 'Lab assessments will only need to be repeated at Baseline if the time between Screening and Baseline is greater than 14 days, or if the subject's health status has changed to warrant a repeat test'. -Changed steroid tapering after Week 12 and during the Maintenance Period from mandatory to optional. -Updated the biomarker lab activities to indicate the exact parameters that will be analyzed at each visit.
29 May 2019	The following changes were implemented with Amendment 3: -Changed the study design from randomized, double-blind, placebo-controlled to open-label.
06 May 2020	The following changes were implemented with Amendment 4: -Expanded the maintenance period by an additional 52 weeks with similar, although reduced study procedures as during Week 12 through Week 52.
04 December 2020	The following changes were implemented with Amendment 5: -Added ustekinumab to approved therapies list for key eligibility criteria. -Removed text from key eligibility criterion requiring open-label (OL) use of tofacitinib if received in a clinical trial. -Clarified endpoint definitions. -Removed discussion of the data monitoring committee (DMC) from the study design. -Clarified text regarding primary and interim analysis and the timing of termination of study enrollment, and explicitly permit additional statistical analysis if needed. -Update eligibility criterion, with details regarding subject eligibility with regards to COVID-19 (coronavirus SARS-CoV-2) infection, to remove requirement for tofacitinib and ustekinumab to have been given in open label fashion if received in a clinical trial, and corrected language on, prohibiting pregnancy and breastfeeding. -Clarified discontinuation of study drug as well as study participation. -Clarified that active tuberculosis (TB) is an adverse event of special interest. -Removed sensitivity analysis for the primary efficacy endpoint. -Added Hepatitis B screening, Hepatitis C screening, HIV test, and SARSCoV-2 molecular test to the list of clinical tests which may be performed during the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported