



Clinical trial results:

A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of BMS -986165 in Subjects with Moderate to Severe Ulcerative Colitis

Summary

EudraCT number	2018-004694-27
Trial protocol	GB HU PL DE BE CZ FR IT
Global end of trial date	04 April 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	IM011-024
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03934216
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	02 May 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of BMS-986165 on clinical remission at the end of the induction period

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 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	Australia: 5
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	131
EEA total number of subjects	81

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)	120
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

131 Participants Randomized and 129 Treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Treatment
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Arm description:

BMS-986-165 6mg BID

Arm type	Experimental
Investigational medicinal product name	BMS-986165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

6mg BID

Arm title	Placebo
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Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

placebo BID

Number of subjects in period 1	Treatment	Placebo
Started	88	43
Completed	30	12
Not completed	58	31
Consent withdrawn by subject	18	6
Non-Compliance with Study Drug	1	1

Adverse event, non-fatal	22	11
Other Reasons	5	5
Randomized but not treated	1	1
Pregnancy	1	-
Lost to follow-up	2	-
Lack of efficacy	8	7

Baseline characteristics

Reporting groups

Reporting group title	Treatment
Reporting group description: BMS-986-165 6mg BID	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Treatment	Placebo	Total
Number of subjects	88	43	131
Age categorical			
Units: Subjects			
Adults (18-64 years)	81	39	120
From 65-84 years	7	4	11
Age Continuous			
Units: Years			
arithmetic mean	41.6	40.3	
standard deviation	± 14.81	± 13.91	-
Sex: Female, Male			
Units: Participants			
Female	40	14	54
Male	48	29	77
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	7	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	2	7
White	80	34	114
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	3	2	5
Not Hispanic or Latino	83	41	124
Unknown or Not Reported	2	0	2

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description:	
BMS-986-165 6mg BID	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Primary: Clinical Remission Response Rate at Week 12

End point title	Clinical Remission Response Rate at Week 12
End point description:	
Clinical remission response rate is the percentage of participants achieving clinical remission, defined as absolute total Mayo Score and absolute Mayo endoscopy, stool frequency, rectal bleeding.	
Will be calculated using a modified Mayo score with the following:	
Stool Frequency (SF) subscore ≤ 1 , with ≥ 1 point decrease from baseline, and	
Rectal Bleeding (RB) subscore = 0, and	
Endoscopic (ES) subscore ≤ 1 (modified, excludes friability)	
The modified Mayo score (0 to 9 points) is the sum of 3 components: the SF, RB, and ES subscores	
Modified Mayo Score: The modified Mayo score is a 9-point scale; a score of 5 to 9 points (inclusive), which is required for randomization, denotes moderate to severe disease (by protocol definition). considered in clinical remission if a Mayo Score of less than or equal to 2 with no individual subscore greater than 1	
End point type	Primary
End point timeframe:	
From first dose to 12 weeks.	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	43		
Units: Percentage of Participants				
number (confidence interval 95%)	14.8 (7.4 to 22.2)	16.3 (5.2 to 27.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Clinical Remission
Comparison groups	Treatment v Placebo

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5935
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.4

Secondary: Clinical Response Rate at 12 weeks

End point title	Clinical Response Rate at 12 weeks
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End point description:

Clinical response is defined as percentage of participants with a reduction in total Mayo Score and reduction in rectal bleeding subscore

Will be defined as the following:

- A decrease from baseline in the modified Mayo score of ≥ 2 points, and
- A decrease from baseline in the modified Mayo score $\geq 30\%$, and
- A decrease in rectal bleeding(RB) subscore of ≥ 1 point or absolute RB subscore ≤ 1

End point type	Secondary
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End point timeframe:

From first dose to 12 weeks

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	43		
Units: Percentage of participants				
number (confidence interval 95%)	37.5 (27.4 to 47.6)	32.6 (18.6 to 46.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Clinical Response
Comparison groups	Treatment v Placebo
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3051
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.7

Secondary: Endoscopic Response at Week 12

End point title	Endoscopic Response at Week 12
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End point description:

Endoscopic response will be defined as percentage of participants with a reduction in the total Ulcerative Colitis Endoscopic Index of Severity score.

The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) scale:

Vascular Pattern:

- Normal (score 0)
- patchy obliteration (score 1)
- Obliterated (score 2)

Bleeding

- None (score 0)
- Mucosal (score 1)
- Luminal mild (score 2)
- Luminal Moderate or severe (score 3)

Erosions and Ulcers

- None (score 0)
- Erosions (score 1)
- Superficial Ulcer (2)
- Deep Ulcer (score 3)

A total score represents the following: remission (0–1); mild (2–4); moderate (5–6); and severe (7–8).

End point type	Secondary
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End point timeframe:

up to 12 Weeks

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	43		
Units: Percentage of Participants				
number (confidence interval 95%)	19.3 (11.1 to 27.6)	27.9 (14.5 to 41.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Endoscopic Response
Comparison groups	Treatment v Placebo

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8764
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.4

Secondary: Histological Improvement Response Rate at 12 Weeks

End point title	Histological Improvement Response Rate at 12 Weeks
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End point description:

Histologic improvement is defined as percentage of participants with a Geboes score of ≤ 3.1

Neutrophils <5% of crypts, with no crypt destruction, erosions, ulcerations, and granulation tissue. Achieving the following scores for the corresponding grades of the Geboes score:

- Score of 0 or 1 for Grade 3 (neutrophils in the epithelium: none or < 5% crypts involved), and
- Score of 0 for Grade 4 (crypt destruction: none), and
- Score of 0 Grade 5 (erosion or ulceration: no erosions, ulcerations, or granulation tissue)

grade 1 = chronic inflammatory infiltrate; grade 2 = lamina propria neutrophils and eosinophils; grade 3 = neutrophils in the epithelium; grade 4 = crypt destruction; grade 5 = erosions or ulceration. A higher score indicates more severe disease

End point type	Secondary
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End point timeframe:

up to 12 Weeks

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	43		
Units: Percentage of Participants				
number (confidence interval 95%)	21.6 (13.0 to 30.2)	16.3 (5.2 to 27.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Histological Response
Comparison groups	Treatment v Placebo

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2235
Method	Stratified Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	3.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events: (From first dose to last dose + 100 days): Approximately 104 Weeks

All-Cause mortality (From randomization to end of study): Approximately 104 Weeks

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all treated participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Treatment
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Reporting group description:

BMS-986165 6mg BID

Reporting group title	BMS-986165 6mg BID during OL period
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Reporting group description:

BMS-986165 6mg BID during OL period after receiving Placebo in Induction period

Reporting group title	Placebo
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Reporting group description:

Placebo BID

Serious adverse events	Treatment	BMS-986165 6mg BID during OL period	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 87 (21.84%)	4 / 32 (12.50%)	2 / 10 (20.00%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Congenital, familial and genetic disorders			
Congenital aural fistula			
subjects affected / exposed	0 / 87 (0.00%)	1 / 32 (3.13%)	0 / 10 (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

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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			
Abdominal pain			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Colitis ulcerative			
subjects affected / exposed	3 / 87 (3.45%)	2 / 32 (6.25%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Impaired gastric emptying			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Respiratory, thoracic and mediastinal disorders			
Nasal septum deviation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Pulmonary embolism			
subjects affected / exposed	0 / 87 (0.00%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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			
Cervical spinal stenosis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
COVID-19			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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
COVID-19 pneumonia			
subjects affected / exposed	8 / 87 (9.20%)	0 / 32 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 87 (0.00%)	1 / 32 (3.13%)	0 / 10 (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
Sepsis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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			
Metabolic acidosis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	0 / 10 (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

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

Non-serious adverse events	Treatment	BMS-986165 6mg BID during OL period	Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	64 / 87 (73.56%)	22 / 32 (68.75%)	6 / 10 (60.00%)
Investigations			
Blood alkaline phosphatase increased subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Haemoglobin decreased subjects affected / exposed	0 / 87 (0.00%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hepatitis B DNA assay positive subjects affected / exposed	0 / 87 (0.00%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
SARS-CoV-2 test positive subjects affected / exposed	0 / 87 (0.00%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Vaccination complication subjects affected / exposed	1 / 87 (1.15%)	1 / 32 (3.13%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
Vascular disorders			
Hypertension subjects affected / exposed	1 / 87 (1.15%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed occurrences (all)	4 / 87 (4.60%) 4	2 / 32 (6.25%) 3	1 / 10 (10.00%) 1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 87 (3.45%)	5 / 32 (15.63%)	0 / 10 (0.00%)
occurrences (all)	4	8	0
Feeling cold			
subjects affected / exposed	0 / 87 (0.00%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	1 / 87 (1.15%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 87 (0.00%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 87 (8.05%)	1 / 32 (3.13%)	0 / 10 (0.00%)
occurrences (all)	7	1	0
Constipation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Colitis ulcerative			
subjects affected / exposed	17 / 87 (19.54%)	8 / 32 (25.00%)	2 / 10 (20.00%)
occurrences (all)	21	11	2
Aphthous ulcer			
subjects affected / exposed	5 / 87 (5.75%)	2 / 32 (6.25%)	1 / 10 (10.00%)
occurrences (all)	9	3	1
Abdominal distension			
subjects affected / exposed	0 / 87 (0.00%)	0 / 32 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 87 (0.00%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Food poisoning			

subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	2 / 32 (6.25%) 2	0 / 10 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	5 / 87 (5.75%) 5	1 / 32 (3.13%) 1	0 / 10 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 87 (3.45%) 3	2 / 32 (6.25%) 2	0 / 10 (0.00%) 0
Skin and subcutaneous tissue disorders Rash papular subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	0 / 32 (0.00%) 0	1 / 10 (10.00%) 1
Rash subjects affected / exposed occurrences (all)	13 / 87 (14.94%) 19	3 / 32 (9.38%) 4	0 / 10 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	0 / 32 (0.00%) 0	1 / 10 (10.00%) 1
Acne subjects affected / exposed occurrences (all)	9 / 87 (10.34%) 9	2 / 32 (6.25%) 3	0 / 10 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 87 (5.75%) 6	4 / 32 (12.50%) 6	0 / 10 (0.00%) 0
Spinal pain subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 32 (3.13%) 1	1 / 10 (10.00%) 1
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	2 / 32 (6.25%) 2	0 / 10 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 87 (6.90%) 8	4 / 32 (12.50%) 5	0 / 10 (0.00%) 0

Influenza			
subjects affected / exposed	3 / 87 (3.45%)	2 / 32 (6.25%)	1 / 10 (10.00%)
occurrences (all)	3	2	1
COVID-19			
subjects affected / exposed	13 / 87 (14.94%)	6 / 32 (18.75%)	0 / 10 (0.00%)
occurrences (all)	13	6	0
Oral herpes			
subjects affected / exposed	2 / 87 (2.30%)	1 / 32 (3.13%)	1 / 10 (10.00%)
occurrences (all)	3	1	3
Upper respiratory tract infection			
subjects affected / exposed	5 / 87 (5.75%)	1 / 32 (3.13%)	0 / 10 (0.00%)
occurrences (all)	7	2	0
Tonsillitis			
subjects affected / exposed	1 / 87 (1.15%)	2 / 32 (6.25%)	0 / 10 (0.00%)
occurrences (all)	2	4	0
Sinusitis			
subjects affected / exposed	5 / 87 (5.75%)	1 / 32 (3.13%)	0 / 10 (0.00%)
occurrences (all)	5	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2019	Includes modifications to the Schedule of Activities and Biomarker sections to provide clarity; added new Section 8.1.1 and language throughout protocol regarding central read versus local read of endoscopy; clarified corticosteroid use as a rescue medication; and added discontinuation criteria and study stopping rules to align with recent FDA communications
09 April 2019	This country-specific amendment applies to all subjects enrolled in Japan. The purpose of this Amendment is to incorporate local regulatory requirements for Japanese sites.
31 July 2019	Adding "or age of majority" to inclusion criterion to align with local regulatory requirements for South Korean sites
01 August 2019	This country-specific amendment applies to all subjects enrolled in the Czech Republic. The purpose of this Amendment is to adjust the maximum age of subjects from 80 to 70 years of age, and to align Section 8.2.5 Pregnancy with local regulatory requirements for Czech Republic sites.

29 August 2019	<p>This country-specific amendment applies to all subjects enrolled in Germany. Modifications include:</p> <ul style="list-style-type: none">• Exclusion Criterion 7)a) has been revised to exclude prisoners or subjects who are involuntarily incarcerated from trial participation.• Section 7.1.1 (Post-Study Treatment Follow-up) has been revised to state that participants who discontinue study treatment will be followed for 28 days or longer, as required, and in line with Section 8.2.3.• Section 8.2.1 and APPENDIX 3 have been revised to state that serious adverse events (AEs) need to be reported 'immediately' to Sponsor or designee but no later than 24 hours after awareness of the event.• Section 8.2.5 (Pregnancy) has been revised to state that study drug treatment must be discontinued immediately in case of pregnancy and that the pregnancy must be reported within 24 hours of awareness of the pregnancy.• APPENDIX 3 has been revised to state that nonserious AEs that cause interruption or discontinuation of study treatment must be followed to resolution or stabilization.
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28 October 2019	<p>Includes the following modifications:</p> <ul style="list-style-type: none"> • add a 52-week open-label extension period to provide the option of additional treatment to subjects deriving clinical benefit at Week 52; • modify the type and/or frequency of various study assessments to improve subject safety and minimize subject burden; provide additional detail for each of the study periods, including clear guidance for management of Week 12 responders and nonresponders in the maintenance period and additional hepatitis B Virus (HBV) and hepatitis C Virus (HCV) screening and monitoring information; • modify several inclusion and exclusion criteria to increase subject eligibility, and add specific randomization criteria to aid in final determination of eligibility; • incorporate several elements from the South Korea and Germany specific v2.0 amendments regarding age of majority, and follow-up after discontinuation and adverse events; • revise or clarify the definitions of key study terms and endpoints; add several exploratory endpoints; • revise or clarify the following study elements: prohibited and restricted treatments; use and tapering of corticosteroids during all study periods; criteria defining treatment failure; criteria leading to discontinuation; and criteria defining inadequate response, loss of response, and intolerance to previous biologic therapy; • clarify sample size calculation, planned exploratory analyses, and other analyses including quality of life and healthcare resource utilization; • remove or modify several contraception requirements to reflect recent toxicology data consistent with these changes; • implement other revisions including modification of text regarding safety reporting requirements; and addition of several new appendices to evaluate UC disease activity, patient-reported outcomes, and healthcare resource utilization.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported