Clinical trial results:
Proof-of-concept study of BI 655130 add-on treatment in patients with mild-to-moderately active ulcerative colitis during TNF inhibitor therapy

Summary

EudraCT number	2016-004572-21
Trial protocol	DK NO DE NL ES GB
Global end of trial date	16 September 2020

Results information

Result version number	v1 (current)
This version publication date	01 October 2021
First version publication date	01 October 2021

Trial information

Trial identification

Sponsor protocol code	1368-0010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03123120
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim Call Center, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim Call Center, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.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	26 October 2020
Is this the analysis of the primary	Yes

completion data?	
Primary completion date	26 March 2020
Global end of trial reached?	Yes
Global end of trial date	16 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this trial were safety and efficacy (proof-of-concept) of induction of mucosal healing by spesolimab (BI 655130) add-on therapy in patients with mild or moderate ulcerative colitis (UC) and persisting endoscopic activity despite pre-existing tumour necrosis factor inhibitor (TNFi) treatment.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2017
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	United Kingdom: 7
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Denmark: 5
Worldwide total number of subjects	39
EEA total number of subjects	32

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)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This randomized, placebo-controlled, double-blind trial over 36 weeks with 24-week follow-up evaluated safety and efficacy of induction of mucosal healing by Spesolimab add-on therapy in patients with mild or moderate ulcerative colitis and persisting endoscopic activity despite pre-existing tumor necrosis factor inhibitor treatment.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - randomized

Arm description:

Matching placebo was administered via intravenous infusion over 12 weeks of treatment. Participants who were randomized into the Placebo treatment were included in this arm.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching placebo was administered via intravenous infusion over 12 weeks of treatment.

Arm title	Spesolimab 1200 mg - randomized

Arm description:

1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment (3 injections of Spesolimab 1200 mg in total during the 12 weeks: at Week 0, 4, and 8 respectively). Participants who were randomized into the Spesolimab 1200 mg treatment were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BI 655130
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment (3 injections of Spesolimab 1200 mg in total during the 12 weeks: at Week 0, 4, and 8 respectively).

Number of subjects in period 1[1]	Placebo - randomized	Spesolimab 1200 mg - randomized
Started	8	14
Completed	8	12
Not completed	0	2
Consent withdrawn by subject	-	1
Lost to follow-up	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo - randomized
Reporting group description:	
Matching placebo was administered via intravenous infusion over 12 weeks of treatment. Participants who were randomized into the Placebo treatment were included in this arm.	
Reporting group title	Spesolimab 1200 mg - randomized
Reporting group description:	
1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment (3 injections of Spesolimab 1200 mg in total during the 12 weeks: at Week 0, 4, and 8 respectively). Participants who were randomized into the Spesolimab 1200 mg treatment were included in this arm.	

Reporting group values	Placebo - randomized	Spesolimab 1200 mg - randomized	Total
Number of subjects	8	14	22
Age categorical			
Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
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)	8	14	22
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: years			
arithmetic mean	45.5	43.1	
standard deviation	± 12.1	± 9.9	-
Sex: Female, Male			
Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: Participants			
Female	1	4	5
Male	7	10	17
Ethnicity (NIH/OMB)			
Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	8	14	22

Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	8	13	21
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Number of participants per Mayo clinical score modified endoscopic subscore value group			
The number of participants per Mayo clinical score (MCS) modified endoscopic subscore (mESS) value group was reported. The MCS mESS ranged from 0 (normal) to 3 (severe disease). The MCS mESS was assessed by a central reader who was independent from the investigator. Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: Subjects			
MCS mESS = 0	0	0	0
MCS mESS = 1	0	0	0
MCS mESS = 2	2	3	5
MCS mESS = 3	6	11	17
Mayo clinical score (MCS) modified endoscopic subscore (mESS)			
The Mayo clinical score (MCS) modified endoscopic subscore (mESS) at baseline was reported. The MCS mESS ranged from 0 (normal) to 3 (severe disease). The MCS mESS was assessed by a central reader who was independent from the investigator. Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.			
Units: Score on a scale			
arithmetic mean	2.8	2.8	
standard deviation	± 0.5	± 0.4	-

End points

End points reporting groups

Reporting group title	Placebo - randomized

Reporting group description:

Matching placebo was administered via intravenous infusion over 12 weeks of treatment. Participants who were randomized into the Placebo treatment were included in this arm.

Reporting group title	Spesolimab 1200 mg - randomized

Reporting group description:

1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment (3 injections of Spesolimab 1200 mg in total during the 12 weeks: at Week 0, 4, and 8 respectively). Participants who were randomized into the Spesolimab 1200 mg treatment were included in this arm.

Subject analysis set title	Placebo - actual
Subject analysis set type	Safety analysis

Subject analysis set description:

Matching placebo were administered via intravenous over 12 weeks of treatment.
Participants who actually administered placebo during the study were included in this group. 1 patient who was assigned to placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group.

Subject analysis set title	Spesolimab 1200 mg - actual
Subject analysis set type	Safety analysis

Subject analysis set description:

1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment.
Participants who actually administered Spesolimab during the study were included in this group. 1 patient who was assigned to Placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group.

Primary: Proportion of participants with endoscopic improvement (MCS mESS ≤1) at Week 12

End point title	Proportion of participants with endoscopic improvement (MCS mESS ≤1) at Week 12

End point description:

Proportion of participants with endoscopic improvement (Mayo clinical score (MCS) modified endoscopic sub-score (mESS) ≤1) at Week 12 was reported. The endoscopic improvement (mucosal healing) was defined as the Mayo clinical score (MCS) modified endoscopic sub-score (mESS) ≤ 1 point. The MCS mESS ranged from 0 (normal) to 3 (severe disease). The mESS was assessed by a central reader who was independent from the investigator. The 95% confidence intervals of the proportion were calculated using the method of Wilson.

Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.

End point type	Primary

End point timeframe:

At Week 12

End point values	Placebo - randomized	Spesolimab 1200 mg - randomized		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	14		
Units: Proportion of participants				
number (confidence interval 95%)	0.375 (0.137 to 0.694)	0.143 (0.040 to 0.399)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Risk difference was calculated as the observed proportion of response from Spesolimab minus the one from Placebo. Newcombe method was used in the calculation of the 95% confidence interval around the risk difference.

Comparison groups	Placebo - randomized v Spesolimab 1200 mg - randomized
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-0.232
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.568
upper limit	0.118

Secondary: Proportion of participants with histological remission at Week 12

End point title	Proportion of participants with histological remission at Week 12

End point description:

Proportion of participants with histological remission at Week 12 was reported. The histological remission was defined as the Robarts histology index (RHI) score ≤ 6. The RHI was a histologic activity score, consists of chronic inflammatory infiltrate, lamina propria neutrophils, neutrophils in epithelium and erosion or ulceration on a scale of 0 to 3. The 4 components were weighted to calculate the RHI, with RHI = 1 × chronic inflammatory infiltrate + 2 × lamina propria neutrophils + 3 × neutrophils in epithelium + 5 × erosion or ulceration. The resulting RHI score ranged from 0 (no disease activity) to 33 (severe disease activity). The 95% confidence intervals of the proportion were calculated using the method of Wilson.

Full analysis set (FAS): This set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Placebo - randomized	Spesolimab 1200 mg - randomized		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	14		
Units: Proportion of participants				
number (confidence interval 95%)	0.500 (0.215 to 0.785)	0.214 (0.076 to 0.476)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Risk difference was calculated as the observed proportion of response from Spesolimab minus the one from Placebo. Newcombe method was used in the calculation of the 95% confidence interval around the risk difference.

Comparison groups	Placebo - randomized v Spesolimab 1200 mg - randomized
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-0.286
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.602
upper limit	0.101

Secondary: Proportion of participants with total clinical remission (tCR) based on total Mayo clinical score at Week 12

End point title	Proportion of participants with total clinical remission (tCR) based on total Mayo clinical score at Week 12

End point description:

Proportion of participants with total clinical remission based on total Mayo clinical score (MCS) at Week 12 was reported. The total clinical remission based on total MCS was defined as the total MCS ≤ 2 points and all sub-scores ≤ 1 point. The total MCS was a composite disease activity score consisting of 4 sub-scores: stool frequency, rectal bleeding, physician's global assessment, and modified endoscopic appearance. Each sub-score ranged from 0 (normal) to 3 (severe disease/worse disease status). The total MCS was by summing up the four sub-scores and ranged from 0 to 12 with higher score indicating worse disease. The 95% confidence intervals of the proportion were calculated using the method of Wilson.

Full analysis set (FAS): This patient set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded from the FAS.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Placebo - randomized	Spesolimab 1200 mg - randomized		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	14		
Units: Proportion of participants				
number (confidence interval 95%)	0.125 (0.022 to 0.471)	0.071 (0.013 to 0.315)		

Statistical analyses

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Risk difference was calculated as the observed proportion of response from Spesolimab minus the one from Placebo. Newcombe method was used in the calculation of the 95% confidence interval around the risk difference.

Comparison groups	Placebo - randomized v Spesolimab 1200 mg - randomized
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-0.054
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.404
upper limit	0.21

Secondary: Proportion of participants with clinical remission (CR) based on Mayo clinical score at Week 12

End point title	Proportion of participants with clinical remission (CR) based on Mayo clinical score at Week 12

End point description:

Proportion of participants with clinical remission (CR) based on Mayo clinical score (MCS) at Week 12 was reported. The CR based on MCS was defined as the total MCS ≤ 2 and Rectal Bleeding Subscore = 0, Stool Frequency Score =0 or 1 and drop ≥ 1 from baseline, and Modified endoscopic sub-score (mESS) ≤ 1. The total MCS consisted of 4 sub-scores: stool frequency, rectal bleeding, physician's global assessment, and modified endoscopic appearance. Each sub-score ranged from 0 (normal) to 3 (severe disease/worse disease status). The total MCS was by summing up the four sub-scores and ranged from 0 to 12 with higher score indicating worse disease. The 95% confidence intervals of the proportion were calculated using the method of Wilson.

Full analysis set (FAS): This set includes all patients in the safety analysis set who had a baseline measurement available for the primary endpoint. Treatment assignment will be as randomized. Patients who were randomized but not treated were excluded.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Placebo - randomized	Spesolimab 1200 mg - randomized		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	14		
Units: Proportion of participants				
number (confidence interval 95%)	0.000 (0.000 to 0.324)	0.143 (0.040 to 0.399)		

Statistical analyses

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Risk difference was calculated as the observed proportion of response from Spesolimab minus the one from Placebo. Newcombe method was used in the calculation of the 95% confidence interval around the risk difference.

Comparison groups	Placebo - randomized v Spesolimab 1200 mg - randomized
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.143
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.197
upper limit	0.399

Secondary: Number of participants with treatment-emergent adverse events (TEAEs)

End point title	Number of participants with treatment-emergent adverse events (TEAEs)

End point description:

Number of participants with any treatment-emergent adverse events (TEAEs) was reported.

Safety Analysis Set (SAF): this patient set included all randomized patients who received at least one dose of trial drug. Treatment assignment was analyzed according to the actual treatment. 1 patient who was assigned to placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group in the SAF.

End point type	Secondary

End point timeframe:

From first does of study medication until end of the follow-up period, up to 36 weeks.

End point values	Placebo - actual	Spesolimab 1200 mg - actual		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	15		
Units: Participants	6	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first does of study medication until end of the follow-up period, up to 36 weeks.

Adverse event reporting additional description:

Safety Analysis Set (SAF): this patient set included all randomized patients who received at least one dose of trial drug. Treatment assignment was analyzed according to the actual treatment. 1 patient who was assigned to placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group in the SAF.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo - actual

Reporting group description:

Matching placebo were administered via intravenous over 12 weeks of treatment.
Participants who actually administered placebo during the study were included in this group. 1 patient who was assigned to placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group.

Reporting group title	Spesolimab 1200 mg - actual

Reporting group description:

1200 milligrams (mg) of Spesolimab (BI 655130) were administered every 4 weeks (q4w) via intravenous infusion over 12 weeks of treatment.
Participants who actually administered Spesolimab during the study were included in this group. 1 patient who was assigned to Placebo accidentally received one dose of Spesolimab and was analyzed in the Spesolimab group.

Serious adverse events	Placebo - actual	Spesolimab 1200 mg - actual	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	2 / 15 (13.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 7 (14.29%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Rectal abscess			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (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	Placebo - actual	Spesolimab 1200 mg - actual	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	15 / 15 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Lymphadenopathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Sputum increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 7 (14.29%)	4 / 15 (26.67%)	
occurrences (all)	1	6	
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye disorders			
Episcleritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ocular discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Colitis ulcerative			
subjects affected / exposed	2 / 7 (28.57%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Stasis dermatitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	

occurrences (all)	1	0	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Foot deformity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Helicobacter gastritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 7 (28.57%)	5 / 15 (33.33%)	
occurrences (all)	2	5	
Upper respiratory tract infection			

subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2017	The following main changes were implemented: - Addition of safety as a trial objective and of TEAEs as secondary endpoint, as safety is a central component of Phase IIa studies. - Change of time point for UC diagnosis to ≥5 months prior to screening in the inclusion criteria to allow stable TNFi treatment for ≥4 months prior to randomization.
13 December 2017	The following main changes were implemented: - Deletion of the lower body weight limit of 60 kg in Inclusion Criterion 2 and corresponding update of the section on dose selection, as a lower weight limit was no longer considered to be needed. - Modification of in Inclusion Criterion 4 to clarify that 'unchanged dose' includes unchanged dose and dosing interval.
04 March 2019	The following main changes were implemented: - Increase of the upper age limit in Inclusion Criterion 1 from 60 to 75 years to facilitate recruitment. - Increase of the upper body weight limit in Inclusion Criterion 2 from 100 to 120 kg to facilitate recruitment; corresponding update of the benefit-risk assessment to justify that this is not expected to affect PK of the trial drug. - Modification of Inclusion Criterion 4 to facilitate recruitment by adding the possibility of TNFi treatment with adalimumab and golimumab with unchanged doses for ≥2 months and specification that patients may or may not have received up to 2 different prior TNFi treatments; corresponding modification of the benefit-risk assessment and discussion of trial design. - Modification of Exclusion Criterion 3 to state that prior use of more than 2 different TNFis was not allowed, to facilitate recruitment. - Change of the timing of the primary endpoint from Week 8 to Week 12, and corresponding update of the wording for the primary objective and all other affected sections. Week 12 was defined as a project standard time point for primary efficacy measurement as initial data indicated a potential for slower onset of action for the spesolimab mechanism of action: The primary endpoint was changed to 'mucosal healing (MCS mESS ≤1) at Week 12' instead of 'at Week 8'; The secondary endpoint 'mucosal healing (MCS mESS ≤1) at Week 12' was deleted; A further endpoint 'mucosal healing (MCS mESS ≤1) at Week 8' was added. - Deletion of the following endpoints at Week 8 from the list of secondary endpoints and moving of these endpoints to the list of further endpoints: 'Modified clinical remission based on MCS (total modified MCS ≤2 and: RBS =0, Stool Frequency Score =0 or 1 and drop ≥1 from baseline, AND mESS ≤1) at Week 8'; 'Clinical remission based on MCS (total MCS ≤2 points, and all subscores ≤1 point) at Week 8'; 'Histological remission (RHI score ≤6) at Week 8'.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported