Clinical trial results:
A Mulitcenter, Open-Label PK Study of Mirikizumab in Pediatric Patients with Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2019-001298-96
Trial protocol	Outside EU/EEA
Global end of trial date	15 March 2023

Results information

Result version number	v1 (current)
This version publication date	28 September 2023
First version publication date	28 September 2023

Trial information

Trial identification

Sponsor protocol code	I6T-MC-AMBU

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04004611
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17410

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002208-PIP01-17
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	15 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed to evaluate how the body processes and removes mirikizumab. The study also evaluated safety and disease response in pediatric participants with UC taking mirikizumab. The study lasted about 52 weeks and included up to 18 visits.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2020
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	Japan: 4
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	United States: 17
Country: Number of subjects enrolled	Israel: 1
Worldwide total number of subjects	26
EEA total number of subjects	0

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)	7
Adolescents (12-17 years)	19
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Mirikizumab (Miri) dose groups to which pediatric participants are assigned at Week (wk) 0 (for induction period) and at wk 12 (for maintenance period) are dependent on participant' s weight and their clinical response status at wk 12 for maintenance period.

Pre-assignment

Screening details:

All participants who achieved a modified Mayo score (MMS) clinical response at wk 12 or wk 24 [non-responders (NR) at wk 12 who received extended intravenous (IV) induction dosing for 12 more wks] were eligible for the maintenance period.

Period 1

Period 1 title	OL Induction Period (Wk 0-12)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV

Arm description:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion every 4 weeks (Q4W) on weeks 0, 4, 8 for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	5 mg/kg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Arm title	OL Induction Period: 10 mg/kg Miri IV

Arm description:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	10 mg/kg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Arm title	OL Induction Period: 300 mg Miri IV

Arm description:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	300 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Number of subjects in period 1	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV	OL Induction Period: 10 mg/kg Miri IV	OL Induction Period: 300 mg Miri IV
Started	10	5	11
Completed	10	5	11

Period 2

Period 2 title	OL Maintenance Period (Wk 12-52)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)

Arm description:

Participants (≤20 kg weight) who were responders to mirikizumab at week 12 in induction received 50 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	50 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (≤20 kg weight) who were responders to mirikizumab at week 12 in induction received 50 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm title	OL Maintenance Period: 100 mg Miri SC

Arm description:

Participants (>20 to ≤40 kg weight) who were responders to mirikizumab at week 12 in induction received 100 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm type	Experimental

Investigational medicinal product name	100 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (>20 to ≤40 kg weight) who were responders to mirikizumab at week 12 in induction received 100 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm title	OL Maintenance Period: 200 mg Miri SC

Arm description:

Participants (>40 kg weight) who were responders to mirikizumab at week 12 in induction received 200 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	200 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (>40 kg weight) who were responders to mirikizumab at week 12 in induction received 200 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.

Arm title	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC

Arm description:

Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 50 mg miri (≤20 kg weight) SC Q4W through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	50 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 50 mg miri (≤20 kg weight) SC Q4W through week 48 or until loss of response was confirmed.

Arm title	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC

Arm description:

Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 100 mg miri (>20 to ≤40 kg weight) SC Q4W through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	100 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 100 mg miri (>20 to ≤40 kg weight) SC Q4W through week 48 or until loss of response was confirmed.

Arm title	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC

Arm description:

Participants (>40 kg) who were non responders to miri at week 12 in induction received 300 mg SC

Q4W for 12 weeks or discontinued after repeat induction, then received 200 mg miri SC Q4W through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	200 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (>40 kg) who were non responders to miri at week 12 in induction received 300 mg SC Q4W for 12 weeks or discontinued after repeat induction, then received 200 mg miri SC Q4W through week 48 or until loss of response was confirmed.

Number of subjects in period 2	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC
Started	1	8	9
Completed	1	7	8
Not completed	0	1	1
Adverse event, non-fatal	-	-	-
Withdrawal by Parent or Guardian	-	1	-
Lack of efficacy	-	-	1

Number of subjects in period 2	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC
Started	1	1	6
Completed	0	1	2
Not completed	1	0	4
Adverse event, non-fatal	-	-	1
Withdrawal by Parent or Guardian	-	-	-
Lack of efficacy	1	-	3

Period 3

Period 3 title	OL Induction and Maintenance Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No

Arm title	OL Induction and Maintenance Period: 5 mg/kg Miri IV

Arm description:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	5 mg/kg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Arm title	OL Induction and Maintenance Period: 10 mg/kg Miri IV

Arm description:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	10 mg/kg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Arm title	OL Induction and Maintenance Period: 300 mg Miri IV

Arm description:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	300 mg mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Number of subjects in period 3	OL Induction and Maintenance Period: 5 mg/kg Miri IV	OL Induction and Maintenance Period: 10 mg/kg Miri IV	OL Induction and Maintenance Period: 300 mg Miri IV
Started	10	5	11
Completed	9	4	6
Not completed	1	1	5
Adverse event, non-fatal	-	-	1
Withdrawal by Parent or Guardian	-	1	-
Lack of efficacy	1	-	4

Baseline characteristics

Reporting groups	
Reporting group title	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion every 4 weeks (Q4W) on weeks 0, 4, 8 for 12 weeks.	
Reporting group title	OL Induction Period: 10 mg/kg Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.	
Reporting group title	OL Induction Period: 300 mg Miri IV
Reporting group description:	
Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.	

Reporting group values	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV	OL Induction Period: 10 mg/kg Miri IV	OL Induction Period: 300 mg Miri IV
Number of subjects	10	5	11
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	9.6	11.6	14.0
standard deviation	± 4.22	± 1.14	± 1.26
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	6	3	6
Male	4	2	5
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	3	0	0
Not Hispanic or Latino	2	3	8
Unknown or Not Reported	5	2	3
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	3	9
More than one race	1	0	0

Unknown or Not Reported	0	0	1
Region of Enrollment			
All randomized participants.			
Units: Subjects			
Israel	0	0	1
Japan	1	2	1
South Korea	4	0	0
United States	5	3	9

Reporting group values	Total		
Number of subjects	26		
Age categorical			
Units: Subjects			

Age continuous			
All randomized participants.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	15		
Male	11		
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	13		
Unknown or Not Reported	10		
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	7		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	17		
More than one race	1		
Unknown or Not Reported	1		
Region of Enrollment			
All randomized participants.			
Units: Subjects			
Israel	1		
Japan	4		
South Korea	4		
United States	17		

End points

End points reporting groups

Reporting group title	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion every 4 weeks (Q4W) on weeks 0, 4, 8 for 12 weeks.	
Reporting group title	OL Induction Period: 10 mg/kg Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.	
Reporting group title	OL Induction Period: 300 mg Miri IV
Reporting group description:	
Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.	
Reporting group title	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)
Reporting group description:	
Participants (≤20 kg weight) who were responders to mirikizumab at week 12 in induction received 50 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.	
Reporting group title	OL Maintenance Period: 100 mg Miri SC
Reporting group description:	
Participants (>20 to ≤40 kg weight) who were responders to mirikizumab at week 12 in induction received 100 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.	
Reporting group title	OL Maintenance Period: 200 mg Miri SC
Reporting group description:	
Participants (>40 kg weight) who were responders to mirikizumab at week 12 in induction received 200 mg SC Q4W from week 12 through week 48 or until loss of response was confirmed.	
Reporting group title	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Reporting group description:	
Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 50 mg miri (≤20 kg weight) SC Q4W through week 48 or until loss of response was confirmed.	
Reporting group title	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC
Reporting group description:	
Participants (≤40 kg) who were non responders to miri at week 12 in induction received 10 mg SC Q4W for 12 weeks or discontinued after repeat induction, and then received 100 mg miri (>20 to ≤40 kg weight) SC Q4W through week 48 or until loss of response was confirmed.	
Reporting group title	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC
Reporting group description:	
Participants (>40 kg) who were non responders to miri at week 12 in induction received 300 mg SC Q4W for 12 weeks or discontinued after repeat induction, then received 200 mg miri SC Q4W through week 48 or until loss of response was confirmed.	
Reporting group title	OL Induction and Maintenance Period: 5 mg/kg Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.	
Reporting group title	OL Induction and Maintenance Period: 10 mg/kg Miri IV
Reporting group description:	
Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.	
Reporting group title	OL Induction and Maintenance Period: 300 mg Miri IV
Reporting group description:	
Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight	

through week 48 or until loss of response was confirmed.

Subject analysis set title	Mirikizumab
Subject analysis set type	Per protocol

Subject analysis set description:

Participants weighing >40 kg received a mirikizumab induction dose of 300 mg via IV infusion and participants weighing ≤40 kg received induction doses of 5 mg/kg or 10 mg/kg via IV infusion at Weeks 0, 4, and 8 for 12 weeks.

Primary: Pharmacokinetics (PK): Clearance of Mirikizumab

End point title	Pharmacokinetics (PK): Clearance of Mirikizumab[1]

End point description:

Clearance of mirikizumab was evaluated. The PK of mirikizumab is characterized at interim analysis points using mixed-effect (population PK) modelling approaches using the available induction and maintenance mirikizumab concentration data. Analysis population description (APD) included all randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Primary

End point timeframe:

Predose on week 4, 8, 12,16, 24, 36, 52 and post dose on week 0 and 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: No inferential statistics was planned for this endpoint.

End point values	Mirikizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Liters per hour per kilogram (L/hr/kg)				
geometric mean (geometric coefficient of variation)	0.000190 (± 59.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission

End point title	Percentage of Participants in Clinical Remission

End point description:

Clinical remission defined as achieving a 9-point modified Mayo score (MMS) for rectal bleeding (RB) = 0, stool frequency (SF) = 0 or 1 and endoscopy (ES) = 0 or 1 (excluding friability). The MMS is a composite score of ulcerative colitis disease activity calculated as the sum of three subscores: SF subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal); RB subscore, based on the participant's diary and scored from 0 (no blood seen) to 3 (blood alone passed); ES subscore, based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding,ulceration. APD included Modified Intention-to-treat population (mITT):All randomized participants who received at least one dose of study drug and who had clinical remission measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	62.5 (30.6 to 86.3)	55.6 (26.7 to 81.1)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Response

End point title	Percentage of Participants in Clinical Response

End point description:

Clinical response defined as a decrease in the 9-point MMS [RB, SF and the ES findings] inclusive of ≥ 2 points and ≥30% from baseline with either a decrease of RB subscore of ≥ or RB subscore of 0 or 1. The MMS is a composite score of ulcerative colitis disease activity calculated as the sum of three subscores: SF subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal); RB subscore, based on the participant's diary and scored from 0 (no blood seen) to 3 (blood alone passed); ES subscore, based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). APD included mITT: All randomized participants who received at least one dose of study drug and who had the clinical response measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	75.0 (40.9 to 92.9)	88.9 (56.5 to 98.0)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who are in MMS Clinical Remission Without the Use of Corticosteroids

End point title	Percentage of Participants Who are in MMS Clinical Remission Without the Use of Corticosteroids

End point description:

Corticosteroid-free clinical remission was defined as an SF subscore = 0 or 1, RB subscore = 0, ES ≤ 1 (excluding friability), and have not received corticosteroids for ≥ 12 weeks in the 52-Week Treatment Period. Each component subscore ranged from 0 to 3 and total score range of the MMS was from 0 to 9, with higher scores indicating more severe disease. APD included mITT: All randomized participants who received at least one dose of study drug and who had the modified mayo score clinical remission without the use of corticosteroids measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	62.5 (30.6 to 86.3)	55.6 (26.7 to 81.1)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission Based on the Pediatric Ulcerative Colitis Activity Index (PUCAI)

End point title	Percentage of Participants in Clinical Remission Based on the Pediatric Ulcerative Colitis Activity Index (PUCAI)

End point description:

The PUCAI is a clinician-administered, 6-item questionnaire that measures: abdominal pain; RB; stool consistency; number of stools; nocturnal stools; and activity level. For PUCAI score all items are answered as an average over the 'past 2 days'. A total disease activity score is calculated from 0 to 85, with Severe 65-85; Moderate:35-60; Mild:10-30, and None:<10. The clinician will record the participant or caregiver/legal guardian responses for the PUCAI electronically as source data in the tablet device at appropriate visits. PUCAI clinical remission is defined as a PUCAI score of <10 points. APD included mITT: All randomized participants who received at least one dose of study drug and who had the clinical remission based on the PUCAI measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	75.0 (40.9 to 92.9)	77.8 (45.3 to 93.7)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Response Based on the PUCAI

End point title	Percentage of Participants in Clinical Response Based on the PUCAI

End point description:

PUCAI clinical response is defined as a reduction in baseline PUCAI score of ≥20 points. APD included mITT: All randomized participants who received at least one dose of study drug and who had the clinical response based on the PUCAI measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to	75.0 (40.9 to	88.9 (56.5 to	0.0 (0.0 to

	79.3)	92.9)	98.0)	79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Endoscopic Remission

End point title	Percentage of Participants in Endoscopic Remission

End point description:

Endoscopic remission at week 52 is defined as achieving a Mayo endoscopic subscore of 0 or 1 (excluding friability) at Week 52. ES subscore is based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). APD included mITT: All randomized participants who received at least one dose of study drug and who had the endoscopic remission measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	62.5 (30.6 to 86.3)	55.6 (26.7 to 81.1)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri	OL Maintenance Period: NR: 300 mg Miri IV		

	IV/100 mg Miri SC	/200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Symptomatic Remission

End point title	Percentage of Participants in Symptomatic Remission

End point description:

Symptomatic remission at week 52 is defined as a Mayo score for RB=0, SF=0 or 1 with ≥ 1 point decrease from baseline.
SF subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal).
RB subscore, based on the participant's diary and scored from 0 (no blood seen) to 3 (blood alone passed).
APD included mITT: All randomized participants who received at least one dose of study drug and who had the symptomatic remission measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	75.0 (40.9 to 92.9)	66.7 (35.4 to 87.9)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to	0.0 (0.0 to		

79.3)	39.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Height Velocity (in Centimeters/Year)

End point title	Height Velocity (in Centimeters/Year)

End point description:

Observed height velocity by gender and age group was calculated. Age groups for which this was summarized were 2 to <8, 8 to <12, and 12 to <18. Observed height velocity by gender and age group was calculated at baseline according to the following formula: (Present Height [cm] - Previous Height [cm])/Interval (months) Between Measurements × 12. 9999=Data Not Available (N/A) and individual values are provided. APD included mITT: All randomized participants who received at least one dose of study drug and who had the height velocity measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Induction and Maintenance Period: 5 mg/kg Miri IV	OL Induction and Maintenance Period: 10 mg/kg Miri IV	OL Induction and Maintenance Period: 300 mg Miri IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[2]	5[3]	11	
Units: centimeter per year (cm/year)				
arithmetic mean (standard deviation)				
Female:2-<8 years (n=1,0,0)	9999 (± 9999)	0 (± 0)	0 (± 0)	
Female:8-<12 years (n=2,0,0)	8.65 (± 3.2)	0 (± 0)	0 (± 0)	
Female:12-<18 years (n=3,2,2)	4.54 (± 4.2)	4.14 (± 1.3)	2.97 (± 0.2)	
Male:2-<8 years (n=1,0,0)	9999 (± 9999)	0 (± 0)	0 (± 0)	
Male:8-<12 years (n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Male:12-<18 years (n=2,1,4)	12.67 (± 1.0)	9999 (± 9999)	3.65 (± 4.3)	

Notes:

[2] - Female:2-<8 years: Individual value= 7.85; Male: 2 - <8 years: Individual value=7.72

[3] - Male: 8-<12 years, Male:12 - <8 years: Individual value= 3.64

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight

End point title	Change from Baseline in Body Weight

End point description:

Change from Baseline in body weight by gender and age group was calculated. 9999=Data Not Available

(N/A) and individual values are provided. APD included mITT: All randomized participants who received at least one dose of study drug and who had the body weight measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	OL Induction and Maintenance Period: 5 mg/kg Miri IV	OL Induction and Maintenance Period: 10 mg/kg Miri IV	OL Induction and Maintenance Period: 300 mg Miri IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[4]	5[5]	11	
Units: kg				
arithmetic mean (standard deviation)				
Female:2-<8 years(n=1,0,0)	9999 (± 9999)	0 (± 0)	0 (± 0)	
Female:8-<12 years(n=2,0,0)	8 (± 1.1)	0 (± 0)	0 (± 0)	
Female:12-<18 years(n=3,2,2)	9 (± 7.1)	9 (± 3.5)	8 (± 2.7)	
Male:2-<8 years(n=1,0,0)	9999 (± 9999)	0 (± 0)	0 (± 0)	
Male:8-<12 years(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Male:12-<18 years(n=2,1,4)	13 (± 11.6)	9999 (± 9999)	2 (± 3.2)	

Notes:

[4] - Female:2-<8 years: Individual value = 5.1; Male:2-<8 years: Individual value = 1.3

[5] - Male: 8 - <12 years: Individual value = 3; Male: 12 - <18 years: Individual value = 3.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Histologic-Endoscopic Mucosal Remission

End point title	Percentage of Participants with Histologic-Endoscopic Mucosal Remission

End point description:

Histologic-endoscopic mucosal remission is defined as achieving both histologic remission and endoscopic remission. Histologic remission is defined as Geboes histological subscores of 0 for parameters: 2B (neutrophils in lamina propria), 3 (neutrophils in epithelium), 4 (crypt destruction), and 5 (erosion or ulceration). APD included mITT: All randomized participants who received at least one dose of study drug and who had the histologic-endoscopic mucosal remission measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	62.5 (30.6 to 86.3)	44.4 (18.9 to 73.3)	0.0 (0.0 to 79.3)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 79.3)	0.0 (0.0 to 39.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in 7-day average of Abdominal Pain Numeric Rating Scale (NRS) score at Week 12

End point title	Change from baseline in 7-day average of Abdominal Pain Numeric Rating Scale (NRS) score at Week 12

End point description:

The Abdominal Pain NRS is a single participant-reported item that measures the "worst abdominal pain in the past 24 hours" using a 6-point scale ranging from 0 (no pain) to 5 (worst possible pain) for 8-11 years old, and 11-point NRS ranging from 0 (no pain) to 10 (worst possible pain) for children < 8 years old as completed by a caregiver and those 12-17 years old. Abdominal pain NRS Score calculated by averaging data from all available daily diary entries of Abdominal Pain NRS for a 7 day period. A negative change from baseline indicates improvement in the participant's Abdominal Pain NRS. 9999=Data Not Available (N/A) and individual values are provided. APD included mITT: All randomized participants who received at least one dose of study drug and who had the 7-day average of Abdominal Pain NRS measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	OL Induction Period: 5 milligram per kilogram (mg/kg) Miri IV	OL Induction Period: 10 mg/kg Miri IV	OL Induction Period: 300 mg Miri IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	5[6]	11	
Units: score on a scale				
arithmetic mean (standard deviation)				
2-<8 years(n=3,0,0)	-3 (± 2.1)	0 (± 0)	0 (± 0)	
8-<12 years(n=2,1,0)	-3 (± 2.1)	9999 (± 9999)	0 (± 0)	
12-<18 years(n=5,3,10)	-4 (± 2.7)	-2 (± 1.5)	-1 (± 2.8)	

Notes:

[6] - 8-<12 years: Individual value=-2

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 7-day Average of Abdominal Pain NRS Score at Week 52

End point title	Change From Baseline in 7-day Average of Abdominal Pain NRS Score at Week 52

End point description:

The Abdominal Pain NRS is a single participant-reported item that measures the "worst abdominal pain in the past 24 hours" using a 6-point scale ranging from 0 (no pain) to 5 (worst possible pain) for 8-11 years old, and 11-point NRS ranging from 0 (no pain) to 10 (worst possible pain) for children < 8 years old as completed by a caregiver and those 12-17 years old. Abdominal Pain NRS Score is calculated by averaging data from all available daily diary entries of abdominal pain NRS for a 7 day period. A negative change from baseline indicates improvement in the participant's Abdominal Pain NRS. 9999=Data Not Available (N/A) and individual values are provided. APD included all randomized participants who received at least one dose of study drug and who had the 7-day average of Abdominal Pain NRS measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	OL Maintenance Period: 50 mg Miri Subcutaneous (SC)	OL Maintenance Period: 100 mg Miri SC	OL Maintenance Period: 200 mg Miri SC	OL Maintenance Period: NR: 10 mg/kg Miri IV/50 mg Miri SC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	8	9	1
Units: score on a scale				
arithmetic mean (standard deviation)				
2-<8 years(n=1,1,0,1,0,0)	9999 (± 9999)	9999 (± 9999)	0 (± 0)	0 (± 0)
8-<12 years(n=0,3,0,0,0,0)	0 (± 0)	-2 (± 1.0)	0 (± 0)	0 (± 0)
12-<18 years(n=0,3,8,0,1,6)	0 (± 0)	-5 (± 3.1)	-4 (± 2.4)	0 (± 0)

End point values	OL Maintenance Period: NR: 10 mg/kg Miri IV/100 mg Miri SC	OL Maintenance Period: NR: 300 mg Miri IV /200 mg Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	6		
Units: score on a scale				
arithmetic mean (standard deviation)				
2-<8 years(n=1,1,0,1,0,0)	0 (± 0)	0 (± 0)		
8-<12 years(n=0,3,0,0,0,0)	0 (± 0)	0 (± 0)		
12-<18 years(n=0,3,8,0,1,6)	9999 (± 9999)	0 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Induction Period (Up to 12 Weeks), Induction and Maintenance Period (Up to 52 Weeks)

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. Participants were analyzed according to the weight/treatment dose group to which they were assigned. Adverse event data is reported for the induction period and combined induction and maintenance periods as per planned analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	OL Induction Period: 5 mg/kg Miri IV

Reporting group description:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion every 4 Q4W on weeks 0, 4, 8 for 12 weeks.

Reporting group title	OL Induction and Maintenance Period: 5 mg/kg Miri IV

Reporting group description:

Participants (≤40 kg weight) received 5 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Reporting group title	OL Induction Period: 10 mg/kg Miri IV

Reporting group description:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Reporting group title	OL Induction and Maintenance Period: 10 mg/kg Miri IV

Reporting group description:

Participants (≤40 kg weight) received 10 mg/kg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Reporting group title	OL Induction Period: 300 mg Miri IV

Reporting group description:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks.

Reporting group title	OL Induction and Maintenance Period: 300 mg Miri IV

Reporting group description:

Participants (>40 kg weight) received 300 mg mirikizumab given as an IV infusion Q4W on weeks 0, 4, 8 for 12 weeks followed by IV or SC mirikizumab based on their week 12 response status and weight through week 48 or until loss of response was confirmed.

Serious adverse events	OL Induction Period: 5 mg/kg Miri IV	OL Induction and Maintenance Period: 5 mg/kg Miri IV	OL Induction Period: 10 mg/kg Miri IV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Gastrointestinal disorders			
appendicitis noninfective			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis ulcerative			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
pseudarthrosis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OL Induction and Maintenance Period: 10 mg/kg Miri IV	OL Induction Period: 300 mg Miri IV	OL Induction and Maintenance Period: 300 mg Miri IV
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
appendicitis noninfective			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (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			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
pseudarthrosis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (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	OL Induction Period: 5 mg/kg Miri IV	OL Induction and Maintenance Period: 5 mg/kg Miri IV	OL Induction Period: 10 mg/kg Miri IV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)	9 / 10 (90.00%)	2 / 5 (40.00%)
General disorders and administration site conditions			
administration site oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
catheter site induration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
fatigue			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
feeling abnormal			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
infusion site reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
injection site erythema			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
injection site oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
injection site pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
injection site pruritus			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
injection site reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
pyrexia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
puncture site pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
puncture site oedema			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
immunosuppression			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
seasonal allergy			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[1]	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
rhinorrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
oropharyngeal pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
pharyngeal swelling			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
throat irritation			
alternative dictionary used:			

MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
insomnia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
procedural anxiety			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
arthropod sting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
infusion related reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
burning sensation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

dizziness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
headache			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	0 / 5 (0.00%)
occurrences (all)	7	8	0
migraine			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
tremor			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
blood loss anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
ear pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
motion sickness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

abdominal pain upper			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
abdominal discomfort			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
anal incontinence			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
constipation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
dyspepsia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
food poisoning			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
gastritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
haemorrhoids			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
lip blister			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
nausea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
vomiting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
dermatitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
rash maculo-papular			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
rash			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
pruritus			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
urticaria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
pollakiuria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Endocrine disorders			
growth hormone deficiency			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
arthralgia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
fracture nonunion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
muscle spasms			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
asymptomatic covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
gastroenteritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
impetigo			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
oral herpes			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
sinusitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
tooth abscess			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
tinea infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OL Induction and Maintenance Period: 10 mg/kg Miri IV	OL Induction Period: 300 mg Miri IV	OL Induction and Maintenance Period: 300 mg Miri IV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	8 / 11 (72.73%)	11 / 11 (100.00%)
General disorders and administration site conditions			
administration site oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
catheter site induration			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
fatigue			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
feeling abnormal			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
infusion site reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
injection site erythema			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
injection site oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
injection site pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	3 / 11 (27.27%)
occurrences (all)	7	0	22
injection site pruritus			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
injection site reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
pyrexia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
puncture site pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
puncture site oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Immune system disorders			
immunosuppression			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
seasonal allergy			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[1]	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
rhinorrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
oropharyngeal pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
pharyngeal swelling			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
throat irritation			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Psychiatric disorders			
insomnia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
procedural anxiety			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
arthropod sting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
infusion related reaction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	2	2
Nervous system disorders			
burning sensation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
dizziness			

alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
headache			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
migraine			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
tremor			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
blood loss anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
ear pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
motion sickness			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

abdominal pain upper			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
abdominal discomfort			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
anal incontinence			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
constipation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
dyspepsia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
food poisoning			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
gastritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
haemorrhoids			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
lip blister			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
nausea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
vomiting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
dermatitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
rash maculo-papular			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
rash			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	2 / 11 (18.18%)
occurrences (all)	0	2	2
pruritus			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
urticaria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Renal and urinary disorders			
pollakiuria			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
growth hormone deficiency			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
arthralgia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
fracture nonunion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
muscle spasms			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Infections and infestations			

covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	2
asymptomatic covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
gastroenteritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
impetigo			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
oral herpes			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
sinusitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
upper respiratory tract infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
tooth abscess			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
tinea infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Notes:

[1] - 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: Gender specific events only occurring in male or female participants have had the number of participants at Risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2019	- Updated the definition of mucosal healing; - Exploratory endpoint has been added; -Removed text referring to randomization; - Clarification provided in schedule of activities; - Updated intestinal dysplasia language; - Added description of UCEIS; - Inclusion and exclusion criteria were revised; - Clarifications on treatments administered, physical examination, clinical laboratory tests, prohibited medications, Permitted medications with dose stabilization.
30 April 2021	- Secondary endpoint has been updated; - Clarification provided in schedule of activities; - Updated age for hormone collection; - Clarified overall design; wording; - Inclusion and exclusion criteria were revised; - Clarifications on treatments administered, physical examination, clinical laboratory tests, prohibited medications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported