Clinical trial results:
A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PARALLEL-ARM, PLACEBO-CONTROLLED MAINTENANCE STUDY OF MIRIKIZUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS (LUCENT 2)

Summary

EudraCT number	2017-003238-96
Trial protocol	DE GB NL LV CZ LT ES BE HU AT SK DK HR IT RO
Global end of trial date	

Results information

Result version number	v1
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	I6T-MC-AMBG

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03524092
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16823

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)	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	Interim
Date of interim/final analysis	03 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of mirikizumab as maintenance therapy in participants who completed as clinical responders in the prior 12-week induction study LUCENT-1 (NCT03518086).

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	19 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 31
Country: Number of subjects enrolled	China: 15
Country: Number of subjects enrolled	Czechia: 52
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 57
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	India: 72
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Japan: 123
Country: Number of subjects enrolled	Latvia: 29
Country: Number of subjects enrolled	Lithuania: 22
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Netherlands: 10

Country: Number of subjects enrolled	Poland: 122
Country: Number of subjects enrolled	Romania: 14
Country: Number of subjects enrolled	Russian Federation: 100
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Slovakia: 21
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	Ukraine: 93
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 140
Worldwide total number of subjects	1177
EEA total number of subjects	468

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)	1083
From 65 to 84 years	94
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was designed to evaluate the safety and efficacy of mirikizumab (miri) in achieving remission at Week (Wk) 40 in participants who completed the 12-week induction study I6T-MC-AMAN (NCT03518086) as clinical responders to mirikizumab. Results for maximum extended enrollment (ME2) participants will be posted after the study completion.

Period 1

Period 1 title	Blinded Maintenance Period (Wk 0-40)
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	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)

Arm description:

Participants who were responders to blinded mirikizumab (miri) at Week 12 in induction study (LUCENT-1) randomized to withdraw from mirikizumab and start receiving PBO SC every 4 weeks (Q4W) from Week 0 of maintenance study (LUCENT-2) until Week 40 or until loss of response was confirmed.

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

Dosage and administration details:

PBO SC every 4 weeks (Q4W).

Arm title	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC

Arm description:

Participants who were responders to blinded mirikizumab at Week 12 in induction study (LUCENT-1) randomized to continue to receive 200 mg mirikizumab SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.

Arm type	Experimental
Investigational medicinal product name	Mirikizumab
Investigational medicinal product code	
Other name	LY3074828
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg mirikizumab SC Q4W.

Arm title	Maintenance Period: PBO IR - PBO SC

Arm description:

Participants who were responders to blinded placebo at Week 12 in induction study (LUCENT-1) continue to receive blinded placebo SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.

Arm type	PBO IR

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PBO SC every 4 weeks (Q4W).

Number of subjects in period 1[1]	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC	Maintenance Period: PBO IR - PBO SC
Started	192	389	135
Received at Least One Dose of Study Drug	192	389	135
Completed	119	347	90
Not completed	73	42	45
Consent withdrawn by subject	7	8	6
Physician decision	-	1	-
Adverse event, non-fatal	16	6	1
Pregnancy	-	-	1
Loss of Response Rescue Period	42	19	29
Lost to follow-up	-	1	-
Lack of efficacy	8	6	7
Protocol deviation	-	1	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: Data is reported separately for Blinded Maintenance Period as Induction Responder (IR) and open label extended Induction period as Induction Nonresponders.

Period 2

Period 2 title	Open Label Extended Induction (Wk 0-12)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Extended Induction: Induction Nonresponders - 300mg Miri IV

Arm description:

Participants who were nonresponders to blinded mirikizumab or placebo in induction study (LUCENT-1), received additional 3 doses of open label 300 mg mirikizumab IV Q4W during extended induction period from Week 0 of LUCENT-2 until Week 12.

Arm type	Induction Nonresponders

Investigational medicinal product name	Mirikizumab
Investigational medicinal product code	
Other name	LY3074828
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mg mirikizumab IV Q4W for 3 doses.

Number of subjects in period 2[2]	Extended Induction: Induction Nonresponders - 300mg Miri IV
Started	461
Completed	271
Not completed	190
Physician decision	1
Consent withdrawn by subject	6
Lack of capacity due to lack of staff	1
Adverse event, non-fatal	11
Covid-19 related study disruption	4
Lack of efficacy	162
Protocol deviation	5

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Included only participants who entered open label extended induction period.

Period 3

Period 3 title	Open Label Maintenance Period (Wk 12-40)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open Label Maintenance Period (Wk 12-40)

Arm description:

Participants who initially did not respond to induction study (LUCENT-1), but responded to extended induction therapy at Week 12 of LUCENT-2 (delayed responders), received 200 mg mirikizumab SC Q4W during open label maintenance period from Week 12 until Week 40 or until early termination (rescue was not available for these participants).

Arm type	Open Label Maintenance Period
Investigational medicinal product name	Mirikizumab
Investigational medicinal product code	
Other name	LY3074828
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg mirikizumab SC Q4W.

Number of subjects in period 3	Open Label Maintenance Period (Wk 12-40)
Started	271
Completed	256
Not completed	15
Adverse event, non-fatal	4
Covid-19 related study disruption	1
Lack of efficacy	9
Protocol deviation	1

Period 4

Period 4 title	Loss of Response Rescue Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV

Arm description:

Participants who received blinded PBO SC or blinded 200 mg mirikizumab SC Q4W during maintenance period and experienced a loss of response at or after Week 12, received rescue therapy with open label 300 mg mirikizumab intravenous (IV) Q4W for 3 doses.

Arm type	LOR Rescue Period
Investigational medicinal product name	Mirikizumab
Investigational medicinal product code	
Other name	LY3074828
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mg mirikizumab IV Q4W.

Number of subjects in period 4[3]	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV
Started	90
Completed	81
Not completed	9
Consent withdrawn by subject	1

Adverse event, non-fatal	2
Pregnancy	1
Lack of efficacy	5

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Included only participants who experienced loss of response and were eligible for loss of response rescue induction.

Baseline characteristics

Reporting groups	
Reporting group title	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)
Reporting group description:	
Participants who were responders to blinded mirikizumab (miri) at Week 12 in induction study (LUCENT-1) randomized to withdraw from mirikizumab and start receiving PBO SC every 4 weeks (Q4W) from Week 0 of maintenance study (LUCENT-2) until Week 40 or until loss of response was confirmed.	
Reporting group title	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Reporting group description:	
Participants who were responders to blinded mirikizumab at Week 12 in induction study (LUCENT-1) randomized to continue to receive 200 mg mirikizumab SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.	
Reporting group title	Maintenance Period: PBO IR - PBO SC
Reporting group description:	
Participants who were responders to blinded placebo at Week 12 in induction study (LUCENT-1) continue to receive blinded placebo SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.	

Reporting group values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC	Maintenance Period: PBO IR - PBO SC
Number of subjects	192	389	135
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: years			
arithmetic mean	41.20	43.30	40.80
standard deviation	± 12.88	± 14.13	± 13.40
Gender categorical			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
Female	78	160	61
Male	114	229	74
Ethnicity			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1). Ethnicity data collected only for United States (US) participants.			
Units: Subjects			
Hispanic or Latino	2	12	2
Not Hispanic or Latino	18	33	8
Unknown or Not Reported	172	344	125
Race			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
American Indian or Alaska Native	1	3	2
Asian	51	93	28
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	6	0

White	138	285	103
More than one race	0	0	2
Unknown or Not Reported	2	2	0
Region of Enrollment			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
Argentina	1	5	0
Australia	0	3	0
Austria	2	2	0
Belgium	1	2	2
Canada	3	5	2
China	3	4	1
Czechia	7	19	11
Denmark	3	3	0
France	10	18	6
Germany	5	13	3
Hungary	1	8	2
India	18	25	16
Ireland	0	1	0
Israel	3	6	1
Italy	3	12	4
Japan	25	47	8
Latvia	8	10	3
Lithuania	6	4	5
Malaysia	0	3	0
Mexico	1	3	2
Netherlands	1	6	0
Poland	15	32	13
Romania	4	2	0
Russia	19	36	16
Serbia	1	9	4
Slovakia	6	7	1
South Korea	3	8	1
Spain	1	6	4
Switzerland	0	4	0
Taiwan	1	1	0
Turkey	0	5	2
Ukraine	18	31	16
United Kingdom	2	4	2
United States	21	45	10

Reporting group values	Total		
Number of subjects	716		
Age categorical Units: Subjects			

Age continuous			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: years arithmetic mean standard deviation	- -		

Gender categorical			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
Female	299		
Male	417		
Ethnicity			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1). Ethnicity data collected only for United States (US) participants.			
Units: Subjects			
Hispanic or Latino	16		
Not Hispanic or Latino	59		
Unknown or Not Reported	641		
Race			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
American Indian or Alaska Native	6		
Asian	172		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	6		
White	526		
More than one race	2		
Unknown or Not Reported	4		
Region of Enrollment			
All randomized participants who are responders to Miri and PBO in induction study (LUCENT-1).			
Units: Subjects			
Argentina	6		
Australia	3		
Austria	4		
Belgium	5		
Canada	10		
China	8		
Czechia	37		
Denmark	6		
France	34		
Germany	21		
Hungary	11		
India	59		
Ireland	1		
Israel	10		
Italy	19		
Japan	80		
Latvia	21		
Lithuania	15		
Malaysia	3		
Mexico	6		
Netherlands	7		
Poland	60		
Romania	6		
Russia	71		
Serbia	14		
Slovakia	14		

South Korea	12		
Spain	11		
Switzerland	4		
Taiwan	2		
Turkey	7		
Ukraine	65		
United Kingdom	8		
United States	76		

End points

End points reporting groups

Reporting group title	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)

Reporting group description:

Participants who were responders to blinded mirikizumab (miri) at Week 12 in induction study (LUCENT-1) randomized to withdraw from mirikizumab and start receiving PBO SC every 4 weeks (Q4W) from Week 0 of maintenance study (LUCENT-2) until Week 40 or until loss of response was confirmed.

Reporting group title	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC

Reporting group description:

Participants who were responders to blinded mirikizumab at Week 12 in induction study (LUCENT-1) randomized to continue to receive 200 mg mirikizumab SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.

Reporting group title	Maintenance Period: PBO IR - PBO SC

Reporting group description:

Participants who were responders to blinded placebo at Week 12 in induction study (LUCENT-1) continue to receive blinded placebo SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.

Reporting group title	Extended Induction: Induction Nonresponders - 300mg Miri IV

Reporting group description:

Participants who were nonresponders to blinded mirikizumab or placebo in induction study (LUCENT-1), received additional 3 doses of open label 300 mg mirikizumab IV Q4W during extended induction period from Week 0 of LUCENT-2 until Week 12.

Reporting group title	Open Label Maintenance Period (Wk 12-40)

Reporting group description:

Participants who initially did not respond to induction study (LUCENT-1), but responded to extended induction therapy at Week 12 of LUCENT-2 (delayed responders), received 200 mg mirikizumab SC Q4W during open label maintenance period from Week 12 until Week 40 or until early termination (rescue was not available for these participants).

Reporting group title	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV

Reporting group description:

Participants who received blinded PBO SC or blinded 200 mg mirikizumab SC Q4W during maintenance period and experienced a loss of response at or after Week 12, received rescue therapy with open label 300 mg mirikizumab intravenous (IV) Q4W for 3 doses.

Subject analysis set title	200 Milligram (mg) Miri SC
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received 200 mg mirikizumab SC every Q4W.

Primary: Percentage of Participants in Clinical Remission at Week 40

End point title	Percentage of Participants in Clinical Remission at Week 40[1]

End point description:

Clinical remission at week 40 is defined as achieving a 9-point modified Mayo score for rectal bleeding=0, stool frequency=0 or 1 with ≥ 1 point decrease from baseline, and endoscopy=0 or 1 (excluding friability). Stool Frequency Subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal); Rectal Bleeding Subscore, based on the participant's diary and scored from 0 (no blood) to 3 (blood only passed); Endoscopy Subscore, based on central reading of colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). Analysis population description (APD): Modified Intention-to-treat population (mITT): All randomized participants who received at least one dose of study drug and who had the modified Mayo score measured correctly at baseline. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Primary

End point timeframe:

Week 40

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	25.1 (18.8 to 31.5)	49.9 (44.7 to 55.0)		

Statistical analyses

Statistical analysis title	Percentage of Participants in Clinical Remission
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	31.2

Secondary: Percentage of Participants in Endoscopic Remission at Week 40

End point title	Percentage of Participants in Endoscopic Remission at Week

End point description:

Endoscopic remission at week 40 is defined as achieving a Mayo endoscopic subscore of 0 or 1 (excluding friability) at Week 40. Endoscopy subscore is based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration). APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least one dose of study drug and who had the modified Mayo score 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 40

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	29.1 (22.4 to 35.7)	58.6 (53.6 to 63.7)		

Statistical analyses

Statistical analysis title	Percentage of Participants in Endoscopic Remission
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.2
upper limit	36.8

Secondary: Percentage of Participants with Histologic Remission at Week 40

End point title	Percentage of Participants with Histologic Remission at Week 40[3]

End point description:

Histologic remission was assessed using the Geboes histologic scoring system developed for assessment of histologic disease activity in ulcerative colitis. Remission was defined as Geboes histological subscore of 0 for grades: 2b (lamina propria neutrophils), and 3 (neutrophils in epithelium), and 4 (crypt destruction), and 5 (erosion or ulceration). APD: Modified Intention-to-treat population (mITT): All randomized participants (pts) who received at least one dose of study drug and who had the modified Mayo score 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 40

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	24.6 (18.3 to 30.9)	48.5 (43.4 to 53.6)		

Statistical analyses

Statistical analysis title	Percentage of Pts with Histologic Remission
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.5
upper limit	30.5

Secondary: Percentage of Participants in Symptomatic Remission at Week 40

End point title	Percentage of Participants in Symptomatic Remission at Week 40[4]

End point description:

Symptomatic remission at week 40 is defined as a Mayo score for rectal bleeding=0, stool frequency=0 or 1 with ≥ 1 point decrease from baseline. Stool frequency subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal). Rectal bleeding subscore, based on the participant's diary and scored from 0 (no blood seen) to 3 (blood alone passed). APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least one dose of study drug and who had the modified Mayo score 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 40

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	39.7 (32.5 to 46.8)	71.0 (66.3 to 75.6)		

Statistical analyses

Statistical analysis title	Percentage of Pts in Symptomatic Remission
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	30.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.9
upper limit	38.6

Secondary: Percentage of Participants in Endoscopic Response at Week 40

End point title	Percentage of Participants in Endoscopic Response at Week

End point description:

Endoscopic response at week 40 is defined as achieving at least a 1 point decrease from baseline in the Mayo endoscopic subscore. APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least one dose of study drug and who had the modified Mayo score 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 40

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	40.8 (33.6 to 48.0)	72.6 (68.0 to 77.2)		

Statistical analyses

Statistical analysis title	Percentage of Participants in Endoscopic Response
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.4
upper limit	39.6

Secondary: Percentage of Participants in Clinical Response at Week 40

End point title	Percentage of Participants in Clinical Response at Week 40[6]

End point description:

Clinical response at week 40 is defined as a decrease in the 9-point modified Mayo score (MMS) [rectal bleeding, stool frequency and the endoscopic findings] inclusive of >= 2 points and >=30% from baseline with either a decrease of rectal bleeding subscore of >=1 or rectal bleeding subscore of 0 or 1.The MMS is a composite score of ulcerative colitis disease activity calculated as the sum of three subscores: Stool frequency subscore, based on the participant's diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal); Rectal bleeding subscore, based on the participant's diary and scored from 0 (no blood seen) to 3 (blood alone passed); Endoscopy subscore, based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding,ulceration). APD: mITT: All randomized participants who received at least one dose of study drug and who had the modified Mayo score measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 40
Participants were analysed per their assigned treatment arm regardless of the treatment they actually

received.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (confidence interval 95%)	49.2 (41.8 to 56.5)	80.3 (76.2 to 84.4)		

Statistical analyses

Statistical analysis title	Percentage of Participants in Clinical Response
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	30.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.3
upper limit	38.9

Secondary: Change from Baseline to Week 40 in Health Related Quality of Life: Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

End point title	Change from Baseline to Week 40 in Health Related Quality of Life: Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score[7]

End point description:

The IBDQ is a 32-item participant-completed questionnaire that measures 4 aspects of subjects' lives: symptoms directly related to the primary bowel disturbance, systemic symptoms, emotional function, and social function. Responses are graded on a 7-point. Likert scale in which 7 denotes "not a problem at all" and 1 denotes "a very severe problem." Scores range from 32 to 224; a higher score indicates a better quality of life. Least square (LS) Mean was calculated using analysis of covariance (ANCOVA) model for post-baseline measures: The ANCOVA model includes: treatment, baseline value, prior biologic or tofacitinib failure (yes/no), baseline corticosteroid use (yes/no), clinical remission status (yes/no) at AMAN Week 12, and region (North America/Europe/Other). Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Induction Baseline, Week 40
APD: mITT: All randomized participants who received at least 1 dose of study drug and had a baseline and at least one post-baseline IBDQ measurement.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: score on a scale				
least squares mean (standard error)	24.51 (± 2.767)	49.75 (± 2.102)		

Statistical analyses

Statistical analysis title	Change from Baseline to Week 40 in IBDQ
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	25.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.16
upper limit	31.32
Variability estimate	Standard error of the mean
Dispersion value	3.094

Notes:

[8] - ANCOVA with modified baseline observation carried forward (mBOCF).

Secondary: Change from Baseline to Week 40 in Fecal Calprotectin

End point title	Change from Baseline to Week 40 in Fecal Calprotectin[9]

End point description:

Fecal calprotectin is an indicator of inflammation in the colon with higher levels indicative of higher levels of inflammation. Least square (LS) Mean was calculated using ANCOVA model for post-baseline measures: The ANCOVA model includes treatment, baseline value, prior biologic or tofacitinib failure (yes/no), corticosteroid use (yes/no) at AMAN baseline, region (North America/Europe/Other), Clinical Remission status (yes/no) at AMAN Week 12. APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least 1 dose of study drug and had a baseline and at least one post-baseline fecal calprotectin measurement. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Induction Baseline, Week 40

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: milligram per kilogram (mg/kg)				
least squares mean (standard error)	-1155.82 (± 221.394)	-1995.47 (± 172.443)		

Statistical analyses

Statistical analysis title	Change from Baseline in Fecal Calprotectin
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [10]
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-839.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1323.08
upper limit	-356.21
Variability estimate	Standard error of the mean
Dispersion value	245.99

Notes:

[10] - ANCOVA with modified baseline observation carried forward (mBOCF).

Secondary: Change From Baseline to Week 40 in Bowel Urgency Based on the Urgency Numeric Rating Scale (NRS)

End point title	Change From Baseline to Week 40 in Bowel Urgency Based on the Urgency Numeric Rating Scale (NRS)[11]

End point description:

The Urgency NRS is a single participant reported item that measures the severity for the urgency (sudden or immediate need) to have a bowel movement in the past 24 hours using an 11-point NRS ranging from 0 (no urgency) to 10 (worst possible urgency). Higher scores indicate more severe urgency. Least square (LS) Mean was calculated using mixed model repeated measures (MMRM) model for post-baseline measures: The MMRM model includes treatment, baseline value, visit, interaction of baseline value-by-visit, interaction of treatment-by-visit, prior biologic or tofacitinib failure (yes/no),

baseline corticosteroid use (yes/no), clinical remission status (yes/no) at AMAN Week 12, and region (North America/Europe/Other). Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Induction Baseline, Week 40
APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least 1 dose of study drug and had a baseline and at least one post-baseline urgency NRS measurement.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	316		
Units: score on a scale				
least squares mean (standard error)	-2.74 (± 0.202)	-3.80 (± 0.139)		

Statistical analyses

Statistical analysis title	Change From Baseline to Week 40 in NRS
Comparison groups	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC) v Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	-0.61
Variability estimate	Standard error of the mean
Dispersion value	0.228

Secondary: Percentage of Participants Hospitalized for Ulcerative Colitis (UC)

End point title	Percentage of Participants Hospitalized for Ulcerative Colitis (UC)[12]

End point description:

Percentage of participants hospitalized for UC. Only hospitalizations associated with an adverse event

with >=24 hours stay were recorded. APD: Modified Intention-to-treat population (mITT): All randomized participants who received at least one dose of study drug. Participants were analysed per their assigned treatment arm regardless of the treatment they actually received.

End point type	Secondary

End point timeframe:

Week 40

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reported only for randomized arms as described in the protocol.

End point values	Maintenance Period: Miri IR - Placebo (PBO) Subcutaneous (SC)	Maintenance Period: Miri IR - 200 Milligram (mg) Miri SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	365		
Units: percentage of participants				
number (not applicable)	1.1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Clearance of Mirikizumab

End point title	Pharmacokinetics (PK): Clearance of Mirikizumab

End point description:

Clearance of mirikizumab was evaluated. APD: All randomized participants who received at least one dose of study drug subcutaneously (both induction responders and nonresponders) and had evaluable PK data.

End point type	Secondary

End point timeframe:

Predose: Weeks 0, 4, 12, 24 and 40

End point values	200 Milligram (mg) Miri SC			
Subject group type	Subject analysis set			
Number of subjects analysed	652			
Units: Liters per Hour (L/h)				
geometric mean (geometric coefficient of variation)	0.0487 (± 54)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 40 Weeks

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Maintenance Period: PBO IR - PBO SC

Reporting group description:

Participants who initially did not respond to induction study (LUCENT-1), but responded to extended induction therapy at Week 12 of LUCENT-2 (delayed responders), received 200 mg mirikizumab SC Q4W during open label maintenance period from Week 12 until Week 40.

Reporting group title	Maintenance Period: Miri IR - PBO SC

Reporting group description:

Participants who were responders to blinded mirikizumab (miri) at Week 12 in induction study (LUCENT-1) randomized to withdraw from mirikizumab and start receiving PBO SC every 4 weeks (Q4W) from Week 0 of maintenance study (LUCENT-2) until Week 40 or until loss of response was confirmed.

Reporting group title	Maintenance Period: Miri IR - 200 mg Miri SC

Reporting group description:

Participants who were responders to blinded mirikizumab at Week 12 in induction study (LUCENT-1) randomized to continue to receive 200 mg mirikizumab SC Q4W from Week 0 of LUCENT-2 until Week 40 or until loss of response was confirmed.

Reporting group title	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV

Reporting group description:

Participants who received blinded PBO SC or blinded 200 mg mirikizumab SC Q4W during maintenance period and experienced a loss of response at or after Week 12, received rescue therapy with open label 300 mg mirikizumab intravenous (IV) Q4W for 3 doses.

Reporting group title	Extended Induction: Induction Nonresponders - 300mg Miri IV

Reporting group description:

Participants who were nonresponders to blinded mirikizumab or placebo in induction study (LUCENT-1), received additional 3 doses of open label 300 mg mirikizumab IV Q4W during extended induction period from Week 0 of LUCENT-2 until Week 12.

Reporting group title	Open Label Maintenance: Delayed Responders - 200 mg Miri SC

Reporting group description:

Participants who initially did not respond to induction study (LUCENT-1), but responded to extended induction therapy at Week 12 of LUCENT-2 (delayed responders), received 200 mg mirikizumab SC Q4W during open label maintenance period from Week 12 until Week 40 or until early termination (rescue was not available for these participants).

Serious adverse events	Maintenance Period: PBO IR - PBO SC	Maintenance Period: Miri IR - PBO SC	Maintenance Period: Miri IR - 200 mg Miri SC
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 135 (5.19%)	15 / 192 (7.81%)	13 / 389 (3.34%)
number of deaths (all causes)	0	1	0

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
gastric cancer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
kaposi's sarcoma			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
lipoma			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal cancer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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

Surgical and medical procedures			
colectomy total			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
retinopexy			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tooth extraction			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
rectocele			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[1]	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
depression suicidal			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neurologic somatic symptom disorder			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Investigations			
blood glucose increased			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
brain contusion			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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
patella fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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
road traffic accident			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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
spinal compression fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Nervous system disorders			
ischaemic stroke			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
migraine			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
presyncope			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
immune thrombocytopenia			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Eye disorders			
maculopathy			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
retinal detachment			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
colitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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 24.1			
subjects affected / exposed	1 / 135 (0.74%)	6 / 192 (3.13%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
inguinal hernia			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
large intestine perforation			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
peptic ulcer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
pneumoperitoneum			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
rectal haemorrhage			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal polyp			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
pruritus			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
ureterolithiasis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Endocrine disorders			
autoimmune thyroiditis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
back pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral disc protrusion			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
sacral pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
bacillus infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
covid-19			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
covid-19 pneumonia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
campylobacter gastroenteritis			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
cellulitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
cytomegalovirus colitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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
diverticulitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
escherichia infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
gastroenteritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
influenza			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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

klebsiella infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
large intestine infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 135 (0.74%)	0 / 192 (0.00%)	0 / 389 (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
sepsis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
subcutaneous abscess			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tonsillitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	0 / 389 (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
Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 135 (0.00%)	1 / 192 (0.52%)	0 / 389 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypokalaemia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 135 (0.00%)	0 / 192 (0.00%)	1 / 389 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV	Extended Induction: Induction Nonresponders - 300mg Miri IV	Open Label Maintenance: Delayed Responders - 200 mg Miri SC
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 90 (3.33%)	21 / 461 (4.56%)	8 / 271 (2.95%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastric cancer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
kaposi's sarcoma			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lipoma			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
rectal cancer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Surgical and medical procedures			
colectomy total			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retinopexy			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
tooth extraction			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Reproductive system and breast disorders			
rectocele			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[1]	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Psychiatric disorders			
depression suicidal			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
neurologic somatic symptom disorder			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 90 (1.11%)	0 / 461 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
blood glucose increased			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Injury, poisoning and procedural			

complications			
brain contusion			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
patella fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
road traffic accident			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
spinal compression fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ischaemic stroke			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
migraine			

alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
presyncope			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Blood and lymphatic system disorders			
immune thrombocytopenia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
maculopathy			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retinal detachment			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Gastrointestinal disorders			
colitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis ulcerative			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	1 / 90 (1.11%)	6 / 461 (1.30%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	1 / 1	0 / 6	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
inguinal hernia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
large intestine perforation			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peptic ulcer			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumoperitoneum			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal haemorrhage			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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

rectal polyp			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Skin and subcutaneous tissue disorders			
pruritus			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureterolithiasis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
autoimmune thyroiditis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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			
arthralgia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 90 (1.11%)	0 / 461 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

back pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
intervertebral disc protrusion			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sacral pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bacillus infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
covid-19			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
covid-19 pneumonia			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
campylobacter gastroenteritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cytomegalovirus colitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
diverticulitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
escherichia infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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

influenza			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
klebsiella infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
large intestine infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
pneumonia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 90 (1.11%)	2 / 461 (0.43%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subcutaneous abscess			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
tonsillitis			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 90 (0.00%)	1 / 461 (0.22%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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
hypokalaemia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	0 / 461 (0.00%)	0 / 271 (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

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Non-serious adverse events	Maintenance Period: PBO IR - PBO SC	Maintenance Period: Miri IR - PBO SC	Maintenance Period: Miri IR - 200 mg Miri SC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 135 (27.41%)	57 / 192 (29.69%)	90 / 389 (23.14%)
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	5 / 135 (3.70%)	2 / 192 (1.04%)	16 / 389 (4.11%)
occurrences (all)	18	5	21
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	8 / 135 (5.93%)	9 / 192 (4.69%)	8 / 389 (2.06%)
occurrences (all)	11	12	8
Gastrointestinal disorders			
colitis ulcerative			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	17 / 135 (12.59%)	35 / 192 (18.23%)	26 / 389 (6.68%)
occurrences (all)	18	35	30
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 135 (2.96%)	8 / 192 (4.17%)	26 / 389 (6.68%)
occurrences (all)	4	8	27
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	9 / 135 (6.67%)	11 / 192 (5.73%)	28 / 389 (7.20%)
occurrences (all)	12	11	38

Non-serious adverse events	Loss of Response (LOR) Rescue Period:LOR Cohort-300 mg Miri IV	Extended Induction: Induction Nonresponders - 300mg Miri IV	Open Label Maintenance: Delayed Responders - 200 mg Miri SC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 90 (14.44%)	44 / 461 (9.54%)	54 / 271 (19.93%)
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	5 / 90 (5.56%)	8 / 461 (1.74%)	13 / 271 (4.80%)
occurrences (all)	5	10	21
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	5 / 90 (5.56%)	7 / 461 (1.52%)	9 / 271 (3.32%)
occurrences (all)	5	7	9
Gastrointestinal disorders			
colitis ulcerative			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 90 (0.00%)	4 / 461 (0.87%)	10 / 271 (3.69%)
occurrences (all)	0	4	11
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	3 / 90 (3.33%)	15 / 461 (3.25%)	19 / 271 (7.01%)
occurrences (all)	5	15	24
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 90 (1.11%)	15 / 461 (3.25%)	14 / 271 (5.17%)
occurrences (all)	1	15	15

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2019	• Replaced Primary objective, major secondary objectives, added Other secondary objectives • Added: 50% biological 50% conventional failure split • Follicle stimulating hormone (FSH) testing optional in women to confirm nonchild-bearing potential • Clarified infusion-reaction related samples • Clarified collection of Endoscopy • Clarified conditions when patients perform health outcome assessments • Clarified when informed consent form (ICF) be obtained • Clarified schedule of activities • Minimized study procedures for participants • Visit window changed between AMAN and AMBG • Clarification of Inclusion Criteria • Added assessments if drug hypersensitivity event observed • Changed the term Study treatment to study drug as study drug is blinded • Clarified term "mucosal healing" • Primary endpoint terminology changed from "durable clinical remission" to "clinical remission"; "remission changed to response" with mirikizumab induction treatment for clarification of treatment • Text deleted for medical monitor consult for endoscopy findings • Added when early termination visit (ETV) endoscopy should be discussed with the medical monitor. • Added Centers for Disease Control and Prevention guidance (CDC) was for the United States (US) and the World Health Organization (WHO) was for countries outside of the US • Deleted clinical study report (CSR) coordinating investigator "with the most enrolled participant's" will be selected by the study team • Clarified use of permitted and prohibited Medications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported