Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Parallel, Placebo-Controlled Induction Study of Mirikizumab in Conventional-Failed and Biologic-Failed Patients with Moderately to Severely Active Ulcerative Colitis (LUCENT 1)

Summary

EudraCT number	2017-003229-14
Trial protocol	DE GB 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	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	I6T-MC-AMAN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03518086
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16591

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	21 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 January 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 safety and efficacy of Mirikizumab in participants with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to, loss of response, or intolerant to conventional or biologic therapy for UC.

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	15 March 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: 14
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	China: 18
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Czechia: 55
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 64
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	India: 83
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 17
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Japan: 137
Country: Number of subjects enrolled	Latvia: 30
Country: Number of subjects enrolled	Lithuania: 22
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Mexico: 12

Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	Poland: 136
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Russian Federation: 107
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Slovakia: 24
Country: Number of subjects enrolled	Korea, Republic of: 28
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	Ukraine: 94
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 151
Worldwide total number of subjects	1281
EEA total number of subjects	505

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)	1184
From 65 to 84 years	97
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized in a 3:1 ratio to 300 milligram (mg) mirikizumab intravenously (IV) every 4 weeks (Q4W) or placebo IV Q4W. Results for maximum extended enrollment (ME2) participants will be posted after the study completion.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo IV Q4W

Arm description:

Placebo given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.

Arm title	300 mg Mirikizumab IV Q4W

Arm description:

300 mg mirikizumab given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Mirikizumab
Investigational medicinal product code	LY3074828
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

300 mg mirikizumab given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.

Number of subjects in period 1	Placebo IV Q4W	300 mg Mirikizumab IV Q4W
Started	322	959
Received at Least One Dose of Study Drug	321	958
Completed	285	920
Not completed	37	39
Consent withdrawn by subject	8	5
Insufficient Diary Data	-	2
Non- compliance to Protocol	-	1
Adverse event, non-fatal	23	15
Site Terminated by Sponsor	-	1
Lost to follow-up	-	3
COVID-19 Related Study Disruption	-	2
Lack of efficacy	5	5
Protocol deviation	1	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo IV Q4W
Reporting group description:	
Placebo given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	
Reporting group title	300 mg Mirikizumab IV Q4W
Reporting group description:	
300 mg mirikizumab given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	

Reporting group values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W	Total
Number of subjects	322	959	1281
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	41.3	42.8	
standard deviation	± 13.78	± 13.83	-
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	140	367	507
Male	182	592	774
Ethnicity (NIH/OMB)			
All randomized participants with non-missing ethnicity data.			
Units: Subjects			
Hispanic or Latino	9	22	31
Not Hispanic or Latino	27	92	119
Unknown or Not Reported	286	845	1131
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	2	10	12
Asian	68	224	292
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	2	10	12
White	247	704	951
More than one race	2	1	3
Unknown or Not Reported	1	9	10
Region of Enrollment			
All randomized participants.			
Units: Subjects			
Argentina	3	8	11
Australia	4	10	14
Austria	2	6	8
Belgium	3	6	9

Canada	11	23	34
China	2	16	18
Croatia	1	1	2
Czechia	20	35	55
Denmark	0	7	7
France	15	49	64
Germany	6	33	39
Hungary	7	16	23
India	21	62	83
Ireland	0	1	1
Israel	3	14	17
Italy	12	25	37
Japan	35	102	137
Latvia	6	24	30
Lithuania	6	16	22
Malaysia	0	6	6
Mexico	2	10	12
Netherlands	2	9	11
Poland	32	104	136
Romania	2	13	15
Russia	28	79	107
Serbia	8	13	21
Slovakia	3	21	24
South Korea	5	23	28
Spain	7	15	22
Switzerland	2	9	11
Taiwan	0	3	3
Turkey	5	6	11
Ukraine	26	68	94
United Kingdom	7	11	18
United States	36	115	151

End points

End points reporting groups

Reporting group title	Placebo IV Q4W
Reporting group description:	
Placebo given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	
Reporting group title	300 mg Mirikizumab IV Q4W
Reporting group description:	
300 mg mirikizumab given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	

Primary: Percentage of Participants With Clinical Remission at Week 12

End point title	Percentage of Participants With Clinical Remission at Week 12
End point description:	
Clinical remission at week 12 is defined as achieving a modified Mayo score (MMS) subscore for rectal bleeding=0,stool frequency=0 or 1 with ≥ 1 point decrease from baseline,and endoscopy=0 or 1 (excluding friability),excluding consideration of Physician's Global Assessment (PGA).Stool frequency subscore,based on the participants (pts) diary and scored from 0 (normal number of stools) to 3 (5 or more stools than normal);Rectal bleeding subscore,based on the pts 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).The confidence interval (CI) of 99.875% was chosen to match the significance level. Analysis population description (APD): Modified Intention-to-treat population (mITT): All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[1]	868[2]		
Units: percentage of participants				
number (confidence interval 99.88%)	13.3 (6.9 to 19.6)	24.2 (19.5 to 28.9)		

Notes:

[1] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[2] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Clinical Remission
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W

Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	11.1
Confidence interval	
level	Other: 99.88 %
sides	2-sided
lower limit	3.2
upper limit	19.1

Secondary: Percentage of Participants With Clinical Response at Week 12

End point title	Percentage of Participants With Clinical Response at Week 12

End point description:

Clinical response at week 12 is defined as decrease in 9-point MMS [rectal bleeding,stool frequency and endoscopic findings] inclusive of >= 2 points and >=30% from baseline with either decrease of rectal bleeding subscore of >=1 or rectal bleeding subscore of 0 or 1.MMS is composite score of ulcerative colitis disease activity calculated as sum of three subscores:Stool frequency subscore, based on pts diary;scored from 0 (normal number of stools) to 3 (5 or more stools than normal);Rectal bleeding subscore, based on pts diary;scored from 0 (no blood seen) to 3 (blood alone passed);Endoscopy subscore, based on colonoscopy or sigmoidoscopy;scored from 0 (normal or inactive disease) to 3 (severe disease,spontaneous bleeding,ulceration).MMS ranges from 0 to 9 points,with higher scores representing more severe disease. CI of 99.875% chosen to match significance level. APD:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[3]	868[4]		
Units: percentage of participants				
number (confidence interval 99.88%)	42.2 (32.9 to 51.5)	63.5 (58.2 to 68.8)		

Notes:

[3] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[4] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Clinical Response
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W

Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.00001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.4
Confidence interval	
level	Other: 99.88 %
sides	2-sided
lower limit	10.8
upper limit	32

Secondary: Percentage of Participants With Endoscopic Remission at Week 12

End point title	Percentage of Participants With Endoscopic Remission at Week 12

End point description:

Endoscopic remission at week 12 is defined as achieving a Mayo endoscopic subscore of 0 or 1 (excluding friability) at Week 12. Endoscopy subscore is based on colonoscopy or sigmoidoscopy and scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration);

The Mayo endoscopic score ranges from 0 to 3 points, with higher scores representing more severe disease.
The confidence interval of 99.875% was chosen to match the significance level.
APD:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[5]	868[6]		
Units: percentage of participants				
number (confidence interval 99.88%)	21.1 (13.4 to 28.8)	36.3 (31.0 to 41.6)		

Notes:

[5] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[6] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Endoscopic Remission
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W

Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.00001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.4
Confidence interval	
level	Other: 99.88 %
sides	2-sided
lower limit	6.3
upper limit	24.5

Secondary: Percentage of Participants With Symptomatic Remission at Week 12

End point title	Percentage of Participants With Symptomatic Remission at Week 12

End point description:

Symptomatic remission at week 12 is defined as a Mayo subscore 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).
The confidence interval of 99.875% was chosen to match the significance level.
APD:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[7]	868[8]		
Units: percentage of participants				
number (confidence interval 99.88%)	27.9 (22.8 to 33.0)	45.5 (42.2 to 48.8)		

Notes:

[7] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[8] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Symptomatic Remission
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W

Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.5
Confidence interval	
level	Other: 99.88 %
sides	2-sided
lower limit	11.4
upper limit	23.6

Secondary: Percentage of Participants With Symptomatic Response at Week 12

End point title	Percentage of Participants With Symptomatic Response at Week 12

End point description:

Symptomatic response at week 12 is defined as ≥30% decrease from baseline in the sum of stool frequency and rectal bleeding 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). The sum of stool frequency and rectal bleeding subscores ranges from 0 to 6. APD:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[9]	868[10]		
Units: percentage of participants				
number (confidence interval 95%)	52.4 (46.7 to 58.1)	72.0 (69.0 to 75.0)		

Notes:

[9] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[10] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Symptomatic Response
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W

Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	26.6

Secondary: Percentage of Participants with Histologic Remission at Week 12

End point title	Percentage of Participants with Histologic Remission at Week 12

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:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[11]	868[12]		
Units: percentage of participants				
number (confidence interval 95%)	15.6 (11.5 to 19.8)	29.3 (26.2 to 32.3)		

Notes:

[11] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[12] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Histologic Remission
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W
Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	13.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	8.6
upper limit	18.7

Secondary: Percentage of Participants With Endoscopic Response at Week 12

End point title	Percentage of Participants With Endoscopic Response at Week 12

End point description:

Endoscopic response at week 12 is defined as achieving at least a 1 point decrease from baseline in the Mayo endoscopic subscore.
The Mayo endoscopic subscore ranges from 0 to 3 points, with higher scores representing more severe disease. APD:mITT: All randomized pts who received at least one dose of study drug and who had MMS measured correctly at baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[13]	868[14]		
Units: percentage of participants				
number (confidence interval 95%)	36.1 (30.6 to 41.5)	55.4 (52.1 to 58.7)		

Notes:

[13] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[14] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Endoscopic Response
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W
Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.00001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.2
upper limit	25.8

Secondary: Change from Baseline to Week 12 in Bowel Urgency Based on the Urgency Numeric Rating Scale (NRS)

End point title	Change from Baseline to Week 12 in Bowel Urgency Based on the Urgency Numeric Rating Scale (NRS)

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), baseline disease activity (MMS: [4-6] or [7-9]), and region (North America/Europe/Other). APD:mITT: All randomized pts who received at least one dose of study drug and had a baseline and at least one post-baseline urgency NRS measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[15]	868[16]		
Units: score on a scale				
least squares mean (standard error)	-1.63 (± 0.141)	-2.59 (± 0.083)		

Notes:

[15] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[16] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Bowel Urgency based on NRS
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W
Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.00001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.95
Confidence interval	
level	Other: 99.88 %
sides	2-sided
lower limit	-1.47
upper limit	-0.44
Variability estimate	Standard error of the mean
Dispersion value	0.159

Notes:

[17] - The confidence interval of 99.875 % was chosen to match the significance level.

Secondary: Change from Baseline to Week 12 in Health Related Quality of Life: Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

End point title	Change from Baseline to Week 12 in Health Related Quality of Life: Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score

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 (Guyatt et al. 1989). 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), baseline disease activity (MMS: [4-6] or [7-9]), and region (North America/Europe/Other). APD: mITT: All randomized pts who received at least one dose of study drug and had a baseline and at least one post-baseline IBDQ measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[18]	868[19]		
Units: score on a scale				
least squares mean (standard error)	25.21 (± 1.798)	38.42 (± 1.108)		

Notes:

[18] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[19] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	IBDQ Total Score
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W
Number of subjects included in analysis	1162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	13.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.28
upper limit	17.15
Variability estimate	Standard error of the mean
Dispersion value	2.005

Secondary: Change from Baseline to Week 12 in Fecal Calprotectin

End point title	Change from Baseline to Week 12 in Fecal Calprotectin

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 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), baseline disease activity (MMS: [4-6] or [7-9]), and region (North America/Europe/Other). APD: mITT: All randomized pts who received at least one dose of study drug and had a baseline and at least one post-baseline urgency fecal calprotectin measurement.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo IV Q4W	300 mg Mirikizumab IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206[20]	665[21]		
Units: milligram per kilogram (mg/kg)				
least squares mean (standard error)	-939.69 (± 196.557)	-1875.29 (± 116.138)		

Notes:

[20] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

[21] - Pts analysed per their assigned treatment arm regardless of the treatment they actually received.

Statistical analyses

Statistical analysis title	Fecal Calprotectin
Comparison groups	Placebo IV Q4W v 300 mg Mirikizumab IV Q4W
Number of subjects included in analysis	871
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-935.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1363.64
upper limit	-507.55
Variability estimate	Standard error of the mean
Dispersion value	218.09

Secondary: Pharmacokinetics (PK): Clearance of Mirikizumab

End point title	Pharmacokinetics (PK): Clearance of Mirikizumab[22]

End point description:

Clearance of mirikizumab was evaluated. Clearance is estimated based on concentration data collected in the time frame of 0-12 weeks. APD: All randomized pts who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Weeks 0-12

Notes:

[22] - 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: No inferential statistics were planned or conducted for this endpoint.

End point values	300 mg Mirikizumab IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	952			
Units: Liters per Hour (L/h)				
geometric mean (geometric coefficient of variation)	0.0224 (± 38)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up To 12 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	24.0

Reporting groups	
Reporting group title	300 mg Mirikizumab IV Q4W
Reporting group description:	
300 mg mirikizumab given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	
Reporting group title	Placebo IV Q4W
Reporting group description:	
Placebo given as an IV infusion Q4W on Weeks 0, 4, 8 for 12 weeks.	

Serious adverse events	300 mg Mirikizumab IV Q4W	Placebo IV Q4W	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 958 (2.82%)	17 / 321 (5.30%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
uterine leiomyoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
spinal compression fracture			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal fracture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
arteriosclerosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
deep vein thrombosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 958 (0.10%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
colitis ulcerative			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	8 / 958 (0.84%)	10 / 321 (3.12%)	
occurrences causally related to treatment / all	1 / 8	3 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
ovarian enlargement			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
penile vein thrombosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
renal colic			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ankylosing spondylitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
acute sinusitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cytomegalovirus colitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis viral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal sepsis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
klebsiella infection			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 958 (0.21%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sinusitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
viral infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
diabetes mellitus			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malnutrition			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 958 (0.00%)	1 / 321 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
type 2 diabetes mellitus			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 958 (0.10%)	0 / 321 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	300 mg Mirikizumab IV Q4W	Placebo IV Q4W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 958 (3.24%)	18 / 321 (5.61%)	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	31 / 958 (3.24%)	18 / 321 (5.61%)	
occurrences (all)	32	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2019	Description of Change: • Made Follicle Stimulating Hormone (FSH) testing optional in women to confirm nonchild-bearing potential. • Additional assessments added to better understand the possible etiology if a drug hypersensitivity event is observed (this includes additional testing on already collected samples). • Updated the schedule of activities to clarify procedures. • Add Major secondary objective for bowel movement urgency improvement; updated secondary objectives; remove mucosal healing and include Ulcerative Colitis Endoscopic Index of Severity (UCEIS) endoscopic remission. • Add to inclusion criteria, additional requirement to confirm UC diagnosis and clarify other criteria. • Clarification of Exclusion Criteria . • Clarification of term "mucosal healing". • Added that participants who do not have the report of a completed, a full colonoscopy will be available in source documents to establish the extent of the disease; participants with rectal sparing on baseline endoscopy must have documentation of rectal involvement on a prior endoscopy. • Clarification of discussion of the screening colonoscopy. • Added that at Week 12 (or Early Termination Visit), a flexible sigmoidoscopy is recommended for all participants. • Clarified the need for an early term endoscopy. • Clarification of guidance for latent tuberculosis infection (LTBI). • To clarify some Clinical Laboratory procedures and Prohibited Medications to provide clarifications.
21 August 2020	Due to the COVID-19 public health emergency that prevents the safe conduct of on-site visits or that otherwise disrupts the ability of the investigators to conduct the trial per the requirements of the protocol, an addendum was written to document allowed changes to the protocol to mitigate COVID-19 restrictions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 March 2020	Lilly made the decision to temporarily pause new participant accrual to LUCENT-1 (all countries with the exception of Japan, S.Korea, Taiwan, China). The interactive web-response system (IWRS) was closed to enter new participants at end of day (8 pm United States Pacific Daylight Time) on 25-March-2020. Enrolled participants could continue in the study provided the investigator affirmed that this was safe and in their best interest and in accordance with any local regulations and health advisories pertaining to the containment of the virus. The interruption was lifted May 7, 2020.	07 May 2020

Notes:

Limitations and caveats

None reported