



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 (current) |
| 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 | Subject, Investigator |

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 $\geq 30\%$ 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 $\geq 30\%$ 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 (\pm 1.798) | 38.42 (\pm 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 | <p>Description of Change:</p> <ul style="list-style-type: none">• 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 | <p>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.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|---|--------------|
| 24 March 2020 | <p>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.</p> <p>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.</p> | 07 May 2020 |

Notes:

Limitations and caveats

None reported