



Clinical trial results:

A Multicenter, Randomized, Double-blind, Placebo-controlled, Proof-of-Concept Study of Ustekinumab in Subjects With Active Systemic Lupus Erythematosus

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-005000-19 |
| Trial protocol | HU DE ES PL |
| Global end of trial date | 07 June 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 27 March 2020 |
| First version publication date | 27 March 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | CR106661 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02349061 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route 202, Raritan, United States, NJ 08869 |
| Public contact | Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 June 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 June 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of ustekinumab as measured by a reduction in disease activity for subjects with active Active Systemic Lupus Erythematosus (SLE).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety and tolerability were evaluated by vital signs, general physical examinations and skin evaluations, adverse events, concomitant medication review, pregnancy testing, administration reactions, chemistry and hematology laboratory tests, and antibodies to ustekinumab.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 22 October 2015 |
| 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: 12 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | Spain: 12 |
| Country: Number of subjects enrolled | Hungary: 8 |
| Country: Number of subjects enrolled | Mexico: 11 |
| Country: Number of subjects enrolled | Poland: 19 |
| Country: Number of subjects enrolled | Taiwan: 13 |
| Country: Number of subjects enrolled | United States: 17 |
| Worldwide total number of subjects | 102 |
| EEA total number of subjects | 44 |

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) | 99 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

166 subjects were screened during the study, 102 were enrolled/randomized and treated.

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Main Study: PCP (Up to Week 24) |
| 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 |
|------------------|---------|

Arm description:

Subjects received placebo matched to ustekinumab intravenously (IV) at Week 0 then followed by placebo subcutaneously (SC) at Week 8 and 16.

| | |
|--|-----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use, Subcutaneous use |

Dosage and administration details:

Subjects received placebo matched to ustekinumab IV at Week 0 followed by placebo SC at Week 8 and 16.

| | |
|------------------|-------------|
| Arm title | Ustekinumab |
|------------------|-------------|

Arm description:

Subjects received an initial body weight range based IV dose approximating 6 milligram per kilogram (mg/kg) of ustekinumab at Week 0 followed by 90 milligram (mg) SC administered every 8 weeks (q8w) at Week 8 and 16.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ustekinumab |
| Investigational medicinal product code | |
| Other name | STELARA |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use, Subcutaneous use |

Dosage and administration details:

Subjects received 6 mg/kg of ustekinumab at Week 0 followed by ustekinumab 90 mg SC administered q8w at Week 8 and 16.

| Number of subjects in period 1 | Placebo | Ustekinumab |
|--------------------------------|---------|-------------|
| Started | 42 | 60 |
| Completed | 33 | 56 |
| Not completed | 9 | 4 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 2 | - |
| Adverse event, non-fatal | 4 | 3 |
| Unspecified | 1 | 1 |
| Lack of efficacy | 1 | - |

Period 2

| | |
|------------------------------|---------------------------|
| Period 2 title | Main Study: Week 24 to 56 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ustekinumab |

Arm description:

Subjects who were assigned to Ustekinumab treatment and who completed placebo controlled period (PCP) continued to receive ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up for 16 weeks after last study agent SC administration.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ustekinumab |
| Investigational medicinal product code | |
| Other name | STELARA |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab 90 mg SC administered q8w at Weeks 24, 32 and 40.

| | |
|------------------|------------------------|
| Arm title | Placebo to Ustekinumab |
|------------------|------------------------|

Arm description:

Subjects who received placebo matched to ustekinumab and completed PCP period in placebo group were crossed-over at Week 24 and received ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up through Week 56 in a blinded fashion for 16 weeks after last study agent SC administration.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ustekinumab |
| Investigational medicinal product code | |
| Other name | STELARA |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab 90 mg SC administered q8w at Weeks 24, 32 and 40.

| Number of subjects in period 2 | Ustekinumab | Placebo to Ustekinumab |
|---------------------------------------|-------------|------------------------|
| Started | 56 | 33 |
| Completed | 53 | 30 |
| Not completed | 3 | 3 |
| Consent withdrawn by subject | - | 1 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 2 | 1 |
| Lack of efficacy | 1 | - |

Period 3

| | |
|------------------------------|---------------------------------------|
| Period 3 title | Study Extension (Week 56 to Week 120) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ustekinumab |

Arm description:

Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ustekinumab |
| Investigational medicinal product code | |
| Other name | STELARA |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab 90 mg SC administered q8w starting at Week 48 or at Week 56 through Week 104.

| | |
|------------------|------------------------|
| Arm title | Placebo to Ustekinumab |
|------------------|------------------------|

Arm description:

Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ustekinumab |
| Investigational medicinal product code | |
| Other name | STELARA |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab 90 mg SC administered q8w starting at Week 48 or at Week 56 through Week 104.

| Number of subjects in period 3^[1] | Ustekinumab | Placebo to Ustekinumab |
|---|-------------|------------------------|
| Started | 29 | 17 |
| Completed | 24 | 14 |
| Not completed | 5 | 3 |
| Consent withdrawn by subject | 2 | 1 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 3 | - |
| Lack of efficacy | - | 1 |

Notes:

[1] - 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: Subjects who were eligible to continue in extension phase are included in this period.

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received placebo matched to ustekinumab intravenously (IV) at Week 0 then followed by placebo subcutaneously (SC) at Week 8 and 16.

| | |
|-----------------------|-------------|
| Reporting group title | Ustekinumab |
|-----------------------|-------------|

Reporting group description:

Subjects received an initial body weight range based IV dose approximating 6 milligram per kilogram (mg/kg) of ustekinumab at Week 0 followed by 90 milligram (mg) SC administered every 8 weeks (q8w) at Week 8 and 16.

| Reporting group values | Placebo | Ustekinumab | Total |
|---|---------|-------------|-------|
| Number of subjects | 42 | 60 | 102 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 42 | 57 | 99 |
| From 65 to 84 years | 0 | 3 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 43.1 | 40 | |
| standard deviation | ± 11.03 | ± 11.95 | - |
| Title for Gender Units: subjects | | | |
| Female | 35 | 58 | 93 |
| Male | 7 | 2 | 9 |

End points

End points reporting groups

| | |
|--|------------------------|
| Reporting group title | Placebo |
| Reporting group description: Subjects received placebo matched to ustekinumab intravenously (IV) at Week 0 then followed by placebo subcutaneously (SC) at Week 8 and 16. | |
| Reporting group title | Ustekinumab |
| Reporting group description: Subjects received an initial body weight range based IV dose approximating 6 milligram per kilogram (mg/kg) of ustekinumab at Week 0 followed by 90 milligram (mg) SC administered every 8 weeks (q8w) at Week 8 and 16. | |
| Reporting group title | Ustekinumab |
| Reporting group description: Subjects who were assigned to Ustekinumab treatment and who completed placebo controlled period (PCP) continued to receive ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up for 16 weeks after last study agent SC administration. | |
| Reporting group title | Placebo to Ustekinumab |
| Reporting group description: Subjects who received placebo matched to ustekinumab and completed PCP period in placebo group were crossed-over at Week 24 and received ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up through Week 56 in a blinded fashion for 16 weeks after last study agent SC administration. | |
| Reporting group title | Ustekinumab |
| Reporting group description: Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120. | |
| Reporting group title | Placebo to Ustekinumab |
| Reporting group description: Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120. | |

Primary: Percentage of Subjects with a Systemic Lupus Erythematosus Responder Index (SRI-4) Composite Response (CR) at Week 24

| | |
|--|---|
| End point title | Percentage of Subjects with a Systemic Lupus Erythematosus Responder Index (SRI-4) Composite Response (CR) at Week 24 |
| End point description: SRI-4: greater than or equal to 4-point reduction in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) total score, no new domain scores in either British Isles Lupus Assessment Group (BILAG) A or B and no worsening (less than 10% increase) from baseline in Physician's Global Assessment of Disease Activity (PGA). CR; SRI-4 response in subjects who do not meet treatment failure criteria. SLEDAI-2K total score range = 0-105, higher score means increased disease activity. BILAG Index: assesses clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system: A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. PGA assess disease activity on a visual analogue scale range= 0-10 (very well-very poor). Full analysis set (FAS) included all randomized subjects who received at least 1 dose (partial or complete, IV or SC) of ustekinumab or placebo. | |
| End point type | Primary |
| End point timeframe: Week 24 | |

| End point values | Placebo | Ustekinumab | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 42 | 60 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 33.3 | 61.7 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|------------------------|
| Comparison groups | Placebo v Ustekinumab |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0057 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.41 |
| upper limit | 7.63 |

Secondary: Change from Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI 2K) Score at Week 24

| | |
|---|---|
| End point title | Change from Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI 2K) Score at Week 24 |
| End point description: | |
| <p>The SLEDAI-2K is an established, validated SLE activity index. It is based on the presence of 24 features in 9 organ systems and measures disease activity in SLE patients in the previous 30 days. It is weighted according to the feature. Features are scored by the assessing physician if present within the last 30 days with more severe features having higher scores, and then simply added to determine the total SLEDAI 2K score, which ranges from 0 to 105, with higher scores representing increased disease activity. FAS included all the randomized subjects who received at least 1 dose (partial or complete, IV or SC) of ustekinumab or placebo. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 24 | |

| End point values | Placebo | Ustekinumab | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 53 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -3.8 (± 5.39) | -4.4 (± 2.91) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|-------------------------------------|
| Comparison groups | Placebo v Ustekinumab |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0929 |
| Method | Mixed model repeated measures model |
| Parameter estimate | Least Squares (LS) Mean Difference |
| Point estimate | -1.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.94 |
| upper limit | 0.23 |

Secondary: Change from Baseline in Physician's Global Assessment of Disease Activity (PGA) Score at Week 24

| | |
|---|--|
| End point title | Change from Baseline in Physician's Global Assessment of Disease Activity (PGA) Score at Week 24 |
| End point description: | |
| PGA was recorded on a visual analogue scale (VAS; 0.0 to 10.0 centimeter [cm]). The scale for the physician's assessment ranges for 'no lupus activity' (0.0) to 'extremely active lupus' (10.0). FAS included all the randomized subjects who received at least 1 dose (partial or complete, IV or SC) of ustekinumab or placebo. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 24 | |

| End point values | Placebo | Ustekinumab | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 55 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -1.93 (± 2.168) | -2.17 (± 1.915) | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Ustekinumab |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3944 |
| Method | Mixed model repeated measures model |
| Parameter estimate | LS Means Difference |
| Point estimate | -0.383 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.271 |
| upper limit | 0.506 |

Secondary: Percentage of Subjects with BILAG-based Combined Lupus Assessment (BICLA) Response at Week 24

| | |
|--|---|
| End point title | Percentage of Subjects with BILAG-based Combined Lupus Assessment (BICLA) Response at Week 24 |
| End point description: BICLA response defined as subjects meeting following criteria: 1. BILAG improvement (all BILAG A scores at baseline improved to either B, C or D and all BILAG B scores at baseline improved to C or D and no worsening in disease activity defined as no new BILAG A scores and ≤ 1 new BILAG B score) and 2. no worsening of total SLEDAI-2K from baseline 3. < 1 cm increase in PGA and 4. no treatment failure criteria met. BILAG: assesses disease extent, severity (range: A [severe] to E [no disease]). SLEDAI-2K: assesses improvement in disease activity (range: 0 to 105; higher score = higher severity). PGA: assesses worsening in subject's general health status (0.0= 'no lupus activity' to 10.0 = 'extremely active lupus'). FAS included all the randomized subjects who received at least 1 dose (partial or complete, IV or SC) of ustekinumab or placebo. | |
| End point type | Secondary |
| End point timeframe: Week 24 | |

| | | | | |
|-------------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | Ustekinumab | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 42 | 60 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 33.3 | 35 | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Ustekinumab |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9939 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 2.34 |

Secondary: Change from Baseline in Number of Joints with Pain and Signs of Inflammation at Week 24

| | |
|---|---|
| End point title | Change from Baseline in Number of Joints with Pain and Signs of Inflammation at Week 24 |
| End point description: Change from baseline in number of joints (active joint) with pain and signs of inflammation (tenderness, swelling or effusion) for subjects with at least 2 affected joints at baseline were reported. An active joint is defined as a joint with pain and signs of inflammation (e.g., tenderness, swelling or effusion). FAS included all the randomized subjects who received at least 1 dose (partial or complete, IV or SC) of ustekinumab or placebo. Population included subjects with at least 2 affected joints at baseline (2 or more affected joints). | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 24 | |

| | | | | |
|--------------------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | Ustekinumab | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 | 51 | | |
| Units: Joints | | | | |
| arithmetic mean (standard deviation) | -2.8 (± 7.31) | -4.5 (± 4.42) | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Ustekinumab |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1032 |
| Method | Mixed model repeated measures model |
| Parameter estimate | LS Means Difference |
| Point estimate | -2.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.78 |
| upper limit | 0.45 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to Week 120

Adverse event reporting additional description:

Safety analysis set was defined as the set of all randomized subjects who have received at least 1 dose (partial or complete, intravenously [IV] or subcutaneously [SC]) of ustekinumab or placebo.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Placebo (Up to Week 24) |
|-----------------------|-------------------------|

Reporting group description:

Subjects received placebo matched to ustekinumab intravenously (IV) at Week 0 then followed by placebo subcutaneously (SC) at Week 8 and 16.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Ustekinumab (Up to Week 24) |
|-----------------------|-----------------------------|

Reporting group description:

Subjects received an initial body weight range based IV dose approximating 6 milligram per kilogram (mg/kg) of ustekinumab at Week 0 followed by 90 mg SC administered every 8 weeks (q8w) at Week 8 and 16.

| | |
|-----------------------|--|
| Reporting group title | Placebo to Ustekinumab (Week 24 to 56) |
|-----------------------|--|

Reporting group description:

Subjects who received placebo matched to ustekinumab and completed PCP period in placebo group were crossed-over at Week 24 and received ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up through Week 56 in a blinded fashion for 16 weeks after last study agent SC administration.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Ustekinumab (Week 24 to 56) |
|-----------------------|-----------------------------|

Reporting group description:

Subjects who were assigned to Ustekinumab treatment and who completed placebo controlled period (PCP) continued to receive ustekinumab 90 mg SC at Weeks 24, 32, and 40 followed by safety follow-up for 16 weeks after last study agent SC administration.

| | |
|-----------------------|---|
| Reporting group title | Placebo to Ustekinumab (Week 56 to 120) |
|-----------------------|---|

Reporting group description:

Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120.

| | |
|-----------------------|------------------------------|
| Reporting group title | Ustekinumab (Week 56 to 120) |
|-----------------------|------------------------------|

Reporting group description:

Per the amended study design, open-label ustekinumab 90 mg q8w SC administration will continue to be provided through Week 104 (study extension) to eligible subjects followed by safety follow-up through Week 120.

| Serious adverse events | Placebo (Up to Week 24) | Ustekinumab (Up to Week 24) | Placebo to Ustekinumab (Week 24 to 56) |
|---|-------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 42 (9.52%) | 5 / 60 (8.33%) | 5 / 33 (15.15%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Keratoacanthoma | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Injury, poisoning and procedural complications | | | |
| Humerus Fracture | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Raynaud's Phenomenon | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |
| Coronary Artery Occlusion | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 0 / 33 (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 |
| Posterior Reversible Encephalopathy Syndrome | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |

| | | | |
|--|----------------|----------------|----------------|
| Hypochromic Anaemia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 0 / 33 (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 |
| Gastrointestinal disorders | | | |
| Gastric Ulcer | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Pancreatitis Acute | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 0 / 33 (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 | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus Nephritis | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |
| Systemic Lupus Erythematosus | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 0 / 33 (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 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic Sepsis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 0 / 33 (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 |
| Salmonella Sepsis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stenotrophomonas Infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (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 |
| Viral Infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Ustekinumab (Week 24 to 56) | Placebo to Ustekinumab (Week 56 to 120) | Ustekinumab (Week 56 to 120) |
|---|-----------------------------|---|------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 56 (12.50%) | 1 / 17 (5.88%) | 4 / 29 (13.79%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Keratoacanthoma | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 | | | |
| Humerus Fracture | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 | | | |
| Hypotension | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Raynaud's Phenomenon | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Coronary Artery Occlusion | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Ischaemic Stroke | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Posterior Reversible Encephalopathy Syndrome | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Hypochromic Anaemia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 | | | |
| Gastric Ulcer | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Pancreatitis Acute | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Lupus Nephritis | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic Lupus Erythematosus | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Neutropenic Sepsis | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Salmonella Sepsis | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 17 (5.88%) | 0 / 29 (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 |
| Stenotrophomonas Infection | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Urinary Tract Infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 0 / 29 (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 |
| Viral Infection | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Placebo (Up to Week 24) | Ustekinumab (Up to Week 24) | Placebo to Ustekinumab (Week 24 to 56) |
|--|-------------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 25 / 42 (59.52%) | 30 / 60 (50.00%) | 21 / 33 (63.64%) |
| Vascular disorders | | | |
| Peripheral Arterial Occlusive Disease | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 3 / 60 (5.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 2 / 60 (3.33%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 2 | 3 |
| Reproductive system and breast disorders | | | |
| Menstruation Irregular | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 42 (4.76%) | 1 / 60 (1.67%) | 1 / 33 (3.03%) |
| occurrences (all) | 2 | 1 | 3 |
| Aspartate Aminotransferase Increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 2 / 60 (3.33%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 3 | 4 |
| Injury, poisoning and procedural complications | | | |
| Limb Injury | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 42 (11.90%) | 4 / 60 (6.67%) | 1 / 33 (3.03%) |
| occurrences (all) | 5 | 4 | 1 |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 60 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 4 | 0 | 4 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 60 (1.67%) | 2 / 33 (6.06%) |
| occurrences (all) | 3 | 1 | 4 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Eye disorders | | | |
| Dry Eye | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 4 / 60 (6.67%) | 3 / 33 (9.09%) |
| occurrences (all) | 0 | 5 | 3 |
| Nausea | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 3 / 60 (5.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 3 | 3 | 1 |
| Hepatobiliary disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Hypertransaminasaemia subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 60 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Actinic Keratosis subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 2 | 0 / 60 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Skin Lesion subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 60 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Renal and urinary disorders | | | |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 60 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 3 / 42 (7.14%) 3 | 0 / 60 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Back Pain subjects affected / exposed occurrences (all) | 2 / 42 (4.76%) 2 | 2 / 60 (3.33%) 2 | 0 / 33 (0.00%) 0 |
| Systemic Lupus Erythematosus subjects affected / exposed occurrences (all) | 2 / 42 (4.76%) 2 | 3 / 60 (5.00%) 3 | 2 / 33 (6.06%) 3 |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 2 / 60 (3.33%) 2 | 1 / 33 (3.03%) 1 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 2 / 42 (4.76%) 2 | 1 / 60 (1.67%) 1 | 3 / 33 (9.09%) 3 |
| Gastroenteritis Viral subjects affected / exposed occurrences (all) | 3 / 42 (7.14%) 3 | 0 / 60 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Nasopharyngitis | | | |

| | | | |
|------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 42 (7.14%) | 6 / 60 (10.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 3 | 7 | 4 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 3 / 60 (5.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 3 | 1 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 3 / 60 (5.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Tooth Abscess | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 9 / 42 (21.43%) | 5 / 60 (8.33%) | 3 / 33 (9.09%) |
| occurrences (all) | 9 | 6 | 4 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 4 / 42 (9.52%) | 6 / 60 (10.00%) | 6 / 33 (18.18%) |
| occurrences (all) | 4 | 6 | 10 |
| Infected Bite | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea Versicolour | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth Infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 60 (1.67%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 1 | 2 |
| Vulvitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 60 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Ustekinumab (Week 24 to 56) | Placebo to Ustekinumab (Week 56 to 120) | Ustekinumab (Week 56 to 120) |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 34 / 56 (60.71%) | 8 / 17 (47.06%) | 22 / 29 (75.86%) |
| Vascular disorders Peripheral Arterial Occlusive Disease subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 29 (0.00%) 0 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 2 1 / 56 (1.79%) 1 | 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 | 1 / 29 (3.45%) 1 0 / 29 (0.00%) 0 |
| Reproductive system and breast disorders Menstruation Irregular subjects affected / exposed occurrences (all) Ovarian Cyst subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 1 / 56 (1.79%) 1 | 1 / 17 (5.88%) 1 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 1 / 29 (3.45%) 1 |
| Investigations Alanine Aminotransferase Increased subjects affected / exposed occurrences (all) Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 1 / 56 (1.79%) 1 | 1 / 17 (5.88%) 2 1 / 17 (5.88%) 2 | 1 / 29 (3.45%) 1 1 / 29 (3.45%) 1 |
| Injury, poisoning and procedural complications Limb Injury subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 29 (0.00%) 0 |
| Nervous system disorders | | | |

| | | | |
|---|----------------------|---------------------|----------------------|
| Headache subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 0 / 17 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Blood and lymphatic system disorders | | | |
| Leukopenia subjects affected / exposed occurrences (all) | 4 / 56 (7.14%) 10 | 1 / 17 (5.88%) 1 | 4 / 29 (13.79%) 7 |
| Neutropenia subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 8 | 1 / 17 (5.88%) 1 | 3 / 29 (10.34%) 6 |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 17 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Eye disorders | | | |
| Dry Eye subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 17 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hepatobiliary disorders | | | |
| Hypertransaminaemia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 29 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Actinic Keratosis subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 29 (0.00%) 0 |
| Skin Lesion subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 2 | 1 / 17 (5.88%) 1 | 1 / 29 (3.45%) 2 |
| Renal and urinary disorders | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| Proteinuria subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 0 / 17 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Back Pain subjects affected / exposed occurrences (all) | 5 / 56 (8.93%) 6 | 0 / 17 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Systemic Lupus Erythematosus subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 1 / 17 (5.88%) 2 | 2 / 29 (6.90%) 2 |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 4 / 56 (7.14%) 4 | 0 / 17 (0.00%) 0 | 4 / 29 (13.79%) 4 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 2 / 17 (11.76%) 2 | 0 / 29 (0.00%) 0 |
| Gastroenteritis Viral subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 6 / 56 (10.71%) 7 | 1 / 17 (5.88%) 2 | 2 / 29 (6.90%) 3 |
| Pharyngitis subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 2 | 0 / 17 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Pharyngotonsillitis subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Tooth Abscess subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 0 / 17 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Upper Respiratory Tract Infection | | | |

| | | | |
|------------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 10 / 56 (17.86%) | 1 / 17 (5.88%) | 3 / 29 (10.34%) |
| occurrences (all) | 17 | 1 | 6 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 10 / 56 (17.86%) | 2 / 17 (11.76%) | 6 / 29 (20.69%) |
| occurrences (all) | 17 | 3 | 7 |
| Infected Bite | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 17 (5.88%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory Tract Infection | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 0 / 17 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 2 | 0 | 2 |
| Tinea Versicolour | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 17 (5.88%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tooth Infection | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 17 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Vulvitis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 17 (5.88%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 17 (5.88%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 19 May 2015 | Overall reason for this amendment was to clarify the use of highly effective methods of contraception for subject inclusion and continuation in the study, and correction of minor errors and omissions. |
| 24 November 2015 | Overall reasons for this amendment was to provide clarification regarding 1) subject eligibility and enrollment, 2) use of restricted and prohibited concomitant medications, 3) refine the definition of primary endpoint, 4) specify conditions under which subjects may undergo retesting at screening, 5) elaborate on statistical procedures to be used to conduct interim and planned data analyses, and 6) provide additional information regarding collection of samples. |
| 18 January 2017 | Overall reason for this amendment was to further evaluate the safety and efficacy of long-term ustekinumab administration in subjects with Systemic Lupus Erythematosus (SLE) who participated in CNTO1275SLE2001 study extension. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported