



Clinical trial results:

A Phase 3b, Randomized, Double-blind, Multicenter Study to Evaluate the Safety and Efficacy of Intravenous Re-induction Therapy With Ustekinumab in Patients with Moderately to Severely Active Crohn's Disease

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2018-002629-51 |
| Trial protocol | NL ES SE FR AT GB CZ IT |
| Global end of trial date | 10 January 2023 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 21 January 2024 |
| First version publication date | 21 January 2024 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | CNT01275CRD3008 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03782376 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen-Cilag Ltd. |
| Sponsor organisation address | Archimedesweg 29, Leiden, Netherlands, 2333 CM |
| Public contact | Clinical Registry Group, Janssen-Cilag Ltd., ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen-Cilag Ltd., 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 | 10 January 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 January 2023 |
| 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 achievement of clinical response at Week 16 following a single intravenous (IV) re-induction dose of 6 milligrams per kilogram (mg/kg) ustekinumab, compared with continuing regular subcutaneous (SC) every 8 weeks (q8w) 90 mg ustekinumab administration, in subjects with secondary loss of response (LoR) to SC q8w 90 mg ustekinumab maintenance therapy.

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.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 December 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | France: 14 |
| Country: Number of subjects enrolled | Germany: 69 |
| Country: Number of subjects enrolled | Italy: 10 |
| Country: Number of subjects enrolled | Netherlands: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 11 |
| Country: Number of subjects enrolled | Czechia: 5 |
| Country: Number of subjects enrolled | Russian Federation: 8 |
| Country: Number of subjects enrolled | Spain: 16 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | United States: 67 |
| Worldwide total number of subjects | 215 |
| EEA total number of subjects | 121 |

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) | 203 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 215 subjects were enrolled, of which 159 subjects completed the study.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1: Ustekinumab (IV Re-induction) |

Arm description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received a weight-tiered based re-induction dose of ustekinumab 6 mg/kg as an intravenous IV infusion and placebo matching to ustekinumab as SC injection at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

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

Dosage and administration details:

Subjects received IV infusion of 6 mg/kg Ustekinumab at Week 0.

| | |
|--|------------------|
| 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 SC maintenance injections of 90 mg ustekinumab at Weeks 8 and 16.

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

Dosage and administration details:

Subjects received SC injection of placebo (matched to Ustekinumab) at Week 0.

| | |
|------------------|--|
| Arm title | Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
|------------------|--|

Arm description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received ustekinumab 90 mg as SC injection and placebo matching to ustekinumab as an IV infusion at Week 0. At Weeks 8 and 16, all

subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| | |
|--|------------------|
| 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 SC maintenance injections of 90 mg ustekinumab at Weeks 0, 8, and 16.

| | |
|--|-----------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received IV infusion of placebo (matched to Ustekinumab) at Week 0.

| Number of subjects in period 1 | Group 1: Ustekinumab (IV Re-induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
|--------------------------------|--|---|
| | Started | 108 |
| Completed | 82 | 77 |
| Not completed | 26 | 30 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 7 | 11 |
| Unspecified | 16 | 17 |
| Lost to follow-up | 2 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Group 1: Ustekinumab (IV Re-induction) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received a weight-tiered based re-induction dose of ustekinumab 6 mg/kg as an intravenous IV infusion and placebo matching to ustekinumab as SC injection at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| | |
|-----------------------|--|
| Reporting group title | Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received ustekinumab 90 mg as SC injection and placebo matching to ustekinumab as an IV infusion at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| Reporting group values | Group 1: Ustekinumab (IV Re-induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | Total |
|---|--|---|-------|
| Number of subjects | 108 | 107 | 215 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 102 | 101 | 203 |
| From 65 to 84 years | 6 | 6 | 12 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 41.8 | 40 | |
| standard deviation | ± 13.63 | ± 13.07 | - |
| Title for Gender Units: subjects | | | |
| Female | 62 | 62 | 124 |
| Male | 46 | 45 | 91 |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Group 1: Ustekinumab (IV Re-induction) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received a weight-tiered based re-induction dose of ustekinumab 6 mg/kg as an intravenous IV infusion and placebo matching to ustekinumab as SC injection at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| | |
|-----------------------|--|
| Reporting group title | Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received ustekinumab 90 mg as SC injection and placebo matching to ustekinumab as an IV infusion at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

Primary: Percentage of Subjects With Clinical Response at Week 16

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Clinical Response at Week 16 |
|-----------------|--|

End point description:

Clinical response: greater than or equal to (\geq) 100-point reduction from baseline in Crohn's disease activity index (CDAI) score or a CDAI score $<$ 150 points. CDAI is a measure of severity of illness derived as weighted sum of 8 Crohn's disease (CD)-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates, and general well-being). The last 4 variables were scored on diary over 7 days by subjects. CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects with prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated of worsening CD prior to designated analysis timepoint were considered not in clinical response, regardless of their CDAI score. Full analysis set (FAS) included randomised subjects.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 16

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 49.1 | 37.4 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Ustekinumab IV Vs Ustekinumab SC |
| Statistical analysis description: The fixed sequence testing method was used. Cochran-Mantel Haenszel (CMH)-chi-square test stratified by baseline CDAI score (≤ 300 or > 300), and prior biologic failure status at baseline (yes or no). | |
| Comparison groups | Group 1: Ustekinumab (IV Re-induction) v Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.089 ^[1] |
| Method | Cochran-Mantel Haenszel-chi-square test |
| Parameter estimate | Difference in percentage |
| Point estimate | 11.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 24.5 |

Notes:

[1] - Threshold for significance was 0.05 level.

Secondary: Percentage of Subjects With Clinical Response at Week 8

| | |
|--|---|
| End point title | Percentage of Subjects With Clinical Response at Week 8 |
| End point description: Clinical response was defined as a ≥ 100 -point reduction from the baseline in CDAI score or a CDAI score < 150 point. The CDAI is a measure of severity of illness derived as a weighted sum of 8 different CD-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates, and general well-being). The last 4 variables were scored over 7 days by the subject on a diary card. In general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects who had prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated to be of worsening CD prior to designated analysis timepoint were considered not to be in clinical response, regardless of their CDAI score. FAS included all randomised subjects. | |
| End point type | Secondary |
| End point timeframe: Week 8 | |

| End point values | Group 1: Ustekinumab (IV Re-induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 51.9 | 44.9 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Ustekinumab IV Vs Ustekinumab SC |
| Statistical analysis description: The fixed sequence testing method was used. CMH chi-square test (2-sided) stratified by baseline CDAI score (≤ 300 or > 300), and prior biologic failure status at baseline (yes or no). | |
| Comparison groups | Group 1: Ustekinumab (IV Re-induction) v Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3 [2] |
| Method | CMH chi-square test (2-sided) |
| Parameter estimate | Difference in percentage |
| Point estimate | 7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 20.2 |

Notes:

[2] - Since the primary endpoint did not achieve statistical significance, all p-values for the major secondary endpoints are nominal and are not statistically significant.

Secondary: Percentage of Subjects With Clinical Remission at Week 16

| | |
|--|---|
| End point title | Percentage of Subjects With Clinical Remission at Week 16 |
| End point description: Percentage of subjects with clinical remission at Week 16 were reported. Clinical remission was defined as CDAI score of <150 points. CDAI is a measure of severity of illness derived as weighted sum of 8 different CD-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates and general well-being). The last 4 variables were scored over 7 days by subject on diary card. In general, CDAI score ranges from 0 to approximately 600; higher score=higher disease activities. Subjects who had prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated to be of worsening CD prior to designated analysis timepoint were considered not to be in clinical remission, regardless of their CDAI score. FAS included all randomised subjects. | |
| End point type | Secondary |
| End point timeframe: Week 16 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 33.3 | 27.1 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Ustekinumab IV Vs Ustekinumab SC |
| Statistical analysis description: The fixed sequence testing method was used. CMH chi-square test (2-sided) stratified by baseline CDAI score (≤ 300 or > 300), and prior biologic failure status at baseline (yes or no). | |
| Comparison groups | Group 1: Ustekinumab (IV Re-induction) v Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.338 ^[3] |
| Method | CMH chi-square test (2-sided) |
| Parameter estimate | Difference in percentage |
| Point estimate | 5.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 17.8 |

Notes:

[3] - Since the primary endpoint did not achieve statistical significance, all p-values for the major secondary endpoints are nominal and are not statistically significant.

Secondary: Percentage of Subjects with Normalisation of C-reactive Protein (CRP) and/or Normalisation of Fecal Calprotectin (fCal) Concentration at Week 16

| | |
|-----------------|--|
| End point title | Percentage of Subjects with Normalisation of C-reactive Protein (CRP) and/or Normalisation of Fecal Calprotectin (fCal) Concentration at Week 16 |
|-----------------|--|

End point description:

Percentage of subjects with normalisation at Week 16, among subjects with elevated CRP and/or fCal at baseline were reported. Subjects were considered normalised if at least one biomarker (fCal or CRP) was normalised. Normalised CRP=CRP value less than or equal to (\leq) 3 milligrams per liter(mg/L). Normalised fCal concentrations was defined as ≤ 250 micrograms per gram(mcg/g). When either CRP or fCal value was abnormal at baseline and value of same parameter normalises at analysis time, subjects were considered normalised at designated analysis timepoint. Subjects with prohibited CD-related surgery, prohibited concomitant medication changes, or discontinued drug due to lack of efficacy or adverse event indicated of worsening CD prior to analysis time are considered not normalised. Subjects with insufficient data at analysis timepoint had last value carried forward. FAS included all randomised subjects with either elevated CRP and/or elevated fCal at baseline.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16

| End point values | Group 1: Ustekinumab (IV Re-induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 94 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 33.3 | 14.9 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Ustekinumab IV Vs Ustekinumab SC |
| Statistical analysis description: The fixed sequence testing method was used. CMH chi-square test (2-sided) stratified by baseline CDAI score (≤ 300 or > 300), and prior biologic failure status at baseline (yes or no). | |
| Comparison groups | Group 1: Ustekinumab (IV Re-induction) v Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 ^[4] |
| Method | CMH chi-square test (2-sided) |
| Parameter estimate | Difference in percentage |
| Point estimate | 18.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.8 |
| upper limit | 30.2 |

Notes:

[4] - Since the primary endpoint did not achieve statistical significance, all p-values for the major secondary endpoints are nominal and are not statistically significant.

Secondary: Percentage of Subjects With Clinical Remission at Week 8

| | |
|---|--|
| End point title | Percentage of Subjects With Clinical Remission at Week 8 |
| End point description: Percentage of subjects with clinical remission at Week 8 were reported. Clinical remission was defined as CDAI score of <150 points. CDAI is a measure of severity of illness derived as weighted sum of 8 different CD-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates and general well-being). The last 4 variables were scored over 7 days by subject on diary card. In general, CDAI score ranges from 0 to approximately 600; higher score=higher disease activities. Subjects who had prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated to be of worsening CD prior to designated analysis timepoint were considered not to be in clinical remission, regardless of their CDAI score. FAS included all randomised subjects. | |
| End point type | Secondary |
| End point timeframe: Week 8 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 35.2 | 29.0 | | |

Statistical analyses

| Statistical analysis title | Ustekinumab IV Vs Ustekinumab SC |
|---|---|
| Statistical analysis description: | |
| The fixed sequence testing method was used. CMH chi-square test (2-sided) stratified by baseline CDAI score (≤ 300 or > 300), and prior biologic failure status at baseline (yes or no). | |
| Comparison groups | Group 1: Ustekinumab (IV Re-induction) v Group 2: Ustekinumab (Continuous q8w SC Maintenance) |
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.314 ^[5] |
| Method | CMH chi-square test (2-sided) |
| Parameter estimate | Difference in percentage |
| Point estimate | 6.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.8 |
| upper limit | 18.6 |

Notes:

[5] - Since the primary endpoint did not achieve statistical significance, all p-values for the major secondary endpoints are nominal and are not statistically significant.

Secondary: Percentage of Subjects With Clinical Remission at Week 24

| End point title | Percentage of Subjects With Clinical Remission at Week 24 |
|--|---|
| End point description: | |
| Percentage of subjects with clinical remission at Week 24 were reported. Clinical remission was defined as CDAI score of <150 points. CDAI is a measure of severity of illness derived as weighted sum of 8 different CD-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates and general well-being). The last 4 variables were scored over 7 days by subject on diary card. In general, CDAI score ranges from 0 to approximately 600; higher score=higher disease activities. Subjects who had prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated to be of worsening CD prior to designated analysis timepoint were considered not to be in clinical remission, regardless of their CDAI score. FAS included all randomised subjects. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 24 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 37.0 | 27.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Response at Week 24

| | |
|--|--|
| End point title | Percentage of Subjects With Clinical Response at Week 24 |
| End point description: | |
| <p>Clinical response was defined as a ≥ 100-point reduction from the baseline in CDAI score or a CDAI score < 150 point. The CDAI is a measure of severity of illness derived as a weighted sum of 8 different Crohn's disease-related variables (extra-intestinal manifestations, abdominal mass, weight, hematocrit, total number of liquid stools, abdominal pain/cramping, use of antidiarrheal drug(s) and/or opiates, and general well-being). The last 4 variables were scored over 7 days by the subject on a diary card. In general, CDAI score ranges from 0 to approximately 600; higher score indicates higher disease activities. Subjects who had prohibited CD-related surgery, prohibited concomitant medication changes or discontinued study agent due to lack of efficacy or adverse event indicated to be of worsening CD prior to designated analysis timepoint were considered not to be in clinical response, regardless of their CDAI score. FAS included all randomised subjects.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Week 24 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 47.2 | 39.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normalisation of C-reactive Protein (CRP) and/or Normalisation of Fecal Calprotectin (fCal) Concentration at Week 24

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Normalisation of C-reactive Protein (CRP) and/or Normalisation of Fecal Calprotectin (fCal) |
|-----------------|---|

End point description:

Percentage of subjects with normalisation at Week 24, among subjects with elevated CRP and/or fCal at baseline were reported. Subjects were considered normalised if at least one biomarker (fCal or CRP) was normalised. Normalised CRP=CRP value less than or equal to (\leq) 3 milligrams per liter(mg/L). Normalised fCal concentrations was defined as \leq 250 micrograms per gram(mcg/g). When either CRP or fCal value was abnormal at baseline and value of same parameter normalises at analysis time, subjects were considered normalised at designated analysis timepoint. Subjects with prohibited CD-related surgery, prohibited concomitant medication changes, or discontinued drug due to lack of efficacy or adverse event indicated of worsening CD prior to analysis time are considered not normalised. Subjects with insufficient data at analysis timepoint had last value carried forward. FAS included all randomised subjects with either elevated CRP and/or elevated fCal at baseline.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 94 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 26.9 | 21.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Adverse Events (TEAEs)

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Treatment-emergent Adverse Events (TEAEs) |
|-----------------|---|

End point description:

An adverse event was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An adverse event does not necessarily have a causal relationship with the treatment. TEAEs were adverse events with onset during the intervention phase or that were a consequence of a pre-existing condition that had worsened since baseline. Any AE occurring at or after the initial administration of study agent through the end of the trial was considered to be treatment emergent. In this endpoint, TEAEs including all AEs irrespective of being serious or non-serious AE are reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From baseline (Week 0) up to Week 36

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 70.4 | 72.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Serious Adverse Events (TESAEs)

| | |
|--|--|
| End point title | Percentage of Subjects with Treatment-emergent Serious Adverse Events (TESAEs) |
| End point description: | |
| <p>A serious adverse event (SAE) was an adverse event resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; a suspected transmission of any infectious agent via a medicinal product; medically important. TESAEs were adverse events with onset during the intervention phase or that are a consequence of a pre-existing condition that had worsened since baseline. Any AE occurring at or after the initial administration of study agent through the end of the trial was considered to be treatment emergent. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline (Week 0) up to Week 36 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 8.3 | 12.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Infections

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Treatment-emergent Infections |
|-----------------|---|

End point description:

Percentage of subjects with treatment-emergent infections were reported. Any infection occurring at or after the initial administration of study agent through the end of the trial was considered to be treatment emergent. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received.

End point type Secondary

End point timeframe:

From baseline (Week 0) up to Week 36

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 33.3 | 29.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment-emergent Serious Infections

End point title Percentage of Subjects with Treatment-emergent Serious Infections

End point description:

Percentage of subjects with treatment-emergent serious infections was reported. Any infection occurring at or after the initial administration of study agent through the end of the trial was considered to be treatment emergent. safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received.

End point type Secondary

End point timeframe:

From baseline (Week 0) up to Week 36

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 107 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 1.9 | 1.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory Values for Hematology (Hemoglobin) and Chemistry (Albumin, Total Protein)

| | |
|-----------------|---|
| End point title | Change from Baseline in Clinical Laboratory Values for Hematology (Hemoglobin) and Chemistry (Albumin, Total Protein) |
|-----------------|---|

End point description:

Change from baseline in clinical laboratory values for hematology (hemoglobin) and chemistry (albumin, total protein) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints for specified parameters.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16, 24

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 103 | 98 | | |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8: Hematology (Hemoglobin) (n=103, 92) | 2.893 (± 9.5568) | -0.185 (± 7.8669) | | |
| Week 16: Hematology (Hemoglobin) (n=94,85) | 3.245 (± 10.4621) | 0.835 (± 10.4652) | | |
| Week 24: Hematology (Hemoglobin) (n=74,75) | 3.203 (± 11.2408) | -0.400 (± 11.2610) | | |
| Week 8: Chemistry (Albumin) (n=102,98) | 0.765 (± 2.9456) | 0.286 (± 2.6671) | | |
| Week 16: Chemistry (Albumin) (n=97,92) | 0.567 (± 3.0649) | 0.554 (± 3.3753) | | |
| Week 24: Chemistry (Albumin) (n=81,77) | 0.741 (± 2.9613) | 0.221 (± 3.1690) | | |
| Week 8: Chemistry (Total protein) (n=102,98) | 0.588 (± 4.6806) | 0.265 (± 4.3803) | | |
| Week 16: Chemistry (Total protein) (n=97,92) | 0.340 (± 5.2418) | 0.783 (± 4.7690) | | |
| Week 24: Chemistry (Total protein) (n=81,78) | 0.605 (± 4.4150) | 0.333 (± 5.4954) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory Values for Hematology (Hematocrit)

| | |
|---|--|
| End point title | Change from Baseline in Clinical Laboratory Values for Hematology (Hematocrit) |
| End point description: Change from baseline in clinical laboratory values for hematology (hematocrit) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints | |
| End point type | Secondary |
| End point timeframe: Baseline, Weeks 8, 16, 24 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 101 | 88 | | |
| Units: Percentage of red blood cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 (n=101,88) | 0.009 (± 0.0313) | -0.001 (± 0.277) | | |
| Week 16 (n=90,83) | 0.010 (± 0.0306) | 0.001 (± 0.0356) | | |
| Week 24 (n=74,71) | 0.009 (± 0.0358) | 0.001 (± 0.0349) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory values for Hematology (Total White Blood Cell [WBC], Neutrophils, Absolute Lymphocyte, Eosinophils, Platelets)

| | |
|--|--|
| End point title | Change from Baseline in Clinical Laboratory values for Hematology (Total White Blood Cell [WBC], Neutrophils, Absolute Lymphocyte, Eosinophils, Platelets) |
| End point description: Change from baseline in clinical laboratory values for hematology (total WBC, neutrophils, absolute lymphocyte, eosinophils, platelets) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints for specific parameters | |
| End point type | Secondary |
| End point timeframe: Baseline, Weeks 8, 16, 24 | |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|--|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 103 | 92 | | |
| Units: 10 ⁹ cells/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8: Total WBC (n=103,92) | -0.386 (± 1.8358) | -0.272 (± 1.7301) | | |
| Week 16: Total WBC (n=94,85) | -0.329 (± 2.2700) | -0.124 (± 2.1404) | | |
| Week 24: Total WBC (n=74,75) | -0.149 (± 2.2347) | 0.104 (± 1.6612) | | |
| Week 8: Neutrophils (n=103, 92) | -0.235 (± 1.7610) | -0.241 (± 1.6154) | | |
| Week 16: Neutrophils (n=94,85) | -0.195 (± 2.0172) | -0.053 (± 2.1811) | | |
| Week 24: Neutrophils (n=74,75) | -0.038 (± 2.2944) | 0.133 (± 1.4312) | | |
| Week 8: Absolute Lymphocytes (n=103,92) | -0.101 (± 0.4962) | -0.020 (± 0.3415) | | |
| Week 16: Absolute Lymphocytes (n=94,85) | -0.088 (± 0.5690) | -0.052 (± 0.3997) | | |
| Week 24: Absolute Lymphocytes (n=74,75) | -0.088 (± 0.6599) | -0.021 (± 0.3960) | | |
| Week 8: Eosinophils (n=103,92) | -0.009 (± 0.0876) | -0.004 (± 0.1153) | | |
| Week 16: Eosinophils (n=94,85) | -0.014 (± 0.1176) | -0.013 (± 0.1330) | | |
| Week 24: Eosinophils (n=74,75) | -0.001 (± 0.0912) | -0.008 (± 0.1136) | | |
| Week 8: Platelets (n=103,92) | -13.65 (± 56.553) | -0.67 (± 51.591) | | |
| Week 16: Platelets (n=93,85) | -13.28 (± 60.105) | 4.53 (± 60.785) | | |
| Week 24: Platelets (n=73,73) | -10.89 (± 62.671) | -0.53 (± 56.624) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory values for Chemistry (Alkaline Phosphatase, Alanine Transaminase [ALT], Aspartate Transaminase [AST])

| | |
|-----------------|---|
| End point title | Change from Baseline in Clinical Laboratory values for Chemistry (Alkaline Phosphatase, Alanine Transaminase [ALT], Aspartate Transaminase [AST]) |
|-----------------|---|

End point description:

Change from baseline in clinical laboratory values for chemistry (alkaline, ALT, AST) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints for specified parameters.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:
Baseline, Weeks 8, 16, 24

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 102 | 98 | | |
| Units: Units per Liter (U/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8: Alkaline Phosphatase (n=102,98) | -1.343 (± 10.7404) | -0.582 (± 10.3565) | | |
| Week 16: Alkaline Phosphatase (n=97,91) | -0.072 (± 12.9488) | 0.923 (± 11.5154) | | |
| Week 24: Alkaline Phosphatase (n=81,77) | -0.296 (± 14.2649) | 0.078 (± 16.1594) | | |
| Week 8: ALT (n=101,97) | -0.347 (± 9.3642) | -0.412 (± 7.9001) | | |
| Week 16: ALT (n=95,89) | -0.811 (± 8.3898) | -0.101 (± 9.9750) | | |
| Week 24: ALT (n=80,76) | 0.463 (± 10.1470) | 2.224 (± 15.5979) | | |
| Week 8: AST (n=101,97) | -0.525 (± 12.0147) | 0.144 (± 4.8584) | | |
| Week 16: AST (n=96,92) | -0.208 (± 12.6366) | 0.163 (± 5.4557) | | |
| Week 24: AST (n=81,77) | 0.741 (± 5.6718) | 1.519 (± 7.3047) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory values for Chemistry (Total Bilirubin, Direct Bilirubin, Creatinine)

| | |
|------------------------|---|
| End point title | Change from Baseline in Clinical Laboratory values for Chemistry (Total Bilirubin, Direct Bilirubin, Creatinine) |
| End point description: | Change from baseline in clinical laboratory values for chemistry (total bilirubin, direct bilirubin, creatinine) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints for specified parameters. |
| End point type | Secondary |
| End point timeframe: | Baseline, Weeks 8, 16, 24 |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 102 | 98 | | |
| Units: micromole per liter (mcmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8: Total Bilirubin (n=101,97) | 0.639 (± 2.5303) | -0.131 (± 2.9617) | | |
| Week 16: Total Bilirubin (n=97,92) | 1.476 (± 3.4135) | 0.555 (± 3.6679) | | |
| Week 24: Total Bilirubin (n=81,77) | 0.687 (± 3.0396) | 0.254 (± 3.1664) | | |
| Week 8: Direct Bilirubin (n=100,97) | 0.086 (± 0.5495) | -0.010 (± 0.5998) | | |
| Week 16: Direct Bilirubin (n=92,90) | 0.154 (± 0.6910) | 0.071 (± 0.7628) | | |
| Week 24: Direct Bilirubin (n=80,76) | 0.109 (± 0.5393) | 0.009 (± 0.7612) | | |
| Week 8: Creatinine (n=102,98) | -0.446 (± 8.9118) | -0.308 (± 9.6489) | | |
| Week 16: Creatinine (n=97,92) | 0.624 (± 9.7987) | 1.117 (± 9.0316) | | |
| Week 24: Creatinine (n=81,77) | 1.717 (± 9.5267) | 0.336 (± 8.4020) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Laboratory Values for Chemistry (Sodium, Potassium, Chloride, Blood Urea Nitrogen [BUN]/urea, Calcium, Phosphate)

| | |
|------------------------|---|
| End point title | Change from Baseline in Clinical Laboratory Values for Chemistry (Sodium, Potassium, Chloride, Blood Urea Nitrogen [BUN]/urea, Calcium, Phosphate) |
| End point description: | Change from baseline in clinical laboratory values for chemistry (sodium, potassium, chloride, BUN/urea, calcium, phosphate) was reported. Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjects were analysed according to the actual treatment received. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' signifies subjects who were evaluated at specified timepoints for specified parameters. |
| End point type | Secondary |
| End point timeframe: | Baseline, Weeks 8, 16, 24 |

| End point values | Group 1: Ustekinumab (IV Re- induction) | Group 2: Ustekinumab (Continuous q8w SC Maintenance) | | |
|--------------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 102 | 98 | | |
| Units: millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Sodium: Week 8 (n=102,98) | 0.108 (± 2.5714) | -0.061 (± 2.2375) | | |
| Sodium: Week 16 (n=97,92) | -0.165 (± 2.2299) | 0.011 (± 2.3370) | | |
| Sodium: Week 24 (n=81,77) | 0.235 (± 2.2928) | -0.117 (± 2.0454) | | |
| Potassium: Week 8 (n=101,98) | 0.126 (± 0.3596) | 0.050 (± 0.3269) | | |
| Potassium: Week 16 (n=97,92) | 0.105 (± 0.3745) | -0.002 (± 0.3933) | | |
| Potassium: Week 24 (n=81,77) | 0.067 (± 0.3732) | 0.001 (± 0.3185) | | |
| Chloride: Week 8 (n=102,98) | 0.078 (± 2.9136) | -0.520 (± 2.4714) | | |
| Chloride: Week 16 (n=97,92) | -0.299 (± 2.4798) | -0.489 (± 2.5398) | | |
| Chloride: Week 24 (n=81,77) | 0.160 (± 2.4107) | -0.481 (± 2.2160) | | |
| BUN/urea: Week 8 (n=102,98) | 0.279 (± 1.0050) | 0.248 (± 1.0710) | | |
| BUN/urea: Week 16 (n=97,92) | 0.204 (± 1.2812) | 0.029 (± 1.2841) | | |
| BUN/urea: Week 24 (n=81,77) | 0.304 (± 1.2031) | 0.179 (± 1.0629) | | |
| Calcium: Week 8 (n=102,98) | 0.022 (± 0.0967) | 0.013 (± 0.0968) | | |
| Calcium: Week 16 (n=97,92) | 0.007 (± 0.1010) | 0.007 (± 0.1098) | | |
| Calcium: Week 24 (n=81,77) | 0.008 (± 0.1101) | 0.004 (± 0.1109) | | |
| Phosphate: Week 8 (n=102,98) | 0.005 (± 0.2015) | 0.046 (± 0.2024) | | |
| Phosphate: Week 16 (n=97,92) | 0.006 (± 0.1946) | 0.026 (± 0.1905) | | |
| Phosphate: Week 24 (n=81,77) | 0.018 (± 0.1612) | 0.021 (± 0.1938) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (Week 0) up to Week 36

Adverse event reporting additional description:

Safety analysis set included all randomised subjects who received at least 1 administration of study agent. Subjectss were analysed according to the actual treatment received.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Group 2: Ustekinumab (Continuous q8w SC maintenance) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary LoR to ustekinumab administered as SC injection q8w maintenance therapy received ustekinumab 90 mg as SC injection and placebo matching to ustekinumab as an IV infjusion at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| | |
|-----------------------|--|
| Reporting group title | Group 1: Ustekinumab (IV re-induction) |
|-----------------------|--|

Reporting group description:

Subjects who initially responded to ustekinumab induction therapy followed by a secondary loss of response (LoR) to ustekinumab administered as subcutaneous (SC) injection every 8 weeks (q8w) maintenance therapy received a weight-tiered based re-induction dose of ustekinumab 6 milligrams per kilogram (mg/kg) as an intravenous (IV) infusion and placebo matching to ustekinumab as SC injection at Week 0. At Weeks 8 and 16, all subjects received ustekinumab 90 mg maintenance dose as SC injection. At Week 24, all subjects underwent study assessments before resuming their standard-of-care therapy at the discretion of the treating physician. Subjects were followed-up for safety up to Week 36.

| Serious adverse events | Group 2: Ustekinumab (Continuous q8w SC maintenance) | Group 1: Ustekinumab (IV re- induction) | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 107 (12.15%) | 9 / 108 (8.33%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant Melanoma | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (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 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 3 / 107 (2.80%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's Disease | | | |
| subjects affected / exposed | 4 / 107 (3.74%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileal Stenosis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small Intestinal Obstruction | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Small Intestinal Stenosis | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus Urinary | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Atrophy | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral Stenosis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (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 | | | |
| Abdominal Abscess | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Abscess | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth Abscess | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (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 | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Group 2: Ustekinumab (Continuous q8w SC maintenance) | Group 1: Ustekinumab (IV re- induction) | |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 77 / 107 (71.96%) | 73 / 108 (67.59%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Pituitary Tumour Benign | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Superficial Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) | |
| occurrences (all) | 0 | 2 | |
| General disorders and administration site conditions | | | |

| | | | |
|--|-----------------|-----------------|--|
| Asthenia | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Chills | | | |
| subjects affected / exposed | 2 / 107 (1.87%) | 0 / 108 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 107 (2.80%) | 0 / 108 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Influenza Like Illness | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) | |
| occurrences (all) | 0 | 2 | |
| Injection Site Erythema | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences (all) | 2 | 1 | |
| Injection Site Mass | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 107 (3.74%) | 2 / 108 (1.85%) | |
| occurrences (all) | 6 | 2 | |
| Immune system disorders | | | |
| Seasonal Allergy | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Heavy Menstrual Bleeding | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) | |
| occurrences (all) | 0 | 2 | |
| Pelvic Fluid Collection | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scrotal Dermatitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Female Genital Tract Fistula | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences (all) | 1 | 1 | |
| Cough | | | |
| subjects affected / exposed | 6 / 107 (5.61%) | 1 / 108 (0.93%) | |
| occurrences (all) | 6 | 1 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Dyspnoea Exertional | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 2 | |
| Nasal Congestion | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Productive Cough | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Rhinitis Allergic | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinorrhoea | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Tonsillar Disorder subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Psychiatric disorders | | | |
| Affective Disorder subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Conversion Disorder subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Depression subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 2 / 108 (1.85%) 2 | |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 2 / 108 (1.85%) 2 | |
| Restlessness subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Investigations | | | |
| Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Blood Alkaline Phosphatase Increased subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 0 / 108 (0.00%) 0 | |
| Blood Creatinine Increased subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Blood Magnesium Decreased subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| C-Reactive Protein Increased | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 0 / 108 (0.00%) 0 | |
| Gamma-Glutamyltransferase Increased subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Sars-Cov-2 Test Positive subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Vitamin D Decreased subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 1 / 108 (0.93%) 1 | |
| Weight Increased subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot Fracture subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Infusion Related Reaction subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Injection Related Reaction subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Ligament Rupture subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Procedural Pain subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Skin Laceration subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Spinal Compression Fracture | | | |

| | | | |
|--|----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Thermal Burn subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Vaccination Complication subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 1 / 108 (0.93%) 1 | |
| Tendon Rupture subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Cardiac disorders Atrial Fibrillation subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Nervous system disorders Carotid Arteriosclerosis subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 2 / 108 (1.85%) 2 | |
| Dizziness Postural subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 5 / 107 (4.67%) 7 | 8 / 108 (7.41%) 15 | |
| Migraine subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Ophthalmic Migraine subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|----------------------|----------------------|--|
| Anaemia subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 3 / 108 (2.78%) 3 | |
| Iron Deficiency Anaemia subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 1 / 108 (0.93%) 1 | |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 2 | 0 / 108 (0.00%) 0 | |
| Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Eye disorders Eye Irritation subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Photophobia subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Uveitis subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Gastrointestinal disorders Abdominal Discomfort subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 2 / 108 (1.85%) 2 | |
| Abdominal Pain | | | |

| | | |
|----------------------------------|-------------------|-------------------|
| subjects affected / exposed | 3 / 107 (2.80%) | 5 / 108 (4.63%) |
| occurrences (all) | 3 | 6 |
| Abdominal Mass | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Abdominal Distension | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Food Poisoning | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Faecaloma | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Eosinophilic Oesophagitis | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Dyspepsia | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) |
| occurrences (all) | 0 | 2 |
| Diarrhoea | | |
| subjects affected / exposed | 2 / 107 (1.87%) | 0 / 108 (0.00%) |
| occurrences (all) | 2 | 0 |
| Crohn's Disease | | |
| subjects affected / exposed | 29 / 107 (27.10%) | 23 / 108 (21.30%) |
| occurrences (all) | 31 | 23 |
| Constipation | | |
| subjects affected / exposed | 2 / 107 (1.87%) | 0 / 108 (0.00%) |
| occurrences (all) | 3 | 0 |
| Anal Skin Tags | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Anal Fistula | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Anal Fissure | | |

| | | |
|----------------------------------|-----------------|-----------------|
| subjects affected / exposed | 4 / 107 (3.74%) | 0 / 108 (0.00%) |
| occurrences (all) | 4 | 0 |
| Anal Eczema | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Abdominal Tenderness | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Abdominal Pain Upper | | |
| subjects affected / exposed | 2 / 107 (1.87%) | 2 / 108 (1.85%) |
| occurrences (all) | 2 | 2 |
| Abdominal Pain Lower | | |
| subjects affected / exposed | 2 / 107 (1.87%) | 0 / 108 (0.00%) |
| occurrences (all) | 2 | 0 |
| Gastrointestinal Inflammation | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Large Intestine Polyp | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haemorrhoids | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) |
| occurrences (all) | 0 | 2 |
| Haematochezia | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Gastrooesophageal Reflux Disease | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 2 / 108 (1.85%) |
| occurrences (all) | 1 | 2 |
| Nausea | | |
| subjects affected / exposed | 4 / 107 (3.74%) | 1 / 108 (0.93%) |
| occurrences (all) | 4 | 1 |
| Rectal Haemorrhage | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Stomatitis | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Subileus subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Toothache subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 1 / 108 (0.93%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 2 / 108 (1.85%) 2 | |
| Proctalgia subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Hepatobiliary disorders Cholecystitis subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Cholestasis subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Acne subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Decubitus Ulcer subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Dermal Cyst | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Dermatitis | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Eczema | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Erythema Nodosum | | | |
| subjects affected / exposed occurrences (all) | 3 / 107 (2.80%) 3 | 0 / 108 (0.00%) 0 | |
| Intertrigo | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Psoriasis | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 1 / 108 (0.93%) 1 | |
| Urticaria | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Pelvi-Ureteric Obstruction | | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 | |
| Arthralgia | | | |

| | | |
|--|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 4 / 107 (3.74%) 4 | 3 / 108 (2.78%) 3 |
| Back Pain | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 4 / 108 (3.70%) 4 |
| Greater Trochanteric Pain Syndrome | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Groin Pain | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Muscle Contracture | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Neck Pain | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Osteoarthritis | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Pain in Jaw | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Polyarthritis | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Rheumatic Disorder | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Spondylitis | | |
| subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Fistula | | |
| subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Infections and infestations | | |

| | | |
|---|-------------------------|-------------------------|
| Enteritis Infectious subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Abscess Soft Tissue subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Anal Abscess subjects affected / exposed occurrences (all) | 2 / 107 (1.87%) 2 | 1 / 108 (0.93%) 1 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Covid-19 subjects affected / exposed occurrences (all) | 16 / 107 (14.95%) 16 | 12 / 108 (11.11%) 12 |
| Coronavirus Infection subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Clostridium Difficile Infection subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |
| Erythema Migrans subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 4 / 107 (3.74%) 4 | 2 / 108 (1.85%) 2 |
| Gastroenteritis Viral subjects affected / exposed occurrences (all) | 1 / 107 (0.93%) 1 | 0 / 108 (0.00%) 0 |
| Gastrointestinal Infection subjects affected / exposed occurrences (all) | 0 / 107 (0.00%) 0 | 1 / 108 (0.93%) 1 |

| | | |
|-----------------------------------|-----------------|-----------------|
| Herpes Zoster | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infected Fistula | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Infection | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Influenza | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 4 / 108 (3.70%) |
| occurrences (all) | 1 | 5 |
| Lower Respiratory Tract Infection | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Nasopharyngitis | | |
| subjects affected / exposed | 5 / 107 (4.67%) | 3 / 108 (2.78%) |
| occurrences (all) | 8 | 5 |
| Otitis Externa | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pharyngitis Streptococcal | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) |
| occurrences (all) | 0 | 1 |
| Pyelitis | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pyelonephritis | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) |
| occurrences (all) | 1 | 0 |
| Sinusitis | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 2 / 108 (1.85%) |
| occurrences (all) | 0 | 2 |
| Upper Respiratory Tract Infection | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 5 / 108 (4.63%) |
| occurrences (all) | 0 | 5 |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| Ureaplasma Infection | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 3 / 107 (2.80%) | 3 / 108 (2.78%) | |
| occurrences (all) | 3 | 3 | |
| Vulvovaginal Candidiasis | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Gout | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences (all) | 1 | 1 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences (all) | 1 | 1 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Iron Deficiency | | | |
| subjects affected / exposed | 0 / 107 (0.00%) | 1 / 108 (0.93%) | |
| occurrences (all) | 0 | 1 | |
| Type 2 Diabetes Mellitus | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin D Deficiency | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 107 (0.93%) | 1 / 108 (0.93%) | |
| occurrences (all) | 1 | 1 | |
| Zinc Deficiency | | | |
| subjects affected / exposed | 1 / 107 (0.93%) | 0 / 108 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 19 July 2019 | The purpose of this amendment was to include information regarding the planned primary endpoint database lock at Week 16 and the final database lock. Other clarifications and changes were made to address investigator and site questions surrounding operational elements of the study. |
| 08 April 2020 | The purpose of this amendment was to allow for self-administration of subcutaneous study intervention at Weeks 8 and 16 outside a study site (eg, at home), in cases where a study site visit is not possible under restrictions and limitations during the Coronavirus Disease-2019 (COVID-19) pandemic. Guidance on other aspects of study conduct during the COVID-19 pandemic is also included. |
| 19 May 2020 | The purpose of this amendment was to allow subcutaneous injections of study intervention at Week 8 and Week 16 to be self-administered outside a study site, in cases where a site visit is not possible. |
| 05 August 2020 | The purpose of this amendment was to increase enrollment into the study, through allowing subjects who have previously received a dose interval shortening of 90mg SC ustekinumab less than every 8 weeks and clarify ileocolonoscopy as an exploratory endpoint for subjects who agree to this procedure. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|---|--------------|
| 26 March 2020 | Enrollment was temporarily held early in the COVID-19 pandemic. | 01 July 2020 |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Some exploratory endpoints including endoscopic assessments for baseline and week 16 and clinical data for 24 weeks are not reported in this summary and will be included in the manuscript.

Notes: