



Clinical trial results:

A Phase 3 Open-label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Subcutaneously Administered Ustekinumab in the Treatment of Moderate to Severe Chronic Plaque Psoriasis in Pediatric Subjects 6 to <12 Years of Age

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2016-000121-40 |
| Trial protocol | BE HU DE PL FR NL Outside EU/EEA |
| Global end of trial date | 06 October 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 16 April 2021 |
| First version publication date | 16 April 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | CNT01275PSO3013 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02698475 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route202, Raritan, United States, 08869 |
| Public contact | Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000311-PIP01-08 |
| 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 | 06 October 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of ustekinumab in pediatric subjects greater than or equal to (\geq) 6 years to less than ($<$) 12 years of age with moderate to severe chronic plaque psoriasis.

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 evaluations were based on the incidence and type of adverse events (AEs), laboratory analyte values, vital sign measurements, physical examinations, concomitant medication review, injection-site reactions, allergic reactions, tuberculosis evaluations reported during the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 07 June 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 52 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Germany: 7 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Poland: 12 |
| Country: Number of subjects enrolled | United States: 8 |
| Worldwide total number of subjects | 44 |
| EEA total number of subjects | 34 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age $<$ 37 | 0 |

| | |
|--|----|
| wk | |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 44 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 52 subjects were screened, of which 44 subjects were enrolled in the study and 39 subjects completed the main study period. 28 subjects entered the long-term extension period.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Ustekinumab Standard Dosage (Main Study) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--|
| Arm title | Ustekinumab Standard Dosage (Main Study) |
|-----------|--|

Arm description:

Subjects received ustekinumab standard weight-based dose at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing up to Week 40. Ustekinumab was administered as subcutaneous (SC) injections of 0.75 milligrams per kilogram (mg/kg) for subjects with weight less than (<) 60 kilograms (kg), 45 mg for subjects with weight greater than or equal to (\geq) 60 kg to less than or equal to (\leq) 100 kg, and 90 mg for subjects with weight >100 kg. Subjects had a safety follow-up till Week 56.

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

Dosage and administration details:

Subjects received weight-based dose of ustekinumab as SC injections at Week 0 and 4 followed by q12w dosing up to Week 40.

| Number of subjects in period 1 | Ustekinumab Standard Dosage (Main Study) |
|--------------------------------|--|
| Started | 44 |
| Completed | 41 |
| Not completed | 3 |
| Lack of efficacy | 1 |
| Protocol deviation | 2 |

Period 2

| | |
|------------------------------|-----------------------------------|
| Period 2 title | Ustekinumab Standard Dosage (LTE) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|---|
| Arm title | Ustekinumab Standard Dosage (Long-term extension [LTE]) |
|------------------|---|

Arm description:

Subjects who had a beneficial response from Ustekinumab treatment continued receiving ustekinumab weight based dose in a every 12 weeks (q12w) regimen from Week 56 onwards until commercially available or up to Week 264. Ustekinumab was administered as SC injections of 0.75 mg/kg for subjects with weight <60 kg, 45 mg for subjects with weight >=60 kg to <=100 kg, and 90 mg for subjects with weight >100 kg.

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

Dosage and administration details:

Subjects received weight-based dose of ustekinumab as SC injections at Week 56 followed by q12w dosing until commercially available or up to Week 264.

| Number of subjects in period 2^[1] | Ustekinumab Standard Dosage (Long-term extension [LTE]) |
|---|---|
| Started | 28 |
| Completed | 0 |
| Not completed | 28 |
| Trial site terminated by sponsor | 1 |
| Other | 1 |
| LTE protocol-specified criteria 9.1.5 | 22 |
| Lost to follow-up | 1 |
| Withdrawal by subject | 3 |

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: The number of subjects starting the long-term extension (LTE) period is different from the main study period as per study design because only few subjects entered the LTE period.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Ustekinumab Standard Dosage (Main Study) |
|-----------------------|--|

Reporting group description:

Subjects received ustekinumab standard weight-based dose at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing up to Week 40. Ustekinumab was administered as subcutaneous (SC) injections of 0.75 milligrams per kilogram (mg/kg) for subjects with weight less than (<) 60 kilograms (kg), 45 mg for subjects with weight greater than or equal to (>=) 60 kg to less than or equal to (<=) 100 kg, and 90 mg for subjects with weight >100 kg. Subjects had a safety follow-up till Week 56.

| Reporting group values | Ustekinumab Standard Dosage (Main Study) | Total | |
|---|--|-------|--|
| Number of subjects | 44 | 44 | |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 44 | 44 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65 to 84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 8.9 | | |
| standard deviation | ± 1.74 | - | |
| Title for Gender Units: subjects | | | |
| Female | 27 | 27 | |
| Male | 17 | 17 | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Ustekinumab Standard Dosage (Main Study) |
|-----------------------|--|

Reporting group description:

Subjects received ustekinumab standard weight-based dose at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing up to Week 40. Ustekinumab was administered as subcutaneous (SC) injections of 0.75 milligrams per kilogram (mg/kg) for subjects with weight less than (<) 60 kilograms (kg), 45 mg for subjects with weight greater than or equal to (>=) 60 kg to less than or equal to (<=) 100 kg, and 90 mg for subjects with weight >100 kg. Subjects had a safety follow-up till Week 56.

| | |
|-----------------------|---|
| Reporting group title | Ustekinumab Standard Dosage (Long-term extension [LTE]) |
|-----------------------|---|

Reporting group description:

Subjects who had a beneficial response from Ustekinumab treatment continued receiving ustekinumab weight based dose in a every 12 weeks (q12w) regimen from Week 56 onwards until commercially available or up to Week 264. Ustekinumab was administered as SC injections of 0.75 mg/kg for subjects with weight <60 kg, 45 mg for subjects with weight >=60 kg to <=100 kg, and 90 mg for subjects with weight >100 kg.

Primary: Percentage of Subjects With Physician's Global Assessment (PGA) Score of Cleared (0) or Minimal (1) at Week 12

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Physician's Global Assessment (PGA) Score of Cleared (0) or Minimal (1) at Week 12 ^[1] |
|-----------------|---|

End point description:

The PGA is used to determine the subject's psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling. The subject's psoriasis was assessed as cleared (0), minimal (1), mild (2), moderate (3), marked (4), or severe (5). Higher scores indicated worse disease. Analysis set: Full analysis set (FAS), consisted of all enrolled and treated participants who received at least 1 injection of ustekinumab (partial or complete). Treatment Failure (TF) criteria: discontinued study agent due to lack of efficacy or adverse event (AE) of worsening of psoriasis or who started protocol-prohibited medication/therapy. Participants who met TF criteria prior to Week 12 or with missing data at Week 12 were considered non-responders at Week 12.

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

End point timeframe:

Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 77.3 (62.2 to 88.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12

| | |
|-----------------|---|
| End point title | Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12 |
|-----------------|---|

End point description:

PASI system is used for assessing and grading the severity of psoriatic lesions and their response to therapy. The body is divided into 4 regions: head, trunk, upper and lower extremities. Each of these areas is assessed separately for the percentage of area involved and gives a numeric score ranging from 0 (no involvement) to 6 (90%-100% involvement). For erythema, induration, and scaling, which are each rated on a scale of 0 (None) to 4 (very severe). PASI produces a numeric score ranging from 0 (no psoriasis) to 72 (disease severity). Higher score indicates more severe disease. Subjects with ≥ 75 % improvement in PASI from Baseline were considered PASI 75 responders. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met TF criteria prior to Week 12 or with missing data at Week 12 were considered non-responders at Week 12.

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

End point timeframe:

Week 12

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 84.1 (69.9 to 93.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Children Dermatology Life Quality Index (CDLQI) Score at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in Children Dermatology Life Quality Index (CDLQI) Score at Week 12 |
|-----------------|--|

End point description:

CDLQI was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in subjects with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30, with lower scores indicating better quality of life. The higher the score, the greater the impairment in quality of life (QoL). Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. For subjects meeting one or more TF criteria, were considered to have 0 improvement from baseline. Here "N" (number of subjects analyzed) signifies subjects who were evaluable for this outcome measure at both baseline and Week 12.

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

End point timeframe:

Baseline and Week 12

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -6.3 (± 6.43) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved PASI 90 Response at Week 12

| | |
|-----------------|---|
| End point title | Percentage of Subjects who Achieved PASI 90 Response at Week 12 |
|-----------------|---|

End point description:

PASI system is used for assessing and grading the severity of psoriatic lesions and their response to therapy. The body is divided into 4 regions: head, trunk, upper and lower extremities. Each of these areas is assessed separately for the percentage of area involved and gives a numeric score ranging from 0 (no involvement) to 6 (90%-100% involvement). For erythema, induration, and scaling, which are each rated on a scale of 0 (None) to 4 (very severe). PASI produces a numeric score ranging from 0 (no psoriasis) to 72 (disease severity). Higher score indicates more severe disease. Subjects with ≥ 90 % improvement in PASI from Baseline were considered PASI 90 responders. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met TF criteria prior to Week 12 or with missing data at Week 12 were considered non-responders at Week 12.

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

End point timeframe:

Week 12

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 63.6 (47.8 to 77.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with a PGA Score of Cleared (0), Cleared (0) or Minimal (1), Mild or Better (<=2) at Weeks 4, 8, 12, 16, 28, 40, and 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects with a PGA Score of Cleared (0), Cleared (0) or Minimal (1), Mild or Better (<=2) at Weeks 4, 8, 12, 16, 28, 40, and 52 |
|-----------------|--|

End point description:

The PGA is used to determine the subject's psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling. The subject's psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), marked (4), or severe (5). Higher scores indicate worse disease. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met 1 or more TF criteria were considered as non-responders after TF. In addition, subjects with missing data at Week 12 were also considered as non-responders at Week 12. 'n' (number analyzed): subjects evaluated at given timepoints.

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

End point timeframe:

Weeks 4, 8, 12, 16, 28, 40, and 52

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|---------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 4: PGA Score 0 (n=42) | 4.8 | | | |
| Week 4: PGA Score 0 or 1 (n=42) | 33.3 | | | |
| Week 4: PGA Score 0 or 1 or 2 (n=42) | 66.7 | | | |
| Week 8: PGA Score 0 (n=41) | 26.8 | | | |
| Week 8: PGA Score 0 or 1 (n=41) | 63.4 | | | |
| Week 8: PGA Score 0 or 1 or 2 (n=41) | 85.4 | | | |
| Week 12: PGA Score 0 (n=44) | 38.6 | | | |
| Week 12: PGA Score 0 or 1 (n=44) | 77.3 | | | |
| Week 12: PGA Score 0 or 1 or 2 (n=44) | 90.9 | | | |
| Week 16: PGA Score 0 (n=42) | 45.2 | | | |
| Week 16: PGA Score 0 or 1 (n=42) | 85.7 | | | |
| Week 16: PGA Score 0 or 1 or 2 (n=42) | 95.2 | | | |
| Week 28: PGA Score 0 (n=42) | 45.2 | | | |
| Week 28: PGA Score 0 or 1 (n=42) | 83.3 | | | |
| Week 28: PGA Score 0 or 1 or 2 (n=42) | 95.2 | | | |
| Week 40: PGA Score 0 (n=42) | 52.4 | | | |
| Week 40: PGA Score 0 or 1 (n=42) | 76.2 | | | |
| Week 40: PGA Score 0 or 1 or 2 (n=42) | 90.5 | | | |
| Week 52: PGA Score 0 (n=41) | 56.1 | | | |
| Week 52: PGA Score 0 or 1 (n=41) | 75.6 | | | |
| Week 52: PGA Score 0 or 1 or 2 (n=41) | 90.2 | | | |

Statistical analyses

Secondary: Percentage of Subjects who Achieved a PASI 50, PASI 75, PASI 90 and PASI 100 Response at Weeks 4, 8, 12, 16, 28, 40, and 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects who Achieved a PASI 50, PASI 75, PASI 90 and PASI 100 Response at Weeks 4, 8, 12, 16, 28, 40, and 52 |
|-----------------|---|

End point description:

PASI system is used for assessing and grading the severity of psoriatic lesions and their response to therapy. The body is divided into 4 regions: head, trunk, upper and lower extremities. Each of these areas is assessed separately for the percentage of area involved and gives a numeric score ranging from 0 (no involvement) to 6 (90%-100% involvement). For erythema, induration, and scaling, which are each rated on a scale of 0 (None) to 4 (very severe). PASI produces a numeric score ranging from 0 (no psoriasis) to 72 (disease severity). PASI 50, 75, 90, and 100 refers to $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and 100% improvement in PASI from Baseline respectively. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met TF criteria prior to Week 12 or with missing data were considered non-responders at Week 12. 'n' (number analyzed): subjects evaluated at given timepoints.

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

End point timeframe:

Weeks 4, 8, 12, 16, 28, 40, and 52

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 4: PASI 100 (n=42) | 2.4 | | | |
| Week 4: PASI 90 (n=42) | 16.7 | | | |
| Week 4: PASI 75 (n=42) | 26.2 | | | |
| Week 4: PASI 50 (n=42) | 52.4 | | | |
| Week 8: PASI 100 (n=41) | 17.1 | | | |
| Week 8: PASI 90 (n=41) | 43.9 | | | |
| Week 8: PASI 75 (n=41) | 58.5 | | | |
| Week 8: PASI 50 (n=41) | 82.9 | | | |
| Week 12: PASI 100 (n=44) | 34.1 | | | |
| Week 12: PASI 90 (n=44) | 63.6 | | | |
| Week 12: PASI 75 (n=44) | 84.1 | | | |
| Week 12: PASI 50 (n=44) | 93.2 | | | |
| Week 16: PASI 100 (n=42) | 40.5 | | | |
| Week 16: PASI 90 (n=42) | 66.7 | | | |
| Week 16: PASI 75 (n=42) | 83.3 | | | |
| Week 16: PASI 50 (n=42) | 97.6 | | | |
| Week 28: PASI 100 (n=42) | 38.1 | | | |
| Week 28: PASI 90 (n=42) | 81.0 | | | |
| Week 28: PASI 75 (n=42) | 92.9 | | | |
| Week 28: PASI 50 (n=42) | 92.9 | | | |
| Week 40: PASI 100 (n=42) | 42.9 | | | |
| Week 40: PASI 90 (n=42) | 78.6 | | | |

| | | | | |
|--------------------------|------|--|--|--|
| Week 40: PASI 75 (n=42) | 90.5 | | | |
| Week 40: PASI 50 (n=42) | 92.9 | | | |
| Week 52: PASI 100 (n=41) | 53.7 | | | |
| Week 52: PASI 90 (n=41) | 70.7 | | | |
| Week 52: PASI 75 (n=41) | 87.8 | | | |
| Week 52: PASI 50 (n=41) | 92.7 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in PASI Score at Weeks 4, 8, 12, 16, 28, 40, and 52

| | |
|-----------------|--|
| End point title | Percent Change from Baseline in PASI Score at Weeks 4, 8, 12, 16, 28, 40, and 52 |
|-----------------|--|

End point description:

PASI system is used for assessing and grading the severity of psoriatic lesions and their response to therapy. The body is divided into 4 regions: head, trunk, upper and lower extremities. Each of these areas is assessed separately for the percentage of area involved and gives a numeric score ranging from 0 (no involvement) to 6 (90%-100% involvement). For erythema, induration, and scaling, which are each rated on a scale of 0 (None) to 4 (very severe). PASI produces a numeric score ranging from 0 (no psoriasis) to 72 (disease severity). PASI 100 responders were defined as 100% improvement in PASI from Baseline respectively. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. For subjects meeting one or more TF criteria, were considered to have 0% improvement from baseline. 'n' (number analyzed): subjects evaluated at given timepoints.

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

End point timeframe:

Baseline and Weeks 4, 8, 12, 16, 28, 40, 52

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=42) | 52.9 (± 27.33) | | | |
| Week 8 (n=41) | 78.9 (± 21.44) | | | |
| Week 12 (n=42) | 89.7 (± 13.80) | | | |
| Week 16 (n=42) | 90.4 (± 13.77) | | | |
| Week 28 (n=42) | 90.4 (± 21.55) | | | |
| Week 40 (n=42) | 89.9 (± 23.01) | | | |
| Week 52 (n=41) | 89.1 (± 24.28) | | | |

Statistical analyses

Secondary: Percentage of Subjects who Achieved PASI 100, PASI 90, PASI 75 or PASI 50 Response in PASI Components (Induration, Erythema, and Scaling) and Region Components (Head, Trunk, Upper Extremities, and Lower Extremities) at Week 12

| | |
|-----------------|--|
| End point title | Percentage of Subjects who Achieved PASI 100, PASI 90, PASI 75 or PASI 50 Response in PASI Components (Induration, Erythema, and Scaling) and Region Components (Head, Trunk, Upper Extremities, and Lower Extremities) at Week 12 |
|-----------------|--|

End point description:

PASI system is used for assessing and grading the severity of psoriatic lesions and their response to therapy. The body is divided into 4 regions: head, trunk, upper and lower extremities. Each of these areas is assessed separately for the percentage of area involved and gives a numeric score ranging from 0 (no involvement) to 6 (90%-100% involvement). For erythema, induration, and scaling, which are each rated on a scale of 0 (None) to 4 (very severe). PASI produces a numeric score ranging from 0 (no psoriasis) to 72 (disease severity). PASI 50, 75, 90, and 100 refers to $\geq 50\%$, $\geq 75\%$, $\geq 90\%$, and 100% improvement in PASI from Baseline respectively. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects meeting one or more TF criteria were considered as non-responders.

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

End point timeframe:

Week 12

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Induration: PASI 100 | 43.2 | | | |
| Induration: PASI 90 | 61.4 | | | |
| Induration: PASI 75 | 77.3 | | | |
| Induration: PASI 50 | 93.2 | | | |
| Scaling: PASI 100 | 38.6 | | | |
| Scaling: PASI 90 | 63.6 | | | |
| Scaling: PASI 75 | 84.1 | | | |
| Scaling: PASI 50 | 90.9 | | | |
| Erythema: PASI 100 | 38.6 | | | |
| Erythema: PASI 90 | 61.4 | | | |
| Erythema: PASI 75 | 81.8 | | | |
| Erythema: PASI 50 | 93.2 | | | |
| Head: PASI 100 | 52.3 | | | |
| Head: PASI 90 | 65.9 | | | |
| Head: PASI 75 | 79.5 | | | |
| Head: PASI 50 | 93.2 | | | |
| Trunk: PASI 100 | 61.4 | | | |
| Trunk: PASI 90 | 61.4 | | | |
| Trunk: PASI 75 | 79.5 | | | |
| Trunk: PASI 50 | 88.6 | | | |
| Upper extremities: PASI 100 | 65.9 | | | |

| | | | | |
|-----------------------------|------|--|--|--|
| Upper extremities: PASI 90 | 65.9 | | | |
| Upper extremities: PASI 75 | 79.5 | | | |
| Upper extremities: PASI 50 | 84.1 | | | |
| Lower extremities: PASI 100 | 68.2 | | | |
| Lower extremities: PASI 90 | 68.2 | | | |
| Lower extremities: PASI 75 | 72.7 | | | |
| Lower extremities: PASI 50 | 93.2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDLQI Score at Weeks 4, 12, 28, and 52

| | |
|--|--|
| End point title | Change from Baseline in CDLQI Score at Weeks 4, 12, 28, and 52 |
| End point description: | |
| CDLQI was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30. The higher the score, the greater the impairment in quality of life (QoL). Analysis set: FAS. TF criteria-discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met TF criteria prior to Week 12 were assigned 0 change. 'n' (number analyzed): subjects evaluated at given timepoints. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Weeks 4, 12, 28, 52 | |

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 44 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=42) | -4.1 (± 4.88) | | | |
| Week 12 (n=42) | -6.3 (± 6.43) | | | |
| Week 28 (n=42) | -6.6 (± 5.79) | | | |
| Week 52 (n=41) | -6.4 (± 6.10) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with a CDLQI Score of 0 or 1 at Week 12 in Subjects with a Baseline CDLQI Score Greater than (>) 1

| | |
|-----------------|---|
| End point title | Percentage of Subjects with a CDLQI Score of 0 or 1 at Week |
|-----------------|---|

End point description:

CDLQI was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30. The higher the score, the greater impairment in quality of life. Analysis set: FAS with CDLQI score >1 at baseline. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met 1 or more TF criteria prior to Week 12 or with missing data were considered as nonresponders. Here "N" (number of subjects analyzed) signifies subjects who were evaluable for this endpoint.

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

End point timeframe:

Week 12

| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 39 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 61.5 (44.6 to 76.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with a CDLQI Score of 0 or 1 at Weeks 4, 12, 28 and 52 in Subjects with a Baseline CDLQI Score >1

| | |
|-----------------|--|
| End point title | Percentage of Subjects with a CDLQI Score of 0 or 1 at Weeks 4, 12, 28 and 52 in Subjects with a Baseline CDLQI Score >1 |
|-----------------|--|

End point description:

CDLQI was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30. The higher the score, the greater impairment in quality of life. Analysis set: FAS with CDLQI >1 at baseline. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met 1 or more TF criteria were considered as nonresponders after TF. Here "N" (number of subjects analyzed) signifies subjects who were evaluable for this endpoint and 'n' (number analyzed): subjects evaluated at given timepoints.

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

End point timeframe:

Weeks 4, 12, 28, and 52

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 39 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 4 (n=37) | 38.7 | | | |
| Week 12 (n=39) | 61.5 | | | |
| Week 28 (n=37) | 62.2 | | | |
| Week 52 (n=36) | 58.3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDLQI Component Scores at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in CDLQI Component Scores at Week 12 |
|-----------------|---|

End point description:

CDLQI was used to assess the impact of psoriasis on subject health-related quality of life. The CDLQI has 10 items assessing health-related quality of life (HRQOL) in patients with skin disease each measured on a scale from 0 (Not at all) to 3 (Very much). The total score ranges from 0 to 30. The total score ranges from 0 to 30. The higher the score, the greater impairment in quality of life. Analysis set: FAS. TF criteria- discontinued study agent due to lack of efficacy or AE of worsening of psoriasis or who started protocol-prohibited medication/therapy. Subjects who met TF criteria prior to Week 12 were assigned 0 change. Here 'N' (number of subjects analyzed) included all subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Week 12

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Ustekinumab Standard Dosage (Main Study) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Symptoms and feelings | -1.9 (± 1.81) | | | |
| Leisure | -1.7 (± 2.19) | | | |
| School or holidays | -0.5 (± 0.80) | | | |
| Personal relationships | -0.8 (± 1.71) | | | |
| Sleep | -0.4 (± 0.91) | | | |
| Treatment | -0.9 (± 1.14) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving a PGA Score of Cleared (0), Cleared (0) or Minimal (1), Mild or Better (<=2) at Weeks 80, 104, 128, 152 and 176

| | |
|-----------------|--|
| End point title | Percentage of Subjects Achieving a PGA Score of Cleared (0), Cleared (0) or Minimal (1), Mild or Better (<=2) at Weeks 80, 104, 128, 152 and 176 |
|-----------------|--|

End point description:

The PGA is used to determine the subject's psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling. The subject's psoriasis was assessed as cleared (0), minimal (1), mild (2), moderate (3), marked (4), or severe (5). Higher scores indicated worse disease. Analysis set: FAS; all subjects enrolled in the LTE who received at least an injection of ustekinumab at Week 56 (partial or complete). Here "N" (number of subjects analyzed) signifies subjects who were evaluable for this endpoint and 'n' (number analyzed): subjects evaluated at given timepoints.

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

End point timeframe:

Weeks 80, 104, 128, 152, 176

| End point values | Ustekinumab Standard Dosage (Long-term extension [LTE]) | | | |
|--|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 80: PGA score 0 (n=25) | 64 | | | |
| Week 80: PGA score 0 or 1 (n=25) | 80 | | | |
| Week 80: PGA score 0 or 1 or 2 (n=25) | 100 | | | |
| Week 104: PGA score 0 (n=20) | 50 | | | |
| Week 104: PGA score 0 or 1 (n=20) | 70 | | | |
| Week 104: PGA score 0 or 1 or 2 (n=20) | 100 | | | |
| Week 128: PGA score 0 (n=20) | 60 | | | |
| Week 128: PGA score 0 or 1 (n=20) | 80 | | | |
| Week 128: PGA score 0 or 1 or 2 (n=20) | 95 | | | |
| Week 152: PGA score 0 (n=13) | 53.8 | | | |
| Week 152: PGA score 0 or 1 (n=13) | 61.5 | | | |
| Week 152: PGA score 0 or 1 or 2 (n=13) | 100 | | | |
| Week 176: PGA score 0 (n=3) | 33.3 | | | |
| Week 176: PGA score 0 or 1 (n=3) | 66.7 | | | |
| Week 176: PGA score 0 or 1 or 2 (n=3) | 100 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 264

Adverse event reporting additional description:

Safety analysis set consisted of all enrolled subjects who received at least 1 injection of ustekinumab (partial or complete) during the study.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Ustekinumab Standard Dosage (Main Study) |
|-----------------------|--|

Reporting group description:

Subjects received ustekinumab standard weight-based dose at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing up to Week 40. Ustekinumab was administered as subcutaneous (SC) injections of 0.75 milligrams per kilogram (mg/kg) for subjects with weight less than (<) 60 kilograms (kg), 45 mg for subjects with weight greater than or equal to (>=) 60 kg to less than or equal to (<=) 100 kg, and 90 mg for subjects with weight >100 kg. Subjects had a safety follow-up till Week 56.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Ustekinumab Standard Dosage (LTE) |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects who had a beneficial response from Ustekinumab treatment continued receiving ustekinumab weight based dose in a every 12 weeks (q12w) regimen from Week 56 onwards until commercially available or up to Week 264. Ustekinumab was administered as SC injections of 0.75 mg/kg for subjects with weight <60 kg, 45 mg for subjects with weight >=60 kg to <=100 kg, and 90 mg for subjects with weight >100 kg.

| Serious adverse events | Ustekinumab Standard Dosage (Main Study) | Ustekinumab Standard Dosage (LTE) | |
|---|--|-----------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 1 / 28 (3.57%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Eyelid Injury | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Attention Deficit/Hyperactivity Disorder | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 28 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infectious Mononucleosis | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 28 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Ustekinumab Standard Dosage (Main Study) | Ustekinumab Standard Dosage (LTE) | |
|--|--|-----------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 44 (61.36%) | 17 / 28 (60.71%) | |
| General disorders and administration site conditions | | | |
| Injection Site Erythema | | | |
| subjects affected / exposed | 6 / 44 (13.64%) | 2 / 28 (7.14%) | |
| occurrences (all) | 16 | 2 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 28 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 2 / 28 (7.14%) | |
| occurrences (all) | 0 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | 3 / 28 (10.71%) | |
| occurrences (all) | 2 | 4 | |

| | | | |
|---|------------------------|-----------------------|--|
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 3 / 28 (10.71%) 3 | |
| Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all) | 3 / 44 (6.82%) 4 | 0 / 28 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 3 / 28 (10.71%) 3 | |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) | 3 / 44 (6.82%) 3 | 3 / 28 (10.71%) 3 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 11 / 44 (25.00%) 12 | 8 / 28 (28.57%) 11 | |
| Otitis Media subjects affected / exposed occurrences (all) | 3 / 44 (6.82%) 3 | 2 / 28 (7.14%) 2 | |
| Pharyngitis subjects affected / exposed occurrences (all) | 6 / 44 (13.64%) 11 | 1 / 28 (3.57%) 2 | |
| Respiratory Tract Infection subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 2 / 28 (7.14%) 3 | |
| Tonsillitis subjects affected / exposed occurrences (all) | 4 / 44 (9.09%) 4 | 0 / 28 (0.00%) 0 | |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 6 / 44 (13.64%) 12 | 2 / 28 (7.14%) 17 | |
| Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 2 / 28 (7.14%) 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|---|
| 18 May 2017 | The overall reason for this amendment was to allow pediatric subjects who demonstrated clinical benefit through Week 52 of the main study to continue receiving ustekinumab. Additionally, longer-term safety and efficacy data in this patient population was collected. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

| |
|--|
| Due to the study design, the population was limited in the long-term extension period and decreased over time as subjects met discontinuation criteria and exited the study. |
|--|

Notes: