



Clinical trial results:

A Phase 3, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study of the Efficacy and Safety of Apremilast (CC-10004) in Subjects with Moderate to Severe Genital Psoriasis

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2018-002608-15 |
| Trial protocol | FR BE IT |
| Global end of trial date | 09 February 2022 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 15 December 2022 |
| First version publication date | 15 December 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------------|
| Sponsor protocol code | CC-10004-PSOR-025 |
|-----------------------|-------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03777436 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Amgen Inc. |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, |
| Public contact | Study Director, Amgen Inc., +1 866-572-6436, medinfo@amgen.com |
| Scientific contact | Study Director, Amgen Inc., +1 866-572-6436, medinfo@amgen.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 | 09 February 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 February 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the clinical efficacy of oral apremilast 30 mg twice daily (BID), compared to placebo, in participants with moderate to severe genital psoriasis during the 16-week Placebo-controlled Phase.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines and in accordance with the general ethical principles outlined in the Declaration of Helsinki. Essential documents will be retained in accordance with ICH GCP. The study sponsor declares that the information provided in this report is an accurate representation of the data captured and analyses performed for this study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 February 2019 |
| 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 | Belgium: 7 |
| Country: Number of subjects enrolled | Canada: 45 |
| Country: Number of subjects enrolled | Germany: 66 |
| Country: Number of subjects enrolled | France: 11 |
| Country: Number of subjects enrolled | Italy: 19 |
| Country: Number of subjects enrolled | United States: 141 |
| Worldwide total number of subjects | 289 |
| EEA total number of subjects | 103 |

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) | 255 |
| From 65 to 84 years | 34 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 49 centers in Belgium, Canada, France, Germany, Italy, and the United States from February 2019 to February 2022.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive either apremilast or matched placebo for the first 16 weeks (Placebo-controlled Phase) of the study. At Week 16, eligible participants may have continued on active treatment by entering a 16-week extension phase (Apremilast Extension Phase). Total treatment duration = 32 weeks.

Period 1

| | |
|------------------------------|--------------------------|
| Period 1 title | Placebo-controlled Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo-controlled Phase: Placebo |

Arm description:

Participants received placebo as oral tablets twice daily (BID) for up to 16 weeks (Week 0 to Week 16).

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered orally.

| | |
|------------------|--|
| Arm title | Placebo-controlled Phase: Apremilast 30 mg |
|------------------|--|

Arm description:

Participants received apremilast 30 mg as oral tablets BID for up to 16 weeks (Week 0 to Week 16).

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Apremilast |
| Investigational medicinal product code | CC-10004 |
| Other name | Otezla |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered orally.

| Number of subjects in period 1 | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg |
|----------------------------------|-----------------------------------|--|
| | | |
| Started | 146 | 143 |
| Took at Least 1 Dose of IP | 145 | 143 |
| Completed | 111 | 119 |
| Not completed | 35 | 24 |
| Consent withdrawn by subject | 19 | 3 |
| Physician decision | - | 1 |
| Due to COVID-19 control measures | 1 | - |
| Adverse event, non-fatal | 8 | 10 |
| Non-compliance with study drug | - | 2 |
| Lost to follow-up | 7 | 7 |
| Lack of efficacy | - | 1 |

Period 2

| | |
|------------------------------|----------------------------|
| Period 2 title | Apremilast Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--|
| Arm title | Apremilast Extension Phase: Apremilast 30 mg |
|------------------|--|

Arm description:

Eligible participants who completed the Placebo-controlled Phase entered the Apremilast Extension Phase and received apremilast 30 mg as oral tablets BID for up to an additional 16 weeks (Week 16 to Week 32).

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Apremilast |
| Investigational medicinal product code | CC-10004 |
| Other name | Otezla |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered orally.

| Number of subjects in period 2^[1] | Apremilast Extension Phase: Apremilast 30 mg |
|---|--|
| Started | 229 |
| Took at Least 1 Dose of IP | 228 |
| Completed | 201 |
| Not completed | 28 |
| Consent withdrawn by subject | 13 |
| Adverse event, non-fatal | 6 |
| Miscellaneous | 1 |
| Lost to follow-up | 7 |
| Lack of efficacy | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 1 participant did not enter the Apremilast Extension Phase as they were lost to follow-up.

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Placebo-controlled Phase: Placebo |
| Reporting group description: | |
| Participants received placebo as oral tablets twice daily (BID) for up to 16 weeks (Week 0 to Week 16). | |
| Reporting group title | Placebo-controlled Phase: Apremilast 30 mg |
| Reporting group description: | |
| Participants received apremilast 30 mg as oral tablets BID for up to 16 weeks (Week 0 to Week 16). | |

| Reporting group values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | Total |
|------------------------|-----------------------------------|--|-------|
| Number of subjects | 146 | 143 | 289 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|---------|-----|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 46.4 | 43.5 | |
| standard deviation | ± 14.38 | ± 13.36 | - |
| Sex: Female, Male | | | |
| Units: | | | |
| Female | 44 | 43 | 87 |
| Male | 102 | 100 | 202 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 8 | 4 | 12 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 1 |
| Black or African American | 3 | 6 | 9 |
| White | 131 | 131 | 262 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 3 | 2 | 5 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 13 | 18 | 31 |
| Not Hispanic or Latino | 131 | 125 | 256 |
| Unknown or Not Reported | 2 | 0 | 2 |
| Modified Static Physician Global Assessment of Genitalia (sPGA-G) Score | | | |
| The modified sPGA-G is the assessment by the Investigator of the participant's psoriasis lesions' overall disease severity in the genital area at the time of evaluation. The modified sPGA-G is a 5-point scale ranging from clear (0), almost clear (1), mild (2), moderate (3), to severe (4), incorporating an assessment of the severity of the three primary signs of the disease: erythema, plaque elevation, and scaling. | | | |
| Units: Subjects | | | |
| 3 (Moderate) | 128 | 123 | 251 |
| 4 (Severe) | 18 | 20 | 38 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Placebo-controlled Phase: Placebo |
| Reporting group description: Participants received placebo as oral tablets twice daily (BID) for up to 16 weeks (Week 0 to Week 16). | |
| Reporting group title | Placebo-controlled Phase: Apremilast 30 mg |
| Reporting group description: Participants received apremilast 30 mg as oral tablets BID for up to 16 weeks (Week 0 to Week 16). | |
| Reporting group title | Apremilast Extension Phase: Apremilast 30 mg |
| Reporting group description: Eligible participants who completed the Placebo-controlled Phase entered the Apremilast Extension Phase and received apremilast 30 mg as oral tablets BID for up to an additional 16 weeks (Week 16 to Week 32). | |

Primary: Percentage of Participants With a Modified sPGA-G Response at Week 16

| | |
|--|---|
| End point title | Percentage of Participants With a Modified sPGA-G Response at Week 16 |
| End point description: The modified sPGA-G is the assessment by the Investigator of the participant's psoriasis lesions' overall disease severity in the genital area at the time of evaluation. The modified sPGA-G is a 5-point scale ranging from clear (0), almost clear (1), mild (2), moderate (3), to severe (4), incorporating an assessment of the severity of the 3 primary signs of the disease: erythema, plaque elevation, and scaling. A modified sPGA-G response is defined as modified sPGA-G score of clear (0) or almost clear (1) and with ≥ 2 -point reduction from Baseline at Week 16. Missing values were imputed using the multiple imputation (MI) method. Two-sided 95% confidence intervals (CIs) for the within-group proportions were based on the Wilson-score method. The intent-to-treat (ITT) analysis set consisted of all participants who are randomized regardless of whether the participant received investigational product (IP). | |
| End point type | Primary |
| End point timeframe: Baseline and Week 16 of the Placebo-controlled Phase | |

| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 143 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 19.1 (12.4 to 25.7) | 38.7 (30.4 to 47.0) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Placebo versus (vs.) Apremilast 30 mg |
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0003 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted difference |
| Point estimate | 19.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 9 |
| upper limit | 30.3 |

Secondary: Percentage of Participants With a Static Physician Global Assessment (sPGA) Response at Week 16

| | |
|-----------------|---|
| End point title | Percentage of Participants With a Static Physician Global Assessment (sPGA) Response at Week 16 |
|-----------------|---|

End point description:

The sPGA is the assessment by the Investigator of the overall disease severity at the time of evaluation. The sPGA is a 5-point scale ranging from 0 (clear), 1 (almost clear), 3 (moderate) to 4 (severe), incorporating an assessment of the severity of the 3 primary signs of the disease: erythema, scaling and plaque elevation.

An sPGA response is defined as sPGA score of clear (0) or almost clear (1) and with ≥ 2 -point reduction from Baseline at Week 16.

Missing values were imputed using the MI method. Two-sided 95% CIs for the within-group proportions were based on the Wilson-score method.

The ITT analysis set consisted of all participants who are randomized regardless of whether the participant received IP.

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

End point timeframe:

Baseline and Week 16 of the placebo-controlled phase

| | | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 143 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 7.2 (2.9 to 11.5) | 21.5 (14.4 to 28.5) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Placebo vs. Apremilast 30 mg |
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 289 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0007 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted difference |
| Point estimate | 14.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6 |
| upper limit | 22.5 |

Secondary: Percentage of Participants With a Genital Psoriasis Itch Numeric Rating Scale (GPI-NRS) Response at Week 16

| | |
|-----------------|---|
| End point title | Percentage of Participants With a Genital Psoriasis Itch Numeric Rating Scale (GPI-NRS) Response at Week 16 |
|-----------------|---|

End point description:

The GPI-NRS is a self-reported measure where participants were asked to assess their psoriasis symptoms in the genital area and select a number on a scale of 0-10, where 0 represents no itch, and 10 represents the worst imaginable itch.

A GPI-NRS response is defined as ≥ 4 point reduction (improvement) from Baseline.

Missing values were imputed using the MI method. Two-sided 95% CIs for the within-group proportions were based on the Wilson-score method.

ITT analysis set with Baseline GPI-NRS score ≥ 4 .

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 16 of the placebo-controlled phase | |

| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
|-----------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 121 | 122 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 19.6 (12.2 to 27.0) | 46.0 (36.8 to 55.3) | | |

Statistical analyses

| Statistical analysis title | Placebo vs. Apremilast 30 mg |
|---|--|
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 243 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Adjusted difference |
| Point estimate | 26.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.5 |
| upper limit | 38 |

Secondary: Change from Baseline in Affected Body Surface Area (BSA) at Week 16

| | |
|-----------------|---|
| End point title | Change from Baseline in Affected Body Surface Area (BSA) at Week 16 |
|-----------------|---|

End point description:

The BSA is a measurement of involved skin over the whole body. The overall BSA affected by psoriasis is estimated based on the palm area of the participant's hand. The surface area of the whole body is made up of approximately 100 palms or "handprints" (each entire palmar surface or "handprint" equates to approximately 1% of total BSA).

A negative change from Baseline indicates a reduction of affected BSA.

Based on mixed-effect model for repeated measures (MMRM) model.

ITT analysis set with Baseline and at least one post-baseline value at Week 16.

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

End point timeframe:

Baseline and Week 16 of the placebo-controlled phase

| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
|---|-----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 120 | | |
| Units: Change in percentage of affected BSA | | | | |
| least squares mean (standard error) | -0.79 (\pm 0.669) | -4.12 (\pm 0.664) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Placebo vs. Apremilast 30 mg |
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 231 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0005 |
| Method | MMRM |
| Parameter estimate | Least squares mean difference |
| Point estimate | -3.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.18 |
| upper limit | -1.47 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.942 |

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16

| | |
|-----------------|--|
| End point title | Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16 |
|-----------------|--|

End point description:

The DLQI is a 10 item questionnaire dealing with the participant's skin. With the exception of Item Number 7, the participant responds on a four-point scale, ranging from 0 (not at all) to 3 (very much). Item Number 7 is a multi-part item, the first part of which ascertains whether the participant's skin prevented them from working or studying (Yes or No), and if "No," then the participant is asked how much of a problem the skin has been at work or study over the past week, with response alternatives being 0 (not at all), 1 (a little) and 2 (a lot).

Total scores have a possible range of 0-30, where 0 represents the best score, and 30 represents the worst health-related quality of life.

A negative change from Baseline indicates an improvement in health-related quality of life scores.

Based on MMRM model.

ITT analysis set with Baseline and at least one post-baseline value at Week 16.

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

End point timeframe:

Baseline and Week 16 of the placebo-controlled phase

| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107 | 117 | | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | -2.6 (\pm 0.57) | -5.3 (\pm 0.55) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Placebo vs. Apremilast 30 mg |
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 224 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0008 |
| Method | MMRM |
| Parameter estimate | Least squares mean difference |
| Point estimate | -2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.2 |
| upper limit | -1.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.79 |

Secondary: Change From Baseline in Genital Psoriasis Symptoms Scale (GPSS) Total Score at Week 16

| | |
|-----------------|--|
| End point title | Change From Baseline in Genital Psoriasis Symptoms Scale (GPSS) Total Score at Week 16 |
|-----------------|--|

End point description:

The GPSS is a self-reported measure where participants were asked to assess each of their psoriasis symptoms (itch, pain, discomfort, stinging, burning, redness, scaling, and cracking) in the genital area and select a number on a scale of 0-10, where 0 represents no, and 10 represents the worst imaginable.

Results from each symptom assessment were summed to generate a total GPSS score ranging from 0 (no genital psoriasis symptoms) to 80 (worst imaginable genital psoriasis symptoms).

A negative change from Baseline indicates an improvement in genital psoriasis symptoms.

Based on MMRM model.

ITT analysis set with Baseline and at least one post-baseline value at Week 16.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 16 of the placebo-controlled phase | |

| End point values | Placebo-controlled Phase: Placebo | Placebo-controlled Phase: Apremilast 30 mg | | |
|-------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107 | 116 | | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | -5.3 (\pm 1.85) | -20.5 (\pm 1.83) | | |

Statistical analyses

| Statistical analysis title | Placebo vs. Apremilast 30 mg |
|---|--|
| Comparison groups | Placebo-controlled Phase: Placebo v Placebo-controlled Phase: Apremilast 30 mg |
| Number of subjects included in analysis | 223 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | MMRM |
| Parameter estimate | Difference |
| Point estimate | -15.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.3 |
| upper limit | -10 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.6 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to a maximum of 41.4 weeks

Adverse event reporting additional description:

The safety analysis set consisted of all participants who were randomized and received at least one dose of IP.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Placebo-controlled Phase: Placebo |
|-----------------------|-----------------------------------|

Reporting group description:

Participants received placebo as oral tablets BID for up to 16 weeks (Week 0 to Week 16).

| | |
|-----------------------|--|
| Reporting group title | Apremilast Extension Phase: Apremilast 30 mg |
|-----------------------|--|

Reporting group description:

Eligible participants who completed the Placebo-controlled Phase entered the Apremilast Extension Phase and received apremilast 30 mg as oral tablets BID for up to an additional 16 weeks (Week 16 to Week 32).

| | |
|-----------------------|--|
| Reporting group title | Placebo-controlled Phase: Apremilast 30 mg |
|-----------------------|--|

Reporting group description:

Participants received apremilast 30 mg as oral tablets BID for up to 16 weeks (Week 0 to Week 16).

| Serious adverse events | Placebo-controlled Phase: Placebo | Apremilast Extension Phase: Apremilast 30 mg | Placebo-controlled Phase: Apremilast 30 mg |
|---|-----------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 145 (1.38%) | 2 / 229 (0.87%) | 3 / 143 (2.10%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 229 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 229 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Actinic keratosis | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 1 / 229 (0.44%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 229 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 1 / 229 (0.44%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 229 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 229 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 145 (0.00%) | 0 / 229 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 229 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 145 (0.69%) | 0 / 229 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Placebo-controlled Phase: Placebo | Apremilast Extension Phase: Apremilast 30 mg | Placebo-controlled Phase: Apremilast 30 mg |
|---|--|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 39 / 145 (26.90%) | 53 / 229 (23.14%) | 73 / 143 (51.05%) |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 16 / 145 (11.03%) 18 | 15 / 229 (6.55%) 18 | 33 / 143 (23.08%) 41 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 12 / 145 (8.28%) 13 11 / 145 (7.59%) 12 | 27 / 229 (11.79%) 28 17 / 229 (7.42%) 17 | 37 / 143 (25.87%) 38 32 / 143 (22.38%) 32 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 12 / 145 (8.28%) 13 | 11 / 229 (4.80%) 14 | 12 / 143 (8.39%) 14 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 22 May 2019 | <ul style="list-style-type: none">- Specified that use of strong cytochrome P450 3A4 (CYP3A4) enzyme inducers is not recommended during the study.- Specified prohibitive concomitant use of antifungal and antiseptic treatment in the genital area.- Removed blinded language in reference to the apremilast extension phase and added dispensation of IP bottles at Week 20. |
| 01 May 2020 | <ul style="list-style-type: none">- Updated to reflect the change in sponsor from Celgene to Amgen.- Updated safety reporting and product complaints information to align with Amgen processes. |
| 03 March 2021 | <ul style="list-style-type: none">- Specified that the strata with BSA $\geq 10\%$ would be $\geq 40\%$ of the total enrollment (and the strata with BSA $< 10\%$ would comprise $\leq 60\%$ of the total enrollment).- Updated the sample size from approximately 332 participants to approximately 286 participants.- Updated the power calculation based on the change in sample size. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|---|--------------|
| 01 April 2020 | In April 2020, screening and enrollment were temporarily paused at all participating countries/sites to limit potential COVID-19 exposure for study participants, sponsor employees, and staff at clinical study sites. | 01 June 2020 |

Notes:

Limitations and caveats

None reported