



Clinical trial results:

A Phase 2a, Randomized, Double-blinded, Placebo-controlled Study to Evaluate the Efficacy and Safety of MEDI9929 in Adult Subjects with Moderate-to-Severe Atopic Dermatitis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-000595-10 |
| Trial protocol | DE HU |
| Global end of trial date | 15 July 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 01 November 2017 |
| First version publication date | 01 November 2017 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D5240C00001 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02525094 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | MedImmune Ltd |
| Sponsor organisation address | Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH |
| Public contact | AstraZeneca, AstraZeneca Clinical Study Information Center, +1 1-877-240-9479, information.center@astrazeneca.com |
| Scientific contact | AstraZeneca, AstraZeneca Clinical Study Information Center, +1 1-877-240-9479, information.center@astrazeneca.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 | 15 July 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 July 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of trial was to evaluate the effect of MEDI9929 compared with placebo in adult participants with moderate to-severe Atopic Dermatitis (AD), assessed using the change from baseline in Eczema Area and Severity Index (EASI) at Week 12.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice and applicable regulatory requirements. Subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

All participants received maintenance therapy of Class 3 topical corticosteroids (TCS) cream or ointment for lesional skin from the start of the run-in period (Visit 2, Week -2) to Week 22.

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 29 August 2015 |
| 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 | Australia: 13 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Germany: 36 |
| Country: Number of subjects enrolled | Hungary: 15 |
| Country: Number of subjects enrolled | New Zealand: 1 |
| Country: Number of subjects enrolled | United States: 34 |
| Worldwide total number of subjects | 111 |
| EEA total number of subjects | 51 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 105 |
| From 65 to 84 years | 6 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 29Aug2015 to 15Jul2016.

Pre-assignment

Screening details:

A total of 155 participants were screened, of which 113 were randomized. Out of 113 participants, 111 were treated in the study.

Period 1

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

Arms

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

Arm description:

Participants received 6 subcutaneous doses of placebo every 2 weeks for 12 weeks, with the last dose at Week 10.

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo administered as 6 subcutaneous doses for every 2 weeks for 12 weeks, with the last dose at Week 10.

| | |
|------------------|-----------------|
| Arm title | MEDI9929 280 mg |
|------------------|-----------------|

Arm description:

Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI9929 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

MEDI9929 was administered at the dose of 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10.

| Number of subjects in period 1 | Placebo | MEDI9929 280 mg |
|---------------------------------------|---------|-----------------|
| Started | 56 | 55 |
| Completed | 49 | 48 |
| Not completed | 7 | 7 |
| Consent withdrawn by subject | 5 | 6 |
| Lost to follow-up | 2 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-----------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received 6 subcutaneous doses of placebo every 2 weeks for 12 weeks, with the last dose at Week 10. | |
| Reporting group title | MEDI9929 280 mg |
| Reporting group description: | |
| Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10. | |

| Reporting group values | Placebo | MEDI9929 280 mg | Total |
|--|---------|-----------------|-------|
| Number of subjects | 56 | 55 | 111 |
| Age Categorical | | | |
| Units: Subjects | | | |
| 18-35 years | 28 | 27 | 55 |
| 36-75 years | 28 | 28 | 56 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 38.8 | 38.5 | - |
| standard deviation | ± 15.3 | ± 14.9 | - |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 26 | 23 | 49 |
| Male | 30 | 32 | 62 |
| Eczema Area and Severity Index Score | | | |
| The eczema area and severity index (EASI) evaluates 4 natural anatomical regions for severity (0 [none] to 3 [severe]) and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The total score is the sum of the four body-region scores, maximum=72, minimum=0. The higher values indicating more severe disease. | | | |
| Units: Subjects | | | |
| ≤ 25 points | 36 | 33 | 69 |
| > 25 points | 20 | 22 | 42 |
| Investigator's Global Assessment | | | |
| The investigator's global assessment (IGA) allows investigators to assess overall disease severity at one given time point and consists of a 5-point severity scale from clear to severe disease (0 = clear, 1 = almost clear, 2 = mild disease, 3 = moderate disease, and 4 = severe disease). | | | |
| Units: Subjects | | | |
| Category 2 | 0 | 1 | 1 |
| Category 3 | 46 | 44 | 90 |
| Category 4 | 10 | 10 | 20 |
| Atopic Dermatitis Status | | | |
| Units: Subjects | | | |
| IgE ≥ 150 kU/L and Positive Serum Specific IgEa | 50 | 47 | 97 |
| IgE ≥ 150 kU/L and Negative Serum Specific IgE | 2 | 0 | 2 |
| IgE < 150 kU/L and Positive Serum Specific IgE | 3 | 3 | 6 |

| | | | |
|---|---|---|---|
| IgE < 150 kU/L and Negative Serum Specific IgEb | 1 | 3 | 4 |
| Missing | 0 | 2 | 2 |

Subject analysis sets

| | |
|----------------------------|-----------------|
| Subject analysis set title | MEDI9929 280mg |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10. Participants who received at least one dose of MEDI9929 during the study, regardless of randomized treatment assignment, were analyzed under MEDI9929 group. One participant who randomized to placebo group but received an incorrect first dose of MEDI9929 was included in the "MEDI9929" group. An arbitrary value of '99999' indicates value was not estimable.

| Reporting group values | MEDI9929 280mg | | |
|--|----------------|--|--|
| Number of subjects | 56 | | |
| Age Categorical | | | |
| Units: Subjects | | | |
| 18-35 years | | | |
| 36-75 years | | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 38.5 | | |
| standard deviation | ± 14.9 | | |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| Eczema Area and Severity Index Score | | | |
| The eczema area and severity index (EASI) evaluates 4 natural anatomical regions for severity (0 [none] to 3 [severe]) and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The total score is the sum of the four body-region scores, maximum=72, minimum=0. The higher values indicating more severe disease. | | | |
| Units: Subjects | | | |
| <= 25 points | 99999 | | |
| > 25 points | | | |
| Investigator's Global Assessment | | | |
| The investigator's global assessment (IGA) allows investigators to assess overall disease severity at one given time point and consists of a 5-point severity scale from clear to severe disease (0 = clear, 1 = almost clear, 2 = mild disease, 3 = moderate disease, and 4 = severe disease). | | | |
| Units: Subjects | | | |
| Category 2 | | | |
| Category 3 | | | |
| Category 4 | | | |
| Atopic Dermatitis Status | | | |
| Units: Subjects | | | |
| IgE >= 150 kU/L and Positive Serum Specific IgEa | | | |
| IgE >= 150 kU/L and Negative Serum Specific IgE | | | |
| IgE < 150 kU/L and Positive Serum Specific IgE | | | |

| | | | |
|---|--|--|--|
| IgE < 150 kU/L and Negative Serum Specific IgEb Missing | | | |
|---|--|--|--|

End points

End points reporting groups

| | |
|--|-----------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received 6 subcutaneous doses of placebo every 2 weeks for 12 weeks, with the last dose at Week 10. | |
| Reporting group title | MEDI9929 280 mg |
| Reporting group description: Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10. | |
| Subject analysis set title | MEDI9929 280mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10. Participants who received at least one dose of MEDI9929 during the study, regardless of randomized treatment assignment, were analyzed under MEDI9929 group. One participant who randomized to placebo group but received an incorrect first dose of MEDI9929 was included in the "MEDI9929" group. An arbitrary value of '99999' indicates value was not estimable. | |

Primary: Percentage of Participants Achieving Greater Than or Equal to (>=) 50 Percent (%) Reduction From Baseline in Eczema Area and Severity Index (EASI 50) at Week 12

| | |
|--|--|
| End point title | Percentage of Participants Achieving Greater Than or Equal to (>=) 50 Percent (%) Reduction From Baseline in Eczema Area and Severity Index (EASI 50) at Week 12 |
| End point description: The eczema area and severity index (EASI) evaluates 4 natural anatomical regions for severity (0 [none] to 3 [severe]) and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The total score is the sum of the four body-region scores, maximum=72, minimum=0. The higher values indicating more severe disease. The EASI50 responder defined as a participant who achieved at least 50% reduction in EASI score from baseline. Intent-To-Treat (ITT) population included all participants who were randomized and received any study investigational product. | |
| End point type | Primary |
| End point timeframe: Week 12 | |

| End point values | Placebo | MEDI9929 280 mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 48.2 | 64.7 | | |

Statistical analyses

| | |
|----------------------------|---------------------------|
| Statistical analysis title | Placebo vs MEDI9929 280mg |
| Comparison groups | MEDI9929 280 mg v Placebo |

| | |
|---|-----------------|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 4.33 |

Secondary: Percentage of Participants Achieving \geq 75 % Reduction From Baseline in EASI75 at Week 12

| | |
|------------------------|---|
| End point title | Percentage of Participants Achieving \geq 75 % Reduction From Baseline in EASI75 at Week 12 |
| End point description: | The EASI evaluates 4 natural anatomical regions for severity (0 [none] to 3 [severe]) and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The total score is the sum of the four body-region scores, maximum=72, minimum=0. The higher values indicating more severe disease. The EASI75 responder defined as a participant who achieves at least a 75% reduction in EASI score from baseline. ITT population included all participants who were randomized and received any study investigational product. |
| End point type | Secondary |
| End point timeframe: | Week 12 |

| End point values | Placebo | MEDI9929 280 mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 19.8 | 24.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in EASI Total Score at Week 12

| | |
|------------------------|--|
| End point title | Mean Change From Baseline in EASI Total Score at Week 12 |
| End point description: | The EASI evaluates 4 natural anatomical regions for severity (0 [none] to 3 [severe]) and extent of key disease signs and focuses on the key acute and chronic signs of inflammation (erythema, induration/papulation, excoriation, and lichenification). The total score is the sum of the four body-region scores, maximum=72, minimum=0. The higher values indicating more severe disease. ITT population included all participants who were randomized and received any study investigational product. Here, "n" is number of participants analysed for this time point. |

| | |
|------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1) and Week 12 | |

| End point values | Placebo | MEDI9929 280 mg | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=56, 55) | 24.48 (± 11.21) | 24.05 (± 12.38) | | |
| Week 12 (n=50, 49) | -11.23 (± 8.73) | -12.16 (± 9.96) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of 0 (Clear) or 1 (Almost Clear) and at Least a 2-Grade Reduction From Baseline

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of 0 (Clear) or 1 (Almost Clear) and at Least a 2-Grade Reduction From Baseline |
|-----------------|--|

End point description:

The investigator's global assessment (IGA) allows investigators to assess overall disease severity at one given time point and consists of a 5-point severity scale from clear to severe disease (0 = clear, 1 = almost clear, 2 = mild disease, 3 = moderate disease, and 4 = severe disease). A participant has IGA response if they achieve a score of 0 (clear) or 1 (almost clear) and at least a 2-grade reduction from baseline. ITT population included all participants who were randomized and received any study investigational product.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Placebo | MEDI9929 280 mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 12.8 | 19.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in the Scoring of Atopic Dermatitis (SCORAD) at Week 12

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in the Scoring of Atopic Dermatitis (SCORAD) at Week 12 |
|-----------------|---|

End point description:

The scoring of atopic dermatitis (SCORAD) is a clinical tool for assessing the severity (that is, extent, intensity) of atopic dermatitis (AD). The tool evaluates the extent and intensity of the AD lesions, along with participant symptoms. The range of the SCORAD is 0-103, where 0 indicates no eczema. The higher values indicating more severe disease. ITT population included all participants who were randomized and received any study investigational product. Here, "n" is number of participants analysed for this time point.

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

End point timeframe:

Baseline (Day 1) and Week 12

| End point values | Placebo | MEDI9929 280 mg | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=56, 55) | 58.66 (\pm 13.32) | 57.68 (\pm 14.80) | | |
| Week 12 (n=50, 49) | -19.35 (\pm 17.49) | -24.24 (\pm 16.94) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving \geq 50% Reduction From Baseline in SCORAD 50

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving \geq 50% Reduction From Baseline in SCORAD 50 |
|-----------------|--|

End point description:

The SCORAD is a clinical tool for assessing the severity (that is, extent, intensity) of atopic dermatitis (AD). The tool evaluates the extent and intensity of the AD lesions, along with participant symptoms. The range of the SCORAD is 0-103, where 0 indicates no eczema. The higher values indicating more severe disease. The SCORAD 50 responder defined as a participant who achieves at least a 50% reduction in SCORAD score from baseline. ITT population included all participants who were randomized and received any study investigational product.

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

End point timeframe:

Week 12

| | | | | |
|-----------------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | MEDI9929 280 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 29.4 | 41.0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving \geq 75% Reduction From Baseline in SCORAD 75

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving \geq 75% Reduction From Baseline in SCORAD 75 |
|-----------------|--|

End point description:

The SCORAD is a clinical tool for assessing the severity (that is, extent, intensity) of atopic dermatitis (AD). The tool evaluates the extent and intensity of the AD lesions, along with participant symptoms. The range of the SCORAD is 0-103, where 0 indicates no eczema. The higher values indicating more severe disease. The SCORAD 75 responder is defined as a participant who achieves at least a 75% reduction in SCORAD score from baseline. ITT population included all participants who were randomized and received any study investigational product.

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

End point timeframe:

Week 12

| | | | | |
|-----------------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | MEDI9929 280 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 7.4 | 9.8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Average Pruritus Numeric Rating Scale (NRS) at Week 12

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in Average Pruritus Numeric Rating Scale (NRS) at Week 12 |
|-----------------|---|

End point description:

Pruritus is assessed using an Numeric Rating Scale (NRS) (0 - 10) with 0= no itch and 10= worst imaginable itch. Daily pruritus assessments were summarized as weekly peak score and a change from baseline in weekly peak score was calculated. ITT population included all participants who were randomized and received any study investigational product. Here, "n" is number of participants analysed for this time point.

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

End point timeframe:

Baseline (Day 1) and Week 12

| End point values | Placebo | MEDI9929 280 mg | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=55, 55) | 5.15 (± 2.10) | 5.26 (± 2.02) | | |
| Week 12 (n=48, 47) | -1.39 (± 1.93) | -1.90 (± 1.99) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in 5-D Pruritus Score at Week 12

End point title | Mean Change from Baseline in 5-D Pruritus Score at Week 12

End point description:

The 5-D pruritus scale is a brief questionnaire designed to assess itch. This scale takes into account the multidimensional nature of pruritus, its impact on quality of life, and is capable of detecting change over time. The 5-D pruritus scale included 5 domains (duration, degree, direction, disability, and distribution of pruritus). The total 5-D score was obtained by scoring each of the domains separately and then summing them together. 5-D total scores ranged between 5 (no pruritus) and 25 (most severe pruritus). The higher values indicating more severe pruritus. ITT population included all participants who were randomized and received any study investigational product. Here, "n" is number of participants analysed for this time point.

End point type | Secondary

End point timeframe:

Baseline (Day 1) and Week 12

| End point values | Placebo | MEDI9929 280 mg | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 55 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=52, 50) | 16.7 (± 3.7) | 16.0 (± 3.7) | | |
| Week 12 (n=47, 46) | -3.9 (± 4.5) | -3.6 (± 4.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

| | |
|-----------------|---|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) ^[1] |
|-----------------|---|

End point description:

An AE is any unfavourable and unintended signs, symptoms, or diseases temporally associated with use of study drug, whether or not considered related to study drug. SAE is any AE that resulted in death, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, life-threatening, a congenital anomaly/birth defect, or an important medical event. TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug until Week 22. As-treated population included all participants who received any study drug. Participants who received at least one dose of MEDI9929 during the study, regardless of randomized treatment assignment, were analyzed under MEDI9929 group. One participant who randomized to placebo group but received an incorrect first dose of MEDI9929 was included in the "MEDI9929" group.

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

End point timeframe:

From treatment administration (Day1) to 22 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed.

| End point values | Placebo | MEDI9929 280mg | | |
|-------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 55 | 56 | | |
| Units: Number of participants | | | | |
| TEAEs | 40 | 38 | | |
| TESAEs | 3 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Trough Serum Concentration of MEDI9929

| | |
|-----------------|--|
| End point title | Mean Trough Serum Concentration of MEDI9929 ^[2] |
|-----------------|--|

End point description:

The mean serum concentrations of MEDI9929 was observed. PK population included all participants who received MEDI9929 and had a sufficient number of serum concentration measurements for computing PK parameters. Here, "N" is number of participants analysed for this end point.

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

End point timeframe:

Week 0 (Pre dose) and Week 12 (post dose)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetic parameters were not analysed for placebo arm.

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | MEDI9929 280 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | 54.9 (± 21.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Detectable MEDI9929 Anti-drug Antibodies at Week 22

| | |
|-----------------|--|
| End point title | Number of Participants who Developed Detectable MEDI9929 Anti-drug Antibodies at Week 22 |
|-----------------|--|

End point description:

A participant was considered ADA-positive across the study if they had a positive reading (titer of 50 or higher) at any time point during the study period. ITT population included all participants who were randomized and received any study investigational product. Here, "N" is the number of participants analysed for this end point.

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

End point timeframe:

Baseline (Day 1) to Week 22

| | | | | |
|-------------------------------|-----------------|-----------------|--|--|
| End point values | Placebo | MEDI9929 280 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 48 | | |
| Units: Number of participants | 2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From treatment administration (Day1) to 22 weeks

Adverse event reporting additional description:

AEs were reported for As-treated population, which included all participants who received any study drug. Participants who received at least one dose of MEDI9929, regardless of randomized treatment, were analyzed under MEDI9929. One participant who randomized to placebo but received an incorrect first dose of MEDI9929 was included in MEDI9929 group

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | MEDI9929 280 mg |
|-----------------------|-----------------|

Reporting group description:

Participants received 6 subcutaneous doses of MEDI9929 280 mg every 2 weeks for 12 weeks, with the last dose at Week 10.

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

Reporting group description:

Participants received 6 subcutaneous doses of placebo every 2 weeks for 12 weeks, with the last dose at Week 10.

| Serious adverse events | MEDI9929 280 mg | Placebo | |
|--|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 3 / 55 (5.45%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 55 (1.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 55 (1.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 56 (1.79%) | 1 / 55 (1.82%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 55 (1.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected dermal cyst | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 55 (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: 1 %

| Non-serious adverse events | MEDI9929 280 mg | Placebo | |
|--|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 56 (51.79%) | 33 / 55 (60.00%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 56 (5.36%) | 1 / 55 (1.82%) | |
| occurrences (all) | 4 | 1 | |
| General disorders and administration site conditions | | | |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 0 / 55 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Injection site erythema | | | |
| subjects affected / exposed | 3 / 56 (5.36%) | 0 / 55 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Immune system disorders | | | |
| Food allergy | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 0 / 55 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---------------------|----------------------|--|
| Abdominal pain subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 0 / 55 (0.00%) 0 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 56 (8.93%) 6 | 3 / 55 (5.45%) 3 | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 0 / 55 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all) | 5 / 56 (8.93%) 6 | 7 / 55 (12.73%) 9 | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 1 / 55 (1.82%) 1 | |
| Rash subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 2 / 55 (3.64%) 4 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 2 / 55 (3.64%) 2 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 1 / 55 (1.82%) 1 | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 0 / 55 (0.00%) 0 | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 56 (3.57%) 2 | 0 / 55 (0.00%) 0 | |
| Infections and infestations Cellulitis | | | |

| | | |
|-----------------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 56 (0.00%) | 2 / 55 (3.64%) |
| occurrences (all) | 0 | 2 |
| Conjunctivitis | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 1 / 55 (1.82%) |
| occurrences (all) | 1 | 1 |
| Folliculitis | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 1 / 55 (1.82%) |
| occurrences (all) | 1 | 1 |
| Herpes simplex | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 1 / 55 (1.82%) |
| occurrences (all) | 1 | 1 |
| Nasopharyngitis | | |
| subjects affected / exposed | 13 / 56 (23.21%) | 11 / 55 (20.00%) |
| occurrences (all) | 15 | 14 |
| Sinusitis | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 2 / 55 (3.64%) |
| occurrences (all) | 2 | 2 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 7 / 55 (12.73%) |
| occurrences (all) | 1 | 8 |
| Urinary tract infection | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 1 / 55 (1.82%) |
| occurrences (all) | 1 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 17 September 2015 | The Protocol was amended to modify the wording for the primary endpoint, secondary endpoints (1, 3, 5, and 6) and exploratory endpoints (1 and 2); Measurement of EASI50 was also added under the secondary endpoints as this endpoint were measured beyond Week 12; Removed "IgE" from the list of biomarkers; A positive QFT-G test for TB does not require an investigator's opinion; Added creatine kinase (CK) and lactate dehydrogenase (LDH) to the list of serum chemistry tests; Added the correct pruritus NRS instead of the incorrectly added eczema-related sleep NRS. Updated the text wherever applicable for more clarification. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported