



Clinical trial results:

A randomized, double-blind, placebo-controlled, parallel-group study to assess the safety, tolerability, pharmacokinetics and preliminary efficacy of CDZ173 in patients with primary Sjögren's syndrome.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-004616-12 |
| Trial protocol | DE HU PL |
| Global end of trial date | 17 May 2017 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 31 May 2018 |
| First version publication date | 31 May 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CCDZ173X2203 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02775916 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 | 17 May 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 17 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of CDZ173 in patients with primary Sjögren's syndrome. To compare the effect of CDZ173 versus placebo on the patient reported outcome of primary Sjögren's syndrome patients after 12 weeks of treatment (study Week 13 (Day 85)).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 01 June 2016 |
| 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 | Germany: 22 |
| Country: Number of subjects enrolled | Hungary: 8 |
| Worldwide total number of subjects | 30 |
| EEA total number of subjects | 30 |

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) | 26 |
| From 65 to 84 years | 4 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 30 patients were randomized in a ratio of 2:1 to receive either CDZ173 or placebo (twice daily at approximately 12 hour intervals) during the 12-week treatment period.

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, Monitor, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | CDZ173 |

Arm description:

Capsule

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | CDZ173 |
| Investigational medicinal product code | CDZ173 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

CDZ173 70mg oral capsule twice a day for 12 weeks

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Capsule matching Placebo

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | CDZ173 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo oral capsule twice a day for 12 weeks

| Number of subjects in period 1 | CDZ173 | Placebo |
|---------------------------------------|--------|---------|
| Started | 20 | 10 |
| Completed | 17 | 10 |
| Not completed | 3 | 0 |
| Adverse event, non-fatal | 1 | - |

| | | |
|---------------------------|---|---|
| Subject/Guardian Decision | 2 | - |
|---------------------------|---|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | CDZ173 |
|-----------------------|--------|

Reporting group description:

Capsule

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

Reporting group description:

Capsule matching Placebo

| Reporting group values | CDZ173 | Placebo | Total |
|---|---------|---------|-------|
| Number of subjects | 20 | 10 | 30 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 17 | 9 | 26 |
| From 65-84 years | 3 | 1 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 48.7 | 44.7 | |
| standard deviation | ± 13.85 | ± 11.58 | - |
| Sex: Female, Male Units: Subjects | | | |
| Female | 17 | 9 | 26 |
| Male | 3 | 1 | 4 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 20 | 10 | 30 |
| Unknown or Not Reported | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|------------------------------|---------|
| Reporting group title | CDZ173 |
| Reporting group description: | |
| Capsule | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Capsule matching Placebo | |

Primary: Safety and tolerability of CDZ173 in patients with primary Sjögren's syndrome up to Day 85

No statistical analysis was planned for this primary outcome.

| | |
|---|--|
| End point title | Safety and tolerability of CDZ173 in patients with primary Sjögren's syndrome up to Day 85 No statistical analysis was planned for this primary outcome. ^[1] |
| End point description: | |
| Safety and tolerability of CDZ173 in patients with primary Sjögren's syndrome up to End of Treatment Day 85 | |
| End point type | Primary |
| End point timeframe: | |
| up to Day 85 | |

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: No statistical analysis was planned for this primary outcome

| End point values | CDZ173 | Placebo | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: count of participants | | | | |
| Participants with at least one AE | 20 | 8 | | |
| Participants with at least one SAE | 1 | 0 | | |
| Death | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the EULAR Sjögren's Syndrome Patient Reported Intensity (ESSPRI) after 12 weeks of Treatment Day 85

| | |
|-----------------|---|
| End point title | Change from Baseline in the EULAR Sjögren's Syndrome Patient Reported Intensity (ESSPRI) after 12 weeks of Treatment Day 85 |
|-----------------|---|

End point description:

The ESSPRI is an established disease outcome measure for Sjögren's syndrome. It consists of a questionnaire developed to assess the patients' symptoms in primary Sjögren's syndrome and covered the three key subjective areas of discomfort, i.e., dryness, pain and fatigue. The full questionnaire had 21 questions. Subsequently, it was noted that the first three questions, Likert scales ranging from 0 –

10, captured the essence of the ESSPRI. This abbreviated version was used to define the "minimal clinically important improvement" (0.67 – 1) and the "patient-acceptable symptom state" (<5). Patients were asked to complete the full ESSPRI questionnaire. However, the mean of the first three questions was used for the primary analysis and for the assessment of eligibility. A reduction from baseline (or, a negative change from baseline) in ESSPRI indicates improvement in patients.

| | |
|--------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Baseline and 12 weeks (Day 85) | |

| End point values | CDZ173 | Placebo | | |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| arithmetic mean (standard deviation) | -1.778 (\pm 2.4509) | -0.741 (\pm 1.3517) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change from Baseline in the ESSPRI at Day 85 |
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.343 |
| upper limit | 1.937 |
| Variability estimate | Standard deviation |
| Dispersion value | 1.332 |

Secondary: Change from Baseline in the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) after 12 weeks of Treatment Day 85

| | |
|-----------------|---|
| End point title | Change from Baseline in the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) after 12 weeks of Treatment Day 85 |
|-----------------|---|

End point description:

The ESSDAI is an established disease outcome measure for Sjögren's syndrome. The instrument contains 12 organ-specific domains contributing to disease activity. For each domain, features of disease activity are scored in 3 or 4 levels according to their severity. These scores are then summed across the 12 domains in a weighted manner to provide the total score. A reduction from baseline (i.e., a negative change from baseline) in the ESSDAI score is indicative of improvement in a patient.

| | |
|--------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 12 weeks (Day 85) | |

| End point values | CDZ173 | Placebo | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| least squares mean (standard error) | -2.82 (\pm 1.165) | -3.34 (\pm 1.168) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change from Baseline in the ESSDAI at Day 85 |
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.52 |
| upper limit | 3.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.466 |

Secondary: Change from Baseline in the Short Form (36) Health Survey (SF-36) after 12 weeks of Treatment Day 85

| | |
|--|--|
| End point title | Change from Baseline in the Short Form (36) Health Survey (SF-36) after 12 weeks of Treatment Day 85 |
| End point description: | |
| <p>The Short Form Health Survey is a survey evaluating individual patient's health status which also monitors and compares patients' disease burden. The SF-36 consists of eight scaled scores (vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health), which are the weighted sums of the questions in their section. An increase in SF-36 score from baseline (i.e., a positive change from baseline) indicates improvement in patients</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 12 weeks (Day 85) | |

| End point values | CDZ173 | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| least squares mean (standard error) | | | | |
| Physical Component Summary Score | 4.82 (± 2.235) | 4.42 (± 2.425) | | |
| Mental Component Summary Score | 5.43 (± 3.415) | 1.10 (± 3.792) | | |

Statistical analyses

| Statistical analysis title | Change from Baseline in SF-36 Physical at Day 85 |
|---|--|
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.08 |
| upper limit | 6.89 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.119 |

| Statistical analysis title | Change from Baseline in SF-36 Mental at Day 85 |
|---|--|
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | 4.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.27 |
| upper limit | 13.93 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.615 |

Secondary: Change in Baseline in Multidimensional Fatigue Inventory (MFI) after 12 weeks of Treatment (Day 85)

| | |
|-----------------|---|
| End point title | Change in Baseline in Multidimensional Fatigue Inventory (MFI) after 12 weeks of Treatment (Day 85) |
|-----------------|---|

End point description:

The Multidimensional Fatigue Inventory is a 20-item self-report instrument designed to measure fatigue that covered the following dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. A reduction from baseline (i.e., a negative change from baseline) in MFI indicates improvement in patients.

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

End point timeframe:

Baseline and 12 weeks (Day 85)

| End point values | CDZ173 | Placebo | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| least squares mean (standard error) | -8.80 (\pm 5.557) | -2.25 (\pm 5.774) | | |

Statistical analyses

| Statistical analysis title | Change in Baseline in MFI at Day 85 |
|---|-------------------------------------|
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | -6.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.76 |
| upper limit | 8.66 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.27 |

Secondary: Change from Baseline in Physician global assessment of the patient's overall disease activity (Physician VAS) after 12 weeks of Treatment Day 85

| | |
|-----------------|--|
| End point title | Change from Baseline in Physician global assessment of the patient's overall disease activity (Physician VAS) after 12 weeks of Treatment Day 85 |
|-----------------|--|

End point description:

A reduction from baseline (i.e., a negative change from baseline) in physician global VAS assessment score indicates improvement in patients.

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

End point timeframe:

Baseline and 12 weeks (Day 85)

| End point values | CDZ173 | Placebo | | |
|-------------------------------------|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| least squares mean (standard error) | -10.06 (\pm 6.584) | 0.91 (\pm 7.699) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in Physician VAS at Day 85 |
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | -10.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -30.94 |
| upper limit | 9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.626 |

Secondary: Change from Baseline in Patient's global assessment of their disease activity (VAS) after 12 weeks of treatment Day 85

| | |
|---|--|
| End point title | Change from Baseline in Patient's global assessment of their disease activity (VAS) after 12 weeks of treatment Day 85 |
| End point description: | |
| A reduction from baseline (or, a negative change from baseline) in patient global VAS assessment score indicates improvement in patients. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 12 weeks | |

| End point values | CDZ173 | Placebo | | |
|-------------------------------------|----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 9 | | |
| Units: total score | | | | |
| least squares mean (standard error) | -4.83 (\pm 7.268) | 2.87 (\pm 8.412) | | |

Statistical analyses

| Statistical analysis title | Change from Baseline in VAS at Day 85 |
|---|---------------------------------------|
| Comparison groups | CDZ173 v Placebo |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (net) |
| Point estimate | -7.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -29.75 |
| upper limit | 14.37 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 10.595 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

Reporting groups

| | |
|------------------------------|------------------|
| Reporting group title | 70 mg CDZ173 bid |
| Reporting group description: | 70 mg CDZ173 bid |
| Reporting group title | Placebo bid |
| Reporting group description: | Placebo bid |

| Serious adverse events | 70 mg CDZ173 bid | Placebo bid | |
|---|------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 10 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 10 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 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 | 70 mg CDZ173 bid | Placebo bid | |
|---|------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 20 (95.00%) | 8 / 10 (80.00%) | |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |

| | | | |
|--|-----------------------|----------------------|--|
| Dizziness subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Headache subjects affected / exposed occurrences (all) | 7 / 20 (35.00%) 11 | 1 / 10 (10.00%) 3 | |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |
| General disorders and administration site conditions | | | |
| Chest Discomfort subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 2 | 1 / 10 (10.00%) 2 | |
| Chills subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Fatigue subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 1 / 10 (10.00%) 1 | |
| Feeling Cold subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 1 / 10 (10.00%) 1 | |
| Eye disorders | | | |
| Dry Eye subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Abdominal Pain Upper subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |

| | | | |
|---|----------------------|----------------------|--|
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 20 (25.00%) 7 | 1 / 10 (10.00%) 1 | |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 5 | 3 / 10 (30.00%) 3 | |
| Nausea subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Toothache subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 3 | 0 / 10 (0.00%) 0 | |
| Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | 0 / 10 (0.00%) 0 | |
| Nasal Congestion subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | 0 / 10 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Dry Skin subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 4 | 0 / 10 (0.00%) 0 | |
| Eczema subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |

| | | | |
|--|------------------------|----------------------|--|
| Hyperhidrosis subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 1 / 10 (10.00%) 1 | |
| Rash subjects affected / exposed occurrences (all) | 10 / 20 (50.00%) 13 | 1 / 10 (10.00%) 2 | |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Back Pain subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Sjogren's Syndrome subjects affected / exposed occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 10 (0.00%) 0 | |
| Infections and infestations Infected Bite subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Tooth Infection subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | 0 / 10 (0.00%) 0 | |
| Vaginal Infection subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 1 / 10 (10.00%) 1 | |
| Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 7 / 20 (35.00%) 9 | 4 / 10 (40.00%) 5 | |

| | | | |
|------------------------------------|-----------------|----------------|--|
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 2 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 15 September 2016 | Amendment 1: The main purpose of this amendment was to include changes in contraceptive requirements based on results from drug-drug interaction study CCDZ173X2104 on hormonal contraception. Exclusion criterion #12 was modified to allow enrolment of women of child-bearing potential using hormonal contraception. In addition, changes were made in the Introduction, and Risks and Benefits sections to reflect the updates in the latest Investigator Brochure. Finally, specifications in inclusion and exclusion criteria, some minor changes, including clarifications on stopping rules, biomarkers assessments, infection monitoring, and typographical corrections, were made to the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported