



Clinical trial results:

A Phase 2, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Study Evaluating the Efficacy and Safety of Ustekinumab (STELARA®) and CNTO 1959 Administered Subcutaneously in Subjects With Active Rheumatoid Arthritis Despite Concomitant Methotrexate Therapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-001122-18 |
| Trial protocol | HU CZ BG |
| Global end of trial date | 05 May 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 06 July 2016 |
| First version publication date | 31 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | CNTO1275ARA2001 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01645280 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|------------------------------------------------------------------------------------------|
| Sponsor organisation name | Janssen-Cilag International NV |
| Sponsor organisation address | Turnhoutseweg 30, 2340, Beerse, Belgium, |
| Public contact | Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 May 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 May 2014 |
| 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 efficacy of ustekinumab and CNTO 1959 in reducing signs and symptoms of disease in subjects with active Rheumatoid Arthritis [RA] despite concomitant methotrexate (MTX) therapy, and to evaluate the safety of ustekinumab and CNTO 1959 in this population.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Known instances of nonconformance were documented and are not considered to have had an impact on the overall conclusions of this study. The study protocol and amendment were reviewed by an Independent Ethics Committee (IEC) or Institutional Review Board (IRB). Safety assessments included monitoring and recording all adverse effects [AE] and serious adverse effects [SAE], laboratory evaluations (hematology, blood chemistry, urinalysis and immunogenicity), vital signs, body weight, electro cardio gram [ECG] and injection site reactions through Week 48.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment | 02 July 2012 |
| 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 | Argentina: 23 |
| Country: Number of subjects enrolled | Bulgaria: 9 |
| Country: Number of subjects enrolled | Chile: 6 |
| Country: Number of subjects enrolled | Colombia: 43 |
| Country: Number of subjects enrolled | Czech Republic: 1 |
| Country: Number of subjects enrolled | Hungary: 19 |
| Country: Number of subjects enrolled | Poland: 35 |
| Country: Number of subjects enrolled | Russian Federation: 86 |
| Country: Number of subjects enrolled | Singapore: 4 |
| Country: Number of subjects enrolled | Ukraine: 46 |
| Country: Number of subjects enrolled | United States: 1 |
| Worldwide total number of subjects | 273 |
| EEA total number of subjects | 64 |

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) | 234 |
| From 65 to 84 years | 39 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Approximately 250 participants were planned, 274 were randomized, and 273 participants were treated.

Pre-assignment

Screening details:

Randomization was to be stratified by investigational site and by participant's C-reactive protein (CRP) level at screening. Based on inclusion criteria of participants with screening CRP greater than or equal to (\geq) 0.80 milligram per deciliter [mg/dL], it was assumed that 60 percent (%) to 80% of participants had CRP \geq 1.50 (mg/dL) at screening.

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, Assessor |

Arms

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

Arm description:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

| | |
|----------------------------------------|------------------------|
| 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:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

| | |
|------------------|---------------------------|
| Arm title | Ustekinumab+MTX 90 mg q8w |
|------------------|---------------------------|

Arm description:

Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

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

Dosage and administration details:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose).

| | |
|------------------|----------------------------|
| Arm title | Ustekinumab+MTX 90 mg q12w |
|------------------|----------------------------|

Arm description:

Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

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

Dosage and administration details:

Weeks 0, 4, then every 12 weeks (Weeks 16 and 28) + MTX (pre-study dose)

| | |
|------------------|-------------------------|
| Arm title | CNT01959+MTX 200 mg q8w |
|------------------|-------------------------|

Arm description:

CNT01959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

| | |
|----------------------------------------|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CNT0 1959 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose)

| | |
|------------------|------------------------|
| Arm title | CNT01959+MTX 50 mg q8w |
|------------------|------------------------|

Arm description:

CNT01959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

| | |
|----------------------------------------|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CNT0 1959 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

at Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28)+ MTX (pre-study dose)

| Number of subjects in period 1 | Placebo+MTX | Ustekinumab+MTX 90 mg q8w | Ustekinumab+MTX 90 mg q12w |
|---------------------------------------|-------------|------------------------------|-------------------------------|
| Started | 55 | 54 | 55 |
| Completed | 50 | 51 | 50 |
| Not completed | 5 | 3 | 5 |
| Adverse event, serious fatal | - | 1 | - |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event, non-fatal | 2 | - | 3 |
| Other | 1 | - | - |
| Lack of efficacy | 2 | 2 | 1 |

| Number of subjects in period 1 | CNT01959+MTX 200 mg q8w | CNT01959+MTX 50 mg q8w |
|---------------------------------------|----------------------------|---------------------------|
| Started | 54 | 55 |
| Completed | 50 | 51 |
| Not completed | 4 | 4 |
| Adverse event, serious fatal | - | - |

| | | |
|------------------------------|---|---|
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | - | 2 |
| Other | - | - |
| Lack of efficacy | 4 | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Reporting group title | Placebo+MTX |
| Reporting group description: At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose) | |
| Reporting group title | Ustekinumab+MTX 90 mg q8w |
| Reporting group description: Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |
| Reporting group title | Ustekinumab+MTX 90 mg q12w |
| Reporting group description: Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy | |
| Reporting group title | CNT01959+MTX 50 mg q8w |
| Reporting group description: CNT01959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |
| Reporting group title | CNT01959+MTX 200 mg q8w |
| Reporting group description: CNT01959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |

| Reporting group values | Placebo+MTX | Ustekinumab+MTX 90 mg q8w | Ustekinumab+MTX 90 mg q12w |
|---------------------------------------------|-------------|------------------------------|-------------------------------|
| Number of subjects | 55 | 54 | 55 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 51 | 46 | 44 |
| From 65 to 84 years | 4 | 8 | 11 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 51.1 | 50.7 | 51.4 |
| standard deviation | ± 10.57 | ± 13.13 | ± 13.59 |
| Title for Gender Units: subjects | | | |
| Female | 48 | 46 | 47 |
| Male | 7 | 8 | 8 |

| Reporting group values | CNT01959+MTX 50 mg q8w | CNT01959+MTX 200 mg q8w | Total |
|---------------------------------------------|---------------------------|----------------------------|-------|
| Number of subjects | 55 | 54 | 273 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 50 | 43 | 234 |
| From 65 to 84 years | 5 | 11 | 39 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|----------------------------------------------------------------------------------|-----------------|-----------------|-----|
| Title for AgeContinuous Units: years arithmetic mean standard deviation | 49.9 ± 12.85 | 54.6 ± 11.34 | - |
| Title for Gender Units: subjects | | | |
| Female | 45 | 42 | 228 |
| Male | 10 | 12 | 45 |

End points

End points reporting groups

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Reporting group title | Placebo+MTX |
| Reporting group description: At Weeks 0, 4, then every 8 weeks (Weeks 12, 20, and 28) + MTX (pre-study dose) | |
| Reporting group title | Ustekinumab+MTX 90 mg q8w |
| Reporting group description: Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |
| Reporting group title | Ustekinumab+MTX 90 mg q12w |
| Reporting group description: Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy | |
| Reporting group title | CNTO1959+MTX 200 mg q8w |
| Reporting group description: CNTO1959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |
| Reporting group title | CNTO1959+MTX 50 mg q8w |
| Reporting group description: CNTO1959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy | |
| Subject analysis set title | Intent-to-treat (ITT) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: The intent-to-treat (ITT) population included all randomized participants. For early escape, data at or prior to Week 16 were carried forward through Week 28. | |

Primary: Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 28

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 28 |
| End point description: The ACR 20 responders are participants with at least 20 percent (%) improvement from Baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: 1) patient's assessment of arthritis pain-visual analog scale, 2) patient's global assessment of disease activity-visual analog scale, 3) physician's global assessment of disease activity-visual analog scale, 4) patient's assessment of physical function as measured by health assessment questionnaire-disability index (HAQ-Di), 5) C-reactive protein (CRP). | |
| End point type | Primary |
| End point timeframe: Week 28 | |

| End point values | Placebo+MTX | Ustekinumab+MTX 90 mg q8w | Ustekinumab+MTX 90 mg q12w | CNTO1959+MTX 50 mg q8w |
|-----------------------------------|-----------------|---------------------------|----------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 54 | 55 | 55 |
| Units: percentage of participants | | | | |
| number (not applicable) | 40 | 52.7 | 54.5 | 38.2 |

| | | | | |
|-----------------------------------|-------------------------|--|--|--|
| End point values | CNT01959+MTX 200 mg q8w | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 54 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 44.4 | | | |

Statistical analyses

| | |
|-----------------------------------------|-----------------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.184 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------------|------------------------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Ustekinumab+MTX 90 mg q12w v Placebo+MTX |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.13 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------------|---------------------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo+MTX v CNT01959+MTX 200 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.642 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------------|--------------------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Comparison groups | Placebo+MTX v CNT01959+MTX 50 mg q8w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.832 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Change From Baseline in Disease Activity Index Score 28 (DAS28; Using C-reactive Protein [CRP]) Score at Week 28

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Disease Activity Index Score 28 (DAS28; Using C-reactive Protein [CRP]) Score at Week 28 |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

The DAS28 calculated from the number of swollen joints (SJC) and painful joints (PJC) using the 28 joints count, CRP milligram per liter (mG/L) and patient's global assessment (PGA) of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤ 3.2 = low disease activity, DAS28 > 3.2 to 5.1 = moderate to high disease activity.

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

End point timeframe:

From Baseline to Week 28

| End point values | Placebo+MTX | Ustekinumab+ MTX 90 mg q8w | Ustekinumab+ MTX 90 mg q12w | CNT01959+MT X 50 mg q8w |
|-------------------------------------|-------------------------|----------------------------------|-----------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 54 | 55 | 55 |
| Units: units on scale | | | | |
| least squares mean (standard error) | -0.94 (\pm 0.174) | -1.52 (\pm 0.185) | -1.49 (\pm 0.183) | 6.07 (\pm 0.821) |

| End point values | CNT01959+MT X 200 mg q8w | | | |
|-------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 54 | | | |
| Units: units on scale | | | | |
| least squares mean (standard error) | -1.21 (\pm 0.17) | | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 5 |
|-----------------------------------------|-----------------------------------------|
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.019 |
| Method | ANCOVA |

| | |
|-----------------------------------------|------------------------------------------|
| Statistical analysis title | Statistical analysis 6 |
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q12w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.025 |
| Method | ANCOVA |

| | |
|-----------------------------------------|---------------------------------------|
| Statistical analysis title | Statistical analysis 7 |
| Comparison groups | Placebo+MTX v CNT01959+MTX 200 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.248 |
| Method | ANCOVA |

| | |
|-----------------------------------------|--------------------------------------|
| Statistical analysis title | Statistical analysis 8 |
| Comparison groups | Placebo+MTX v CNT01959+MTX 50 mg q8w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.045 |
| Method | ANCOVA |

Secondary: Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 12

| | |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With American College of Rheumatology 20 (ACR 20) Response at Week 12 |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

The ACR 20 responders are participants with at least 20 percent (%) improvement from Baseline for tender joint count (TJC), swollen joint count (SJC), and at least 3 of the 5 remaining core set measures: 1) Patient's Assessment of Arthritis Pain-Visual Analog Scale, 2) Patient's Global Assessment of Disease Activity-Visual Analog Scale, 3) Physician's Global Assessment of Disease Activity-Visual Analog Scale, 4) Patient's Assessment of Physical Function as measured by Health Assessment Questionnaire-Disability Index (HAQ-DI), 5) C-reactive Protein (CRP).

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

End point timeframe:

Week 12

| End point values | Placebo+MTX | Ustekinumab+ MTX 90 mg q8w | Ustekinumab+ MTX 90 mg q12w | CNTO1959+MT X 50 mg q8w |
|-----------------------------------|-----------------|----------------------------------|-----------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 54 | 55 | 55 |
| Units: percentage of participants | | | | |
| number (not applicable) | 29.1 | 37 | 34.5 | 20 |

| End point values | CNTO1959+MT X 200 mg q8w | | | |
|-----------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 54 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 33.3 | | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 9 |
|-----------------------------------------|-----------------------------------------|
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.381 |
| Method | Cochran-Mantel-Haenszel |

| Statistical analysis title | Statistical analysis 10 |
|-----------------------------------------|------------------------------------------|
| Comparison groups | Ustekinumab+MTX 90 mg q12w v Placebo+MTX |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.543 |
| Method | Cochran-Mantel-Haenszel |

| Statistical analysis title | Statistical analysis 11 |
|-----------------------------------------|---------------------------------------|
| Comparison groups | Placebo+MTX v CNTO1959+MTX 200 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.629 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------------|--------------------------------------|
| Statistical analysis title | Statistical analysis 12 |
| Comparison groups | Placebo+MTX v CNTO1959+MTX 50 mg q8w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.273 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 28

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 28 |
| End point description: | |
| The Health Assessment Questionnaire-Disability Index (HAQ-DI): participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 28 | |

| End point values | Placebo+MTX | Ustekinumab+ MTX 90 mg q8w | Ustekinumab+ MTX 90 mg q12w | CNTO1959+MT X 50 mg q8w |
|-------------------------------------|-----------------|----------------------------------|-----------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 54 | 55 | 55 |
| Units: units on scale | | | | |
| least squares mean (standard error) | -0.3 (± 0.074) | -0.48 (± 0.072) | -0.44 (± 0.071) | -0.39 (± 0.076) |

| End point values | CNTO1959+MT X 200 mg q8w | | | |
|-------------------------------------|-----------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 54 | | | |
| Units: units on scale | | | | |
| least squares mean (standard error) | -0.41 (± 0.075) | | | |

Statistical analyses

| | |
|-----------------------------------------|-----------------------------------------|
| Statistical analysis title | Statistical analysis 13 |
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.06 |
| Method | ANCOVA |

| | |
|-----------------------------------------|------------------------------------------|
| Statistical analysis title | Statistical analysis 14 |
| Comparison groups | Placebo+MTX v Ustekinumab+MTX 90 mg q12w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.134 |
| Method | ANCOVA |

| | |
|-----------------------------------------|---------------------------------------|
| Statistical analysis title | Statistical analysis 15 |
| Comparison groups | Placebo+MTX v CNTO1959+MTX 200 mg q8w |
| Number of subjects included in analysis | 109 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.28 |
| Method | ANCOVA |

| | |
|-----------------------------------------|--------------------------------------|
| Statistical analysis title | Statistical analysis 16 |
| Comparison groups | Placebo+MTX v CNTO1959+MTX 50 mg q8w |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.345 |
| Method | ANCOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Placebo+MTX |
|-----------------------|-------------|

Reporting group description:

Placebo with Methotrexate concomitant therapy

| | |
|-----------------------|---------------------------|
| Reporting group title | Ustekinumab+MTX 90 mg q8w |
|-----------------------|---------------------------|

Reporting group description:

Ustekinumab 90 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

| | |
|-----------------------|----------------------------|
| Reporting group title | Ustekinumab+MTX 90 mg q12w |
|-----------------------|----------------------------|

Reporting group description:

Ustekinumab 90 mg by SC route at 0, 4 and 12 weeks with Methotrexate concomitant therapy

| | |
|-----------------------|------------------------|
| Reporting group title | CNT01959+MTX 50 mg q8w |
|-----------------------|------------------------|

Reporting group description:

CNT01959 50 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

| | |
|-----------------------|-------------------------|
| Reporting group title | CNT01959+MTX 200 mg q8w |
|-----------------------|-------------------------|

Reporting group description:

CNT01959 200 mg by SC route at 0, 4 and 8 weeks with Methotrexate concomitant therapy

| Serious adverse events | Placebo+MTX | Ustekinumab+MTX 90 mg q8w | Ustekinumab+MTX 90 mg q12w |
|---------------------------------------------------------------------|----------------|------------------------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 4 / 54 (7.41%) | 3 / 55 (5.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast Cancer Stage I | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous Cell Carcinoma of Lung | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 1 / 55 (1.82%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| complications | | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | 0 / 55 (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 |
| Vascular disorders | | | |
| Shock | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cardiac disorders | | | |
| Angina Unstable | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 54 (0.00%) | 0 / 55 (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 |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | 0 / 55 (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 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 1 / 55 (1.82%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | 0 / 55 (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 |
| Gastrointestinal disorders | | | |
| Ileus | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 1 / 55 (1.82%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| Rheumatoid Arthritis | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 54 (0.00%) | 0 / 55 (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 | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lobar Pneumonia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | 0 / 55 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | CNT01959+MTX 50 mg q8w | CNT01959+MTX 200 mg q8w | |
|---------------------------------------------------------------------|------------------------|-------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 3 / 54 (5.56%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast Cancer Stage I | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous Cell Carcinoma of Lung | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Shock | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina Unstable | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Ileus | | | |

| | | | |
|--------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid Arthritis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar Pneumonia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Placebo+MTX | Ustekinumab+MTX 90 mg q8w | Ustekinumab+MTX 90 mg q12w |
|-------------------------------------------------------|------------------|------------------------------|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 55 (32.73%) | 20 / 54 (37.04%) | 17 / 55 (30.91%) |
| Investigations | | | |
| Blood Creatine Phosphokinase Increased | | | |

| | | | |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood Lactate Dehydrogenase Increased | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 4 / 54 (7.41%) | 2 / 55 (3.64%) |
| occurrences (all) | 4 | 4 | 2 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 2 / 54 (3.70%) | 5 / 55 (9.09%) |
| occurrences (all) | 5 | 3 | 5 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 54 (3.70%) | 0 / 55 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 54 (3.70%) | 1 / 55 (1.82%) |
| occurrences (all) | 1 | 2 | 1 |
| Influenza Like Illness | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 2 / 54 (3.70%) | 0 / 55 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 1 / 54 (1.85%) | 1 / 55 (1.82%) |
| occurrences (all) | 2 | 1 | 1 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 1 / 54 (1.85%) | 1 / 55 (1.82%) |
| occurrences (all) | 2 | 1 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Back Pain | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rheumatoid Arthritis | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 54 (3.70%) | 5 / 55 (9.09%) |
| occurrences (all) | 1 | 2 | 7 |
| Spinal Pain | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 1 / 54 (1.85%) | 2 / 55 (3.64%) |
| occurrences (all) | 2 | 1 | 2 |
| Tendonitis | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 54 (3.70%) | 2 / 55 (3.64%) |
| occurrences (all) | 1 | 2 | 2 |
| Influenza | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 1 / 54 (1.85%) | 3 / 55 (5.45%) |
| occurrences (all) | 4 | 2 | 3 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 5 / 54 (9.26%) | 4 / 55 (7.27%) |
| occurrences (all) | 4 | 8 | 6 |
| Respiratory Tract Infection Viral | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | 2 / 55 (3.64%) |
| occurrences (all) | 2 | 0 | 2 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 54 (3.70%) | 2 / 55 (3.64%) |
| occurrences (all) | 2 | 3 | 2 |

| Non-serious adverse events | CNT01959+MTX 50 mg q8w | CNT01959+MTX 200 mg q8w | |
|-------------------------------------------------------|------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 55 (25.45%) | 21 / 54 (38.89%) | |
| Investigations | | | |
| Blood Creatine Phosphokinase Increased | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 54 (1.85%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|------------------------------------------------|--|
| Blood Lactate Dehydrogenase Increased subjects affected / exposed occurrences (all) | 0 / 55 (0.00%) 0 | 1 / 54 (1.85%) 1 | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 1 | 1 / 54 (1.85%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 2 / 55 (3.64%) 2 | 3 / 54 (5.56%) 3 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 1 | 3 / 54 (5.56%) 3 | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Influenza Like Illness subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 1 1 / 55 (1.82%) 2 | 1 / 54 (1.85%) 1 1 / 54 (1.85%) 1 | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 55 (0.00%) 0 | 2 / 54 (3.70%) 2 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 1 0 / 55 (0.00%) 0 | 0 / 54 (0.00%) 0 0 / 54 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Back Pain | | | |

| | | | |
|---------------------------------------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 55 (5.45%) 4 | 1 / 54 (1.85%) 1 | |
| Rheumatoid Arthritis subjects affected / exposed occurrences (all) | 2 / 55 (3.64%) 2 | 4 / 54 (7.41%) 4 | |
| Spinal Pain subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 1 | 0 / 54 (0.00%) 0 | |
| Tendonitis subjects affected / exposed occurrences (all) | 0 / 55 (0.00%) 0 | 1 / 54 (1.85%) 1 | |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 2 / 55 (3.64%) 2 | 4 / 54 (7.41%) 5 | |
| Influenza subjects affected / exposed occurrences (all) | 3 / 55 (5.45%) 3 | 3 / 54 (5.56%) 4 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 55 (5.45%) 6 | 4 / 54 (7.41%) 7 | |
| Respiratory Tract Infection Viral subjects affected / exposed occurrences (all) | 1 / 55 (1.82%) 2 | 1 / 54 (1.85%) 2 | |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 2 / 55 (3.64%) 2 | 2 / 54 (3.70%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 29 March 2012 | The length of study was reduced to a 28-week placebo-controlled period with 20-week follow-up period. The hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) testings were added at the screening. The total blood volume was updated to include the additional laboratory testing added to the protocol. The treatment failure criteria were updated to include all reasons for discontinuation of study agent (such as due to adverse events [AEs]). A 12-lead ECG was added to the Week 28 safety evaluations. Instructions were added to the protocol to avoid unblinding by the Principal Investigator because of serious adverse events (SAEs) related to disease progression. Added that ribonucleic acid (RNA) would be measured from whole blood as well as serum in the study. The unit 10-cm was removed in reference to Visual Analogue Scale (VAS) since an electronic patient-reported outcome e-PRO) device was to be used to collect the VAS in the study. Preplanned surgery/procedure(s) row was removed from the time and events schedule since this row did not pertain to this study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

No notable study limitations were identified by the Sponsor.

Notes: