



Clinical trial results:

An Open-Label, Single-Arm, Extension Study to Demonstrate Long-Term Efficacy and Safety of CT-P13 When Co-administered With Methotrexate in Patients With Rheumatoid Arthritis Who Were Treated With Infliximab (Remicade or CT-P13) in Study CT-P13 3.1

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2011-004468-31 |
| Trial protocol | GB AT ES LV SK LT PL IT |
| Global end of trial date | 12 July 2013 |

Results information

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

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | CT-P13 3.2 |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | CELLTRION, Inc. |
| Sponsor organisation address | 23, Academy-ro, Yeonsu-gu, Incheon, Korea, Republic of, |
| Public contact | SuEun Song, CELLTRION, Inc, SuEun.Song@celltrion.com |
| Scientific contact | Sung Young Lee, CELLTRION, Inc, SungYoung.Lee@celltrion.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 | 10 December 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 July 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 July 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To confirm long-term efficacy and safety of CT-P13.

Protection of trial subjects:

- Hypersensitivity monitoring was performed as following.
- Vital sign: 15 minutes [± 5 minutes] before beginning the infusion, at the start of infusion, every 30 minutes [± 5 minutes] after the start of infusion, at the end of infusion, and 30, 60, and 120 minutes [± 10 minutes] after the end of infusion.
- Throughout the study, patients were monitored for the clinical signs and symptoms of TB.
- Premedications were given for safety of patients
- Emergency equipment and medication were available.
- For patients who experienced or developed life-threatening infusion-related anaphylactic reactions, infliximab treatment was stopped immediately and the patient withdrawn from the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 22 February 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------------------|
| Country: Number of subjects enrolled | Peru: 11 |
| Country: Number of subjects enrolled | Philippines: 27 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 12 |
| Country: Number of subjects enrolled | Bulgaria: 19 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Latvia: 9 |
| Country: Number of subjects enrolled | Lithuania: 18 |
| Country: Number of subjects enrolled | Poland: 86 |
| Country: Number of subjects enrolled | Romania: 10 |
| Country: Number of subjects enrolled | Slovakia: 4 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | Ukraine: 38 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | Chile: 15 |
| Country: Number of subjects enrolled | Colombia: 12 |
| Country: Number of subjects enrolled | Mexico: 28 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 302 |
| EEA total number of subjects | 159 |

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) | 289 |
| From 65 to 84 years | 13 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female patients with rheumatoid arthritis (aged 18 to 75 years old based on Study CT-P13 3.1) who had completed the scheduled visits, including the EOS Visit, in Study CT-P13 3.1

Period 1

| | |
|------------------------------|----------------------------|
| Period 1 title | Phase III (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

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

Arm description:

maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population)

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CT-P13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

CT-P13 (3 mg/kg, IV infusion for 2hr per dose) coadministered MTX between 12.5 to 25 mg/week (oral or parenteral dose) and folic acid (≥ 5 mg/week, oral dose)

| | |
|------------------|--------|
| Arm title | Switch |
|------------------|--------|

Arm description:

switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population)

| | |
|--|---------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | CT-P13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

CT-P13 (3 mg/kg, IV infusion for 2hr per dose) coadministered MTX between 12.5 to 25 mg/week (oral or parenteral dose) and folic acid (≥ 5 mg/week, oral dose)

| Number of subjects in period 1 | Maintenance | Switch |
|---------------------------------------|-------------|--------|
| Started | 159 | 143 |
| Completed | 134 | 127 |
| Not completed | 25 | 16 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 4 | 5 |
| death | 1 | - |
| Adverse event, non-fatal | 16 | 8 |
| Lost to follow-up | 2 | 2 |
| Lack of efficacy | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-------------|
| Reporting group title | Maintenance |
| Reporting group description: maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population) | |
| Reporting group title | Switch |
| Reporting group description: switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population) | |

| Reporting group values | Maintenance | Switch | Total |
|---|-------------|----------|-------|
| Number of subjects | 159 | 143 | 302 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| median | 50 | 49 | |
| full range (min-max) | 18 to 73 | 23 to 74 | - |
| Gender categorical Units: Subjects | | | |
| Female | 126 | 121 | 247 |
| Male | 33 | 22 | 55 |

End points

End points reporting groups

| | |
|--|----------------------------|
| Reporting group title | Maintenance |
| Reporting group description: maintain treatment with CT-P13 in Study CT-P13 3.2 (Safety population) | |
| Reporting group title | Switch |
| Reporting group description: switch from Remicade reference product in Study CT-P13 3.1 to CT-P13 in Study CT-P13 3.2 (Safety population) | |
| Subject analysis set title | Intent-to-Treat Population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All subjects enrolled in Study CT-P13 3.2 were included in Intent-to-Treat Subjects. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All subjects who received a complete or partial dose of IMP were included in the Safety Analysis Set. | |
| Subject analysis set title | Efficacy Population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All subjects who received at least 1 full dose of IMP and had data for at least 1 efficacy assessment were included in the Efficacy Analysis Set. | |

Primary: Treatment-Emergent Serious Adverse Events

| | |
|---|--|
| End point title | Treatment-Emergent Serious Adverse Events ^[1] |
| End point description: Number of Patients with at least one Treatment Emergent Serious Adverse Event | |
| End point type | Primary |
| End point timeframe: up to EOS | |

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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

| End point values | Maintenance | Switch | | |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 ^[2] | 143 ^[3] | | |
| Units: percentage | | | | |
| number (not applicable) | 7.5 | 9.1 | | |

Notes:

[2] - Safety population

[3] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Hypersensitivity and infusion-related reactions

| | |
|-----------------|--|
| End point title | Hypersensitivity and infusion-related reactions ^[4] |
|-----------------|--|

End point description:

Number of patients with at least one Treatment Emergent Adverse Event due to hypersensitivity and infusion-related reactions

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

End point timeframe:

up to EOS

Notes:

[4] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

| End point values | Maintenance | Switch | | |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 ^[5] | 143 ^[6] | | |
| Units: percentage | | | | |
| number (not applicable) | 6.3 | 2.8 | | |

Notes:

[5] - Safety population

[6] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-Emergent Adverse Events

| | |
|-----------------|--|
| End point title | Treatment-Emergent Adverse Events ^[7] |
|-----------------|--|

End point description:

Number of Patients with at least one Treatment Emergent Adverse Event

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

End point timeframe:

up to EOS

Notes:

[7] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

| End point values | Maintenance | Switch | | |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 ^[8] | 143 ^[9] | | |
| Units: percentage | | | | |
| number (not applicable) | 53.5 | 53.8 | | |

Notes:

[8] - Safety population

[9] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-Emergent Adverse Events due to infection

| | |
|-----------------|--|
| End point title | Treatment-Emergent Adverse Events due to infection ^[10] |
|-----------------|--|

End point description:

Number of Patients with at least one Treatment Emergent Adverse Event due to infection

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

End point timeframe:

up to EOS

Notes:

[10] - 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: The End Points such as Treatment-Emergent Serious Adverse Events, Treatment-Emergent Adverse Events, Treatment-Emergent Adverse Events due to infection, Hypersensitivity and infusion-related reactions were described using descriptive statistics.

| End point values | Maintenance | Switch | | |
|-----------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 ^[11] | 143 ^[12] | | |
| Units: percentage | | | | |
| number (not applicable) | 31.4 | 32.9 | | |

Notes:

[11] - Safety population

[12] - Safety population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to EOS

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Maintenance |
|-----------------------|-------------|

Reporting group description: -

| | |
|-----------------------|--------|
| Reporting group title | Switch |
|-----------------------|--------|

Reporting group description: -

| Serious adverse events | Maintenance | Switch | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 159 (7.55%) | 13 / 143 (9.09%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer stage II | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal T-cell lymphoma | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myeloproliferative disorder | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer stage I | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Ovarian cancer stage III | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular disorder | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia megaloblastic | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| 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 | | | |
| Death | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Medical device complication | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Oesophageal perforation | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pseudarthrosis | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid arthritis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 159 (1.26%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist deformity | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected dermal cyst | | | |
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 159 (0.63%) | 0 / 143 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingitis | | | |
| subjects affected / exposed | 0 / 159 (0.00%) | 1 / 143 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Maintenance | Switch | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 159 (19.50%) | 28 / 143 (19.58%) | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 5 / 159 (3.14%) | 9 / 143 (6.29%) | |
| occurrences (all) | 5 | 9 | |
| Latent tuberculosis | | | |
| subjects affected / exposed | 10 / 159 (6.29%) | 5 / 143 (3.50%) | |
| occurrences (all) | 10 | 5 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 159 (5.03%) | 6 / 143 (4.20%) | |
| occurrences (all) | 9 | 6 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 159 (5.03%) | 8 / 143 (5.59%) | |
| occurrences (all) | 9 | 8 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|--|
| 30 May 2012 | <p>Summary of significant changes includes the following:</p> <ul style="list-style-type: none">• Amended the number of study centers/countries• Clarified visit window and visit intervals• Amended Exclusion Criteria 9• Amended safety endpoints analysis• Clarified ACR core set of variables• Amended the immunogenicity analysis• Clarified monitoring and reporting of AEs• Clarified analysis of serum pregnancy test• Clarified analysis of sample for clinical laboratory assessments• Clarified back-up sample of immunogenicity analysis• Clarified concomitant medications• Amended demography and MH• Clarified SAE data entry• Clarified coding of AEs, MH, previous and concomitant treatments• Added rescue therapy• Added reporting of changes in terms of dose of concomitant medication• Other clarifications and administrative changes |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported