



Clinical trial results:

A Double-Blind, Randomized, Parallel-Group, Active Control Study to Compare the Efficacy and Safety of CHS-0214 Versus Enbrel® in Subjects With Chronic Plaque Psoriasis (CHS-0214-04) (RaPsOdy)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-000444-14 |
| Trial protocol | DE GB PL |
| Global end of trial date | 27 April 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 May 2017 |
| First version publication date | 13 May 2017 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | CHS-0214-04 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02134210 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Coherus BioSciences, Inc. |
| Sponsor organisation address | 333 Twin Dolphin Drive, Suite 600, Redwood City, United States, CA 94065 |
| Public contact | Barbara K. Finck, Coherus BioSciences, Inc., +1 650 649 3530, |
| Scientific contact | Barbara K. Finck, Coherus BioSciences, Inc., +1 650 649 3530, |

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 | 31 May 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 July 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 April 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Part 1 of this study was to compare the efficacy and safety of CHS-0214 and Enbrel (EU) 50 mg given twice a week (BIW) for 12 weeks.

The primary objective of Part 2 of this study was to compare the safety and durability of response of CHS-0214 and Enbrel (EU) 50 mg given once a week (QW) from 13 weeks up to 47 weeks of treatment.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with the International Conference on Harmonisation E6 Good Clinical Practice Guidelines. The rationale of the study, procedural details, and investigational goals were explained to each subject, along with potential risks and benefits. Each subject was assured of his/her right to withdraw from the study at any time. Prior to the initiation of any study procedures, each subject signed and dated an approved informed consent form.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 June 2014 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 12 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 201 |
| Country: Number of subjects enrolled | Germany: 24 |
| Country: Number of subjects enrolled | Canada: 74 |
| Country: Number of subjects enrolled | Australia: 18 |
| Country: Number of subjects enrolled | Israel: 14 |
| Country: Number of subjects enrolled | South Africa: 48 |
| Country: Number of subjects enrolled | United States: 142 |
| Worldwide total number of subjects | 521 |
| EEA total number of subjects | 225 |

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) | 486 |
| From 65 to 84 years | 35 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

4-week screening period (Weeks -4 to 0)

Period 1

| | |
|------------------------------|---|
| Period 1 title | Part 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|----------|
| Arm title | CHS-0214 |
|------------------|----------|

Arm description:

Subjects were assigned the treatment as randomized.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | CHS-0214 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A 50 mg dose of CHS-0214 was administered twice a week (BIW) by subcutaneous (SC) injection, from Week 0 Day 0 through Week 12.

| | |
|------------------|-------------|
| Arm title | Enbrel (EU) |
|------------------|-------------|

Arm description:

Subjects were assigned the treatment as randomized.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Enbrel (EU) |
| Investigational medicinal product code | |
| Other name | etanercept |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A 50 mg dose of Enbrel (EU) was administered twice a week (BIW) by subcutaneous (SC) injection, from Week 0 Day 0 through Week 12.

| Number of subjects in period 1 | CHS-0214 | Enbrel (EU) |
|--------------------------------|----------|-------------|
| Started | 261 | 260 |
| Completed | 255 | 241 |
| Not completed | 6 | 19 |
| Consent withdrawn by subject | 4 | 8 |
| Physician decision | - | 1 |
| TB test positive | - | 1 |
| Disease progression | - | 1 |
| Adverse event, non-fatal | - | 5 |
| other | - | 2 |
| Lost to follow-up | 2 | - |
| Protocol deviation | - | 1 |

Period 2

| | |
|------------------------------|---------------------------------------|
| Period 2 title | Part 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer |

Arms

| | |
|--|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | CHS-0214 |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | CHS-0214 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects continued in the blinded groups to which they were originally randomized.
A 50 mg dose of CHS-0214 was administered once a week (QW) by subcutaneous (SC) injection, for maintenance, from Week 13 through Week 47.

| | |
|--|------------------|
| Arm title | Enbrel (EU) |
| Arm description: - | |
| Arm type | Safety |
| Investigational medicinal product name | Enbrel (EU) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects continued in the blinded groups to which they were originally randomized.

A 50 mg dose of Enbrel (EU) was administered once a week (QW) by subcutaneous (SC) injection, for maintenance, from Week 13 through Week 47.

| Number of subjects in period 2 | CHS-0214 | Enbrel (EU) |
|---------------------------------------|----------|-------------|
| Started | 255 | 241 |
| Completed | 227 | 211 |
| Not completed | 28 | 30 |
| Consent withdrawn by subject | 14 | 8 |
| TB test positive | 1 | 3 |
| Disease progression | 2 | 5 |
| Adverse event, non-fatal | 5 | 4 |
| Development of malignancy | - | 1 |
| Pregnancy | 1 | - |
| Did not return for follow up visit | 1 | 1 |
| Lost to follow-up | 4 | 7 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | CHS-0214 |
| Reporting group description: Subjects were assigned the treatment as randomized. | |
| Reporting group title | Enbrel (EU) |
| Reporting group description: Subjects were assigned the treatment as randomized. | |

| Reporting group values | CHS-0214 | Enbrel (EU) | Total |
|---|----------|-------------|-------|
| Number of subjects | 261 | 260 | 521 |
| 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) | 246 | 240 | 486 |
| From 65-84 years | 15 | 20 | 35 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical Units: Subjects | | | |
| Female | 76 | 80 | 156 |
| Male | 185 | 180 | 365 |

Subject analysis sets

| | |
|---|--------------------------|
| Subject analysis set title | CHS-0214 - FAP Part 1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The Full Analysis Population (FAP) included all subjects randomized prior to the dosing suspension who had completed 12 weeks of study drug at the time of the suspension, and subjects randomized after dosing was resumed and received 1 or more doses of study drug. This was the primary efficacy analysis population. | |
| Subject analysis set title | Enbrel (EU) - FAP Part 1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The Full Analysis Population (FAP) included all subjects randomized prior to the dosing suspension who had completed 12 weeks of study drug at the time of the suspension, and subjects randomized after dosing was resumed and received 1 or more doses of study drug. This was the primary efficacy analysis population. | |

| Reporting group values | CHS-0214 - FAP Part 1 | Enbrel (EU) - FAP Part 1 | |
|------------------------|-----------------------|--------------------------|--|
| Number of subjects | 228 | 228 | |

| | | | |
|---|-----|-----|--|
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 217 | 213 | |
| From 65-84 years | 11 | 15 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 66 | 71 | |
| Male | 162 | 157 | |

End points

End points reporting groups

| | |
|---|--------------------------|
| Reporting group title | CHS-0214 |
| Reporting group description: Subjects were assigned the treatment as randomized. | |
| Reporting group title | Enbrel (EU) |
| Reporting group description: Subjects were assigned the treatment as randomized. | |
| Reporting group title | CHS-0214 |
| Reporting group description: - | |
| Reporting group title | Enbrel (EU) |
| Reporting group description: - | |
| Subject analysis set title | CHS-0214 - FAP Part 1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The Full Analysis Population (FAP) included all subjects randomized prior to the dosing suspension who had completed 12 weeks of study drug at the time of the suspension, and subjects randomized after dosing was resumed and received 1 or more doses of study drug. This was the primary efficacy analysis population. | |
| Subject analysis set title | Enbrel (EU) - FAP Part 1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The Full Analysis Population (FAP) included all subjects randomized prior to the dosing suspension who had completed 12 weeks of study drug at the time of the suspension, and subjects randomized after dosing was resumed and received 1 or more doses of study drug. This was the primary efficacy analysis population. | |

Primary: Mean percent change in PASI from baseline (last non-missing value prior to first dose) at Week 12.

| | |
|--|--|
| End point title | Mean percent change in PASI from baseline (last non-missing value prior to first dose) at Week 12. |
| End point description: This was the primary endpoint intended to support the Marketing Authorization Application in the European Union. | |
| End point type | Primary |
| End point timeframe: Baseline (last non-missing value prior to first dose) to Week 12. | |

| End point values | CHS-0214 - FAP Part 1 | Enbrel (EU) - FAP Part 1 | | |
|--------------------------------------|-----------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 228 | 228 | | |
| Units: Mean percent change | | | | |
| arithmetic mean (standard deviation) | -76.7 (± 21.1) | -73.4 (± 25) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Analysis of Mean Percent Change in PASI at Week 12 |
| Comparison groups | CHS-0214 - FAP Part 1 v Enbrel (EU) - FAP Part 1 |
| Number of subjects included in analysis | 456 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[1] |
| Parameter estimate | Estimated treatment difference, weighted |
| Point estimate | -3.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.67 |
| upper limit | 0.84 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.171 |

Notes:

[1] - Cochran-Mantel-Haenszel (CMH) procedure stratified by the randomization strata. Equivalence was established if the limits of the 2-sided 95% CI were completely within the pre-specified equivalence range.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to Week 48

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | CHS-0214 |
|-----------------------|----------|

Reporting group description: -

| | |
|-----------------------|-------------|
| Reporting group title | Enbrel (EU) |
|-----------------------|-------------|

Reporting group description: -

| Serious adverse events | CHS-0214 | Enbrel (EU) | |
|---|-----------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 261 (2.68%) | 10 / 260 (3.85%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 261 (0.77%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pickwickian syndrome | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | 1 / 260 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (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 | | | |
| Bartholin's abscess | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar Pneumonia | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | 0 / 260 (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: 2 %

| Non-serious adverse events | CHS-0214 | Enbrel (EU) | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 191 / 261 (73.18%) | 198 / 260 (76.15%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 6 / 261 (2.30%) | 4 / 260 (1.54%) | |
| occurrences (all) | 7 | 5 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 11 / 261 (4.21%) | 11 / 260 (4.23%) | |
| occurrences (all) | 12 | 11 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 5 / 261 (1.92%) | 7 / 260 (2.69%) | |
| occurrences (all) | 5 | 9 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 13 / 261 (4.98%) | 14 / 260 (5.38%) | |
| occurrences (all) | 13 | 14 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 8 / 261 (3.07%) | 10 / 260 (3.85%) | |
| occurrences (all) | 8 | 16 | |
| General disorders and administration site conditions | | | |
| Injection site bruising | | | |
| subjects affected / exposed | 7 / 261 (2.68%) | 8 / 260 (3.08%) | |
| occurrences (all) | 13 | 8 | |

| | | | |
|---|-------------------------|-------------------------|--|
| Injection site reaction subjects affected / exposed occurrences (all) | 11 / 261 (4.21%) 18 | 46 / 260 (17.69%) 80 | |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 261 (2.30%) 6 | 3 / 260 (1.15%) 3 | |
| Toothache subjects affected / exposed occurrences (all) | 2 / 261 (0.77%) 2 | 6 / 260 (2.31%) 7 | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus subjects affected / exposed occurrences (all) | 8 / 261 (3.07%) 9 | 9 / 260 (3.46%) 9 | |
| Psoriasis subjects affected / exposed occurrences (all) | 10 / 261 (3.83%) 10 | 13 / 260 (5.00%) 13 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 7 / 261 (2.68%) 7 | 4 / 260 (1.54%) 5 | |
| Back pain subjects affected / exposed occurrences (all) | 6 / 261 (2.30%) 6 | 4 / 260 (1.54%) 4 | |
| Infections and infestations | | | |
| Influenza subjects affected / exposed occurrences (all) | 11 / 261 (4.21%) 12 | 11 / 260 (4.23%) 12 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 40 / 261 (15.33%) 54 | 42 / 260 (16.15%) 56 | |
| Pharyngitis subjects affected / exposed occurrences (all) | 5 / 261 (1.92%) 5 | 7 / 260 (2.69%) 7 | |
| Sinusitis | | | |

| | | | |
|-----------------------------------|------------------|-------------------|--|
| subjects affected / exposed | 4 / 261 (1.53%) | 10 / 260 (3.85%) | |
| occurrences (all) | 4 | 12 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 24 / 261 (9.20%) | 27 / 260 (10.38%) | |
| occurrences (all) | 25 | 29 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 261 (3.07%) | 13 / 260 (5.00%) | |
| occurrences (all) | 11 | 14 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 30 June 2014 | <ul style="list-style-type: none">- Study name RaPsOdy was added at the end of the study title- All secondary endpoints were added- Inclusion and exclusion criteria were edited to better define the selection of the study population- Added development of malignancy while on study as a reason for subject withdrawal- Added instruction that subjects who discontinued early would return for all Part 1 study visits- Clarified that "dropouts" referred to subjects who discontinued early and who were randomized but not treated- Revised instructions for used syringes- Edited language around prior and concomitant medications- Clarified that the same Investigator/clinician should have conducted the PASI for each subject at each visit- Added clarification that injection site reactions should have only been reported as adverse events if they were observed by study personnel- Changed Grade 4 adverse event definition from "severe" to "life-threatening"- Clarified that subjects with an indeterminate QuantiFERON-TB Gold test result could have had the test repeated once, and if negative, could have participated in the study |
| 06 November 2014 | <ul style="list-style-type: none">- Prohibited administration of a live vaccine within 4 weeks prior to screening- Added language to clarify text around study drug accountability and retention as a safety measure, and to maintain consistency with the product insert of etanercept- Updated testing methods for positive HIV results |
| 11 March 2015 | <ul style="list-style-type: none">- Revised enrollment numbers- Clarified that a subject's last dose is at Week 47- Added text to clarify requirements for the use of abstinence as a means of birth control- Added requirement that study personnel should visually inspect syringes for particulate matter and/or discoloration prior to dispensing study drug- Clarified TB testing entry criteria and what results permitted a repeat test- Clarified when subjects should have returned for follow-up after last dose of study drug- Added an explanation on how to manage subjects who were enrolled prior to study drug suspension- Prohibited systemic steroids within 4 weeks of randomization- Clarified that subjects who were off study drug during the study drug suspension period could have resumed study drug regardless of how many doses were missed- Expanded the 2 primary endpoints of the study- Added a description of adverse event outcomes- Added language to allow continuation into an open-label extension study in select countries- Redefined the Full Analysis Population and Safety Population |
| 21 September 2015 | <ul style="list-style-type: none">- Added durability of response as an efficacy variable for Part 2- Added detailed information to the interpretation of QuantiFERON-TB Gold testing and how subjects who had an intermediate or low positive result should be managed- Added language stating that the Sponsor may review A/B unblinded Part 1 analyses to assess if the results can support the project regulatory strategy and may release the assessment publically |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-----------------|--|------------------|
| 30 October 2014 | During the conduct of the study, enrollment and dosing of subjects was voluntarily suspended by the Sponsor. During routine visual inspection of study drug in storage, 4 syringes containing CHS-0214 from a lot in use in Study CHS-0214-04 were observed to contain small dark particles. In the interest of patient safety, dosing of the ongoing Phase 3 clinical trials was immediately stopped, and an investigation was initiated to determine the cause and incidence of the observed particulate. A chemical analysis by an independent laboratory determined that the particles were not the result of drug product instability or formulation. Upon conclusion of the investigation, the lot was replaced in clinical inventory, and enrollment and dosing were resumed. | 05 November 2014 |

Notes:

Limitations and caveats

None reported