



Clinical trial results:

A Phase 2, open-label, multicenter study to assess the safety and efficacy of certolizumab pegol in children and adolescents with active Crohn's disease (NURTURE Study)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-004381-24 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 02 July 2012 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 June 2016 |
| First version publication date | 10 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | C87035 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00899678 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UCB Celltech |
| Sponsor organisation address | 208 Bath Road, Slough, United Kingdom, SL1 3 WE |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 2173 4815 15, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 2173 48 15 15, clinicaltrials@ucb.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? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 08 October 2012 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 02 July 2012 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the efficacy of certolizumab pegol in children and adolescents with moderately to severely active Crohn's disease (CD). This study also assesses certolizumab pegol treatment in this population with respect to:

- Safety
 - Tolerability
 - Efficacy (secondary efficacy variables, including the impact upon growth and development)
 - Immunogenicity
 - Pharmacokinetics
 - Subject-reported outcomes
-

Protection of trial subjects:

Not applicable

Background therapy:

Corticosteroids at screening were tapered according to a schedule between Week 2 and Week 8. In the event of a flare in Crohn's disease, corticosteroids could be reintroduced at the same dose as at Week 0.

Evidence for comparator:

Not applicable

| | |
|---|--------------|
| Actual start date of recruitment | 01 June 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | Canada: 23 |
| Country: Number of subjects enrolled | New Zealand: 5 |
| Country: Number of subjects enrolled | United States: 67 |
| Worldwide total number of subjects | 99 |
| EEA total number of subjects | 0 |

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) | 23 |
| Adolescents (12-17 years) | 76 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The Participant Flow refers to the Safety Set (SS) population. The Safety Population includes all subjects enrolled who received at least 1 injection of study treatment.

Pre-assignment

Screening details:

During an Induction Period (Weeks 0 to 6), subjects were administered Certolizumab Pegol (CZP) subcutaneously every 2 weeks (Q2W). Subjects who showed a clinical response at Week 6 were randomized in a 1:1 ratio to one of 2 dose groups. Subjects who did not respond at Week 6 were withdrawn from the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Study Overall (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Induction Only |

Arm description:

Induction Only is the period between the Week 0 dose and prior to first maintenance dose (Week 8). Induction Only includes all subjects who received a dose during the Induction Period but did not receive any treatment during the Maintenance Period. During the Induction Period (Weeks 0 to 6), subjects were administered Certolizumab Pegol (CZP) subcutaneously every 2 weeks (Q2W) (for a total of 3 administrations of drug) at a dose of either:

- 400 mg for subjects \geq 40 kg
- 200 mg for subjects 20 to < 40 kg

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Certolizumab Pegol |
| Investigational medicinal product code | Certolizumab Pegol |
| Other name | Cimzia |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Maintenance High-Dose group: 400 mg Certolizumab Pegol for subjects \geq 40 kg or 200 mg Certolizumab Pegol for subjects 20 to < 40 kg Maintenance Low-Dose

Maintenance Low-Dose group: 200 mg Certolizumab Pegol for subjects \geq 40 kg or 100 mg Certolizumab Pegol for subjects 20 to < 40 kg

| | |
|------------------|----------------------|
| Arm title | Maintenance Low-Dose |
|------------------|----------------------|

Arm description:

Maintenance Low-Dose group*:

200 mg Certolizumab Pegol once every 4 weeks for subjects \geq 40 kg or 100 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg

*prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects \geq 40 kg or 200 mg for subjects 20 to < 40 kg

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Certolizumab Pegol |
| Investigational medicinal product code | Certolizumab Pegol |
| Other name | Cimzia |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Maintenance High-Dose group: 400 mg Certolizumab Pegol for subjects ≥ 40 kg or 200 mg Certolizumab Pegol for subjects 20 to < 40 kg Maintenance Low-Dose

Maintenance Low-Dose group: 200 mg Certolizumab Pegol for subjects ≥ 40 kg or 100 mg Certolizumab Pegol for subjects 20 to < 40 kg

| | |
|------------------|-----------------------|
| Arm title | Maintenance High-Dose |
|------------------|-----------------------|

Arm description:**Maintenance High-Dose group*:**

400 mg Certolizumab Pegol once every 4 weeks for subjects ≥ 40 kg or 200 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg

*prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects ≥ 40 kg or 200 mg for subjects 20 to < 40 kg

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Certolizumab Pegol |
| Investigational medicinal product code | Certolizumab Pegol |
| Other name | Cimzia |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Maintenance High-Dose group: 400 mg Certolizumab Pegol for subjects ≥ 40 kg or 200 mg Certolizumab Pegol for subjects 20 to < 40 kg Maintenance Low-Dose

Maintenance Low-Dose group: 200 mg Certolizumab Pegol for subjects ≥ 40 kg or 100 mg Certolizumab Pegol for subjects 20 to < 40 kg

| Number of subjects in period 1 | Induction Only | Maintenance Low-Dose | Maintenance High-Dose |
|---------------------------------------|----------------|----------------------|-----------------------|
| Started | 27 | 37 | 35 |
| Completed | 2 | 12 | 7 |
| Not completed | 25 | 25 | 28 |
| Consent withdrawn by subject | - | 1 | 2 |
| Other | 1 | 2 | 2 |
| AE, non-serious non-fatal | 3 | 4 | 3 |
| AE, unknown | - | 1 | - |
| SAE, non-fatal | 3 | 5 | 2 |
| Lack of efficacy | 17 | 11 | 18 |
| Protocol deviation | 1 | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-----------------------|
| Reporting group title | Induction Only |
| Reporting group description: | |
| Induction Only is the period between the Week 0 dose and prior to first maintenance dose (Week 8). Induction Only includes all subjects who received a dose during the Induction Period but did not receive any treatment during the Maintenance Period. During the Induction Period (Weeks 0 to 6), subjects were administered Certolizumab Pegol (CZP) subcutaneously every 2 weeks (Q2W) (for a total of 3 administrations of drug) at a dose of either: | |
| - 400 mg for subjects \geq 40 kg | |
| - 200 mg for subjects 20 to < 40 kg | |
| Reporting group title | Maintenance Low-Dose |
| Reporting group description: | |
| Maintenance Low-Dose group*: | |
| 200 mg Certolizumab Pegol once every 4 weeks for subjects \geq 40 kg or 100 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg | |
| *prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects \geq 40 kg or 200 mg for subjects 20 to < 40 kg | |
| Reporting group title | Maintenance High-Dose |
| Reporting group description: | |
| Maintenance High-Dose group*: | |
| 400 mg Certolizumab Pegol once every 4 weeks for subjects \geq 40 kg or 200 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg | |
| *prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects \geq 40 kg or 200 mg for subjects 20 to < 40 kg | |

| Reporting group values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose |
|---|----------------|----------------------|-----------------------|
| Number of subjects | 27 | 37 | 35 |
| Age categorical | | | |
| Units: Subjects | | | |
| 6-11 years | 6 | 9 | 8 |
| 12-17 years | 21 | 28 | 27 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 13.8 | 13.2 | 13.4 |
| standard deviation | \pm 2.67 | \pm 2.41 | \pm 2.46 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 10 | 10 | 21 |
| Male | 17 | 27 | 14 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian / Alaskan Native | 0 | 0 | 0 |
| Asian | 1 | 0 | 0 |
| Black | 3 | 3 | 8 |
| Native Hawaiian or other Pacific islander | 0 | 0 | 0 |
| White | 22 | 32 | 27 |
| Other / Mixed | 1 | 2 | 0 |

| | | | |
|--|--------------------|--------------------|-------------------|
| Weight Units: kilogram arithmetic mean standard deviation | 46.5 ± 12.565 | 45.67 ± 14.638 | 50.35 ± 18.569 |
| Height Units: centimeter arithmetic mean standard deviation | 157.46 ± 13.841 | 155.32 ± 13.589 | 157.22 ± 13.32 |
| Body Mass Index (BMI) Units: kilogram per square meter arithmetic mean standard deviation | 18.39 ± 2.504 | 18.51 ± 3.531 | 19.79 ± 4.897 |
| Body Surface Area (BSA) Units: square meter arithmetic mean standard deviation | 1.42 ± 0.25 | 1.39 ± 0.272 | 1.47 ± 0.319 |

| | | | |
|--|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 99 | | |
| Age categorical Units: Subjects | | | |
| 6-11 years | 23 | | |
| 12-17 years | 76 | | |
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Gender Categorical Units: Subjects | | | |
| Female | 41 | | |
| Male | 58 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian / Alaskan Native | 0 | | |
| Asian | 1 | | |
| Black | 14 | | |
| Native Hawaiian or other Pacific islander | 0 | | |
| White | 81 | | |
| Other / Mixed | 3 | | |
| Weight Units: kilogram arithmetic mean standard deviation | - | | |
| Height Units: centimeter arithmetic mean standard deviation | - | | |
| Body Mass Index (BMI) Units: kilogram per square meter arithmetic mean standard deviation | - | | |

| | | | |
|-------------------------|---|--|--|
| Body Surface Area (BSA) | | | |
| Units: square meter | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | Induction Only |
| Reporting group description: Induction Only is the period between the Week 0 dose and prior to first maintenance dose (Week 8). Induction Only includes all subjects who received a dose during the Induction Period but did not receive any treatment during the Maintenance Period. During the Induction Period (Weeks 0 to 6), subjects were administered Certolizumab Pegol (CZP) subcutaneously every 2 weeks (Q2W) (for a total of 3 administrations of drug) at a dose of either: - 400 mg for subjects ≥ 40 kg - 200 mg for subjects 20 to < 40 kg | |
| Reporting group title | Maintenance Low-Dose |
| Reporting group description: Maintenance Low-Dose group*: 200 mg Certolizumab Pegol once every 4 weeks for subjects ≥ 40 kg or 100 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg *prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects ≥ 40 kg or 200 mg for subjects 20 to < 40 kg | |
| Reporting group title | Maintenance High-Dose |
| Reporting group description: Maintenance High-Dose group*: 400 mg Certolizumab Pegol once every 4 weeks for subjects ≥ 40 kg or 200 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg *prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects ≥ 40 kg or 200 mg for subjects 20 to < 40 kg | |

Primary: Percentage of subjects in clinical remission at Week 62

| | |
|--|--|
| End point title | Percentage of subjects in clinical remission at Week 62 ^[1] |
| End point description: Clinical remission is defined as a Pediatric Crohn's Disease Activity Index (PCDAI) score ≤ 10 . The Pediatric Crohn's Disease Activity Index (PCDAI) consists of 4 domains (laboratory, height/weight, examination, and history) with several assessments that are converted into a PCDAI score which can range from 0 to 100 points, with a higher score indicating more severe disease activity. | |
| End point type | Primary |
| End point timeframe: Week 62 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|-----------------------------------|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[2] | 37 | 35 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| number (95 % CI) | (to) | 24.3 (10.5 to 38.1) | 17.1 (4.7 to 29.6) | |

Notes:

[2] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Pediatric Crohn's Disease Activity Index (PCDAI) scores at Week 62

| | |
|--|---|
| End point title | Absolute Pediatric Crohn's Disease Activity Index (PCDAI) scores at Week 62 |
| End point description: The Pediatric Crohn's Disease Activity Index (PCDAI) consists of 4 domains (laboratory, height/weight, examination, and history) with several assessments that are converted into a PCDAI score which can range from 0 to 100 points, with a higher score indicating more severe disease activity. | |
| End point type | Secondary |
| End point timeframe: Week 62 | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--------------------------------------|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[3] | 11 | 7 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | () | 8.18 (± 6.9) | 7.14 (± 7.83) | |

Notes:

[3] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pediatric Crohn's Disease Activity Index (PCDAI) scores from Week 0 to the end of the study (Week 62)

| | |
|---|---|
| End point title | Change in Pediatric Crohn's Disease Activity Index (PCDAI) scores from Week 0 to the end of the study (Week 62) |
| End point description: The Pediatric Crohn's Disease Activity Index (PCDAI) consists of 4 domains (laboratory, height/weight, examination, and history) with several assessments that are converted into a PCDAI score which can range from 0 to 100 points, with a higher score indicating more severe disease activity. A negative value in change from Baseline indicates an improvement from Baseline to Week 62. | |
| End point type | Secondary |
| End point timeframe: From Week 0 to Week 62 | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--------------------------------------|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[4] | 11 | 7 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | () | -29.77 (± 8.097) | -27.14 (± 5.669) | |

Notes:

[4] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving clinical response from Week 0 to the end of the study (Week 62)

| | |
|-----------------|--|
| End point title | Percentage of subjects achieving clinical response from Week 0 to the end of the study (Week 62) |
|-----------------|--|

End point description:

Clinical response is defined as a decrease from Week 0 in Pediatric Crohn's Disease Activity Index (PCDAI) score of ≥ 15 points and a total PCDAI score ≤ 30 points.

The Pediatric Crohn's Disease Activity Index (PCDAI) consists of 4 domains (laboratory, height/weight, examination, and history) with several assessments that are converted into a PCDAI score which can range from 0 to 100 points, with a higher score indicating more severe disease activity.

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

End point timeframe:

From Week 0 to Week 62

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|-----------------------------------|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[5] | 37 | 35 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| number (95 % CI) | (to) | 29.7 (15 to 44.5) | 20 (6.7 to 33.3) | |

Notes:

[5] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: C-Reactive Protein (CRP) levels at Week 62

| | |
|-----------------|--|
| End point title | C-Reactive Protein (CRP) levels at Week 62 |
|-----------------|--|

End point description:

The C-Reactive Protein (CRP) is a considered marker of inflammation in subjects with Crohn's Disease (CD)

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

End point timeframe:

Week 62

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[6] | 11 | 7 | |
| Units: mg/L | | | | |
| geometric mean (confidence interval 95%) | | | | |
| geometric mean (95 % CI) | (to) | 7.2 (2.5 to 20.7) | 5.8 (2.1 to 15.7) | |

Notes:

[6] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in C-Reactive Protein (CRP) levels from Week 0 to the end of the study (Week 62)

| | |
|-----------------|---|
| End point title | Change in C-Reactive Protein (CRP) levels from Week 0 to the end of the study (Week 62) |
|-----------------|---|

End point description:

The C-Reactive Protein (CRP) is a considered marker of inflammation in subjects with Crohn's Disease (CD).

Changes from Baseline in CRP levels are expressed as a ratio with the value measured at Baseline as the denominator.

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

End point timeframe:

From Week 0 to Week 62

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[7] | 11 | 7 | |
| Units: ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| geometric mean (95 % CI) | (to) | 0.49 (0.17 to 1.41) | 1.84 (0.27 to 12.71) | |

Notes:

[7] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate (ESR) at Week 62

| | |
|---|---|
| End point title | Erythrocyte Sedimentation Rate (ESR) at Week 62 |
| End point description: The Erythrocyte Sedimentation Rate (ESR) is a considered biomarker of inflammation in subjects with Crohn's Disease (CD). | |
| End point type | Secondary |
| End point timeframe: Week 62 | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[8] | 12 | 7 | |
| Units: mm/h | | | | |
| geometric mean (confidence interval 95%) | | | | |
| geometric mean (95 % CI) | (to) | 20.9 (11.8 to 37.2) | 25.2 (12.3 to 51.7) | |

Notes:

[8] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Erythrocyte Sedimentation Rate (ESR) from Week 0 to the end of the study (Week 62)

| | |
|---|--|
| End point title | Change in Erythrocyte Sedimentation Rate (ESR) from Week 0 to the end of the study (Week 62) |
| End point description: The Erythrocyte Sedimentation Rate (ESR) is a considered biomarker of inflammation in subjects with Crohn's Disease (CD). Changes from Baseline in CRP levels are expressed as a ratio with the value measured at baseline as the denominator. | |
| End point type | Secondary |
| End point timeframe: From Week 0 to Week 62 | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|--|------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[9] | 12 | 7 | |
| Units: ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |

| | | | | |
|--------------------------|--------|---------------------|---------------------|--|
| geometric mean (95 % CI) | (to) | 0.57 (0.31 to 1.04) | 1.08 (0.39 to 3.02) | |
|--------------------------|--------|---------------------|---------------------|--|

Notes:

[9] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in growth scores (Tanner stage [assessing puberty]) from Week 0 to the end of the study (Week 62)

| | |
|-----------------|--|
| End point title | Change in growth scores (Tanner stage [assessing puberty]) from Week 0 to the end of the study (Week 62) |
|-----------------|--|

End point description:

The Tanner stage is an assessment of developmental stage on external genitalia and pubic hair (boys), and on breast and pubic hair (girls). Values range from 1 to 5 where a higher number indicates more development.

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

End point timeframe:

From Week 0 to Week 62

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|-------------------------------------|-------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[10] | 10 | 7 | |
| Units: participants | | | | |
| Increase from Stage I to Stage II | | 2 | 0 | |
| Increase from Stage I to Stage III | | 1 | 1 | |
| Increase from Stage II to Stage III | | 0 | 1 | |
| Increase from Stage III to Stage IV | | 2 | 0 | |
| Increase from Stage IV to Stage V | | 0 | 1 | |
| Decrease from Stage IV to Stage III | | 1 | 1 | |
| Subjects remained in Stage I | | 0 | 1 | |
| Subjects remained in Stage III | | 0 | 2 | |
| Subjects remained in Stage IV | | 1 | 0 | |
| Subjects remained in Stage V | | 3 | 0 | |

Notes:

[10] - Subjects from "Induction Only" were not included in the Analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who initiated steroid tapering

| | |
|-----------------|---|
| End point title | Percentage of subjects who initiated steroid tapering |
|-----------------|---|

End point description:

Subjects receiving corticosteroids at Screening may start a defined tapering schedule between Weeks 2 and 8. Corticosteroid tapering must start at the latest by Week 8. Corticosteroid doses are tapered at different rates depending on the subject's dose.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Week 2 up to Week 8 | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|----------------------------------|-------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[11] | 21 | 20 | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| number (95 % CI) | (to) | 71.4 (52.1 to 90.8) | 65 (44.1 to 85.9) | |

Notes:

[11] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in corticosteroid-free remission at the end of the study

| | |
|-----------------|---|
| End point title | Percentage of subjects in corticosteroid-free remission at the end of the study |
|-----------------|---|

End point description:

Corticosteroid use at end of study is defined as 84 days past the last dose of study medication. Remission is assessed at the last visit where Pediatric Crohn's Disease Activity index (PCDAI) data is available.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Last/Withdrawal Visit (up to Week 62) | |

| End point values | Induction Only | Maintenance Low-Dose | Maintenance High-Dose | |
|-----------------------------------|-------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[12] | 21 | 20 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| number (95 % CI) | (to) | 23.8 (5.6 to 42) | 15 (0 to 30.6) | |

Notes:

[12] - Subjects from "Induction Only" were not included in the analysis of this End Point.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected over 68 weeks (from Week -6 to Week 62).

Adverse event reporting additional description:

Adverse Events (AEs) refer to the Safety Set (SS) population.

All subjects in the Safety Population (n=99) participated in the Induction Period. There were 27 subjects who did not continue into the Maintenance Period.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Induction Period |
|-----------------------|------------------|

Reporting group description:

Induction Only is the period between the Week 0 dose and prior to first maintenance dose (Week 8).

Induction Only includes all subjects who received a dose during the Induction Period but did not receive any treatment during the Maintenance Period. During the Induction Period (Weeks 0 to 6), subjects were administered Certolizumab Pegol (CZP) subcutaneously every 2 weeks (Q2W) (for a total of 3 administrations of drug) at a dose of either:

- 400 mg for subjects ≥ 40 kg

- 200 mg for subjects 20 to < 40 kg

| | |
|-----------------------|----------------------|
| Reporting group title | Maintenance Low-Dose |
|-----------------------|----------------------|

Reporting group description:

Maintenance Low-Dose group*: 200 mg Certolizumab Pegol once every 4 weeks for subjects ≥ 40 kg or 100 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg

*prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects ≥ 40 kg or 200 mg for subjects 20 to < 40 kg

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

Overall Study comprises Induction Period and Maintenance Period (Week -6 to Week 62).

| | |
|-----------------------|-----------------------|
| Reporting group title | Maintenance High-Dose |
|-----------------------|-----------------------|

Reporting group description:

Maintenance High-Dose group*: 400 mg Certolizumab Pegol once every 4 weeks for subjects ≥ 40 kg or 200 mg Certolizumab Pegol once every 4 weeks for subjects 20 to < 40 kg

*prior to this dosing regimen, subjects underwent an induction of Certolizumab Pegol administered subcutaneously every 2 weeks (total 3 injections) at of either 400 mg for subjects ≥ 40 kg or 200 mg for subjects 20 to < 40 kg

| Serious adverse events | Induction Period | Maintenance Low-Dose | Overall Study |
|---|------------------|----------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 99 (6.06%) | 4 / 37 (10.81%) | 14 / 99 (14.14%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Weight decreased | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Vomiting | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 0 / 37 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonellosis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 37 (2.70%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 37 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------------|--|--|
| Serious adverse events | Maintenance High-Dose | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 35 (11.43%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal fistula | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis viral | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Induction Period | Maintenance Low-Dose | Overall Study |
|---|------------------|----------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 59 / 99 (59.60%) | 28 / 37 (75.68%) | 78 / 99 (78.79%) |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 37 (0.00%) | 2 / 99 (2.02%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|--|------------------------|-----------------------|-------------------------|
| Weight decreased subjects affected / exposed occurrences (all) | 2 / 99 (2.02%) 2 | 2 / 37 (5.41%) 2 | 4 / 99 (4.04%) 7 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 2 / 37 (5.41%) 2 | 2 / 99 (2.02%) 2 |
| Ligament sprain subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 2 / 37 (5.41%) 2 | 2 / 99 (2.02%) 2 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 9 / 99 (9.09%) 12 | 4 / 37 (10.81%) 10 | 12 / 99 (12.12%) 26 |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 3 / 99 (3.03%) 3 | 3 / 37 (8.11%) 4 | 6 / 99 (6.06%) 7 |
| Injection site pain subjects affected / exposed occurrences (all) | 22 / 99 (22.22%) 55 | 4 / 37 (10.81%) 17 | 22 / 99 (22.22%) 108 |
| Pyrexia subjects affected / exposed occurrences (all) | 9 / 99 (9.09%) 15 | 6 / 37 (16.22%) 7 | 20 / 99 (20.20%) 31 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 3 / 37 (8.11%) 4 | 10 / 99 (10.10%) 12 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 5 / 37 (13.51%) 5 | 9 / 99 (9.09%) 12 |
| Anal inflammation subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 37 (0.00%) 0 | 2 / 99 (2.02%) 2 |
| Constipation | | | |

| | | | |
|---|----------------|-----------------|------------------|
| subjects affected / exposed | 3 / 99 (3.03%) | 3 / 37 (8.11%) | 7 / 99 (7.07%) |
| occurrences (all) | 3 | 3 | 7 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 5 / 37 (13.51%) | 12 / 99 (12.12%) |
| occurrences (all) | 0 | 7 | 15 |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 99 (7.07%) | 3 / 37 (8.11%) | 12 / 99 (12.12%) |
| occurrences (all) | 7 | 5 | 19 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 2 / 37 (5.41%) | 5 / 99 (5.05%) |
| occurrences (all) | 2 | 2 | 6 |
| Mouth ulceration | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 3 / 37 (8.11%) | 8 / 99 (8.08%) |
| occurrences (all) | 2 | 3 | 8 |
| Nausea | | | |
| subjects affected / exposed | 6 / 99 (6.06%) | 3 / 37 (8.11%) | 10 / 99 (10.10%) |
| occurrences (all) | 8 | 3 | 13 |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 1 / 37 (2.70%) | 5 / 99 (5.05%) |
| occurrences (all) | 3 | 1 | 6 |
| Toothache | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 3 / 37 (8.11%) | 3 / 99 (3.03%) |
| occurrences (all) | 1 | 3 | 4 |
| Vomiting | | | |
| subjects affected / exposed | 6 / 99 (6.06%) | 3 / 37 (8.11%) | 13 / 99 (13.13%) |
| occurrences (all) | 7 | 3 | 20 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 3 / 37 (8.11%) | 8 / 99 (8.08%) |
| occurrences (all) | 5 | 3 | 13 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 2 / 37 (5.41%) | 8 / 99 (8.08%) |
| occurrences (all) | 5 | 2 | 9 |
| Rhinorrhoea | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 1 / 37 (2.70%) 1 | 3 / 99 (3.03%) 3 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 1 / 37 (2.70%) | 5 / 99 (5.05%) |
| occurrences (all) | 3 | 1 | 5 |
| Rash | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 3 / 37 (8.11%) | 5 / 99 (5.05%) |
| occurrences (all) | 2 | 6 | 8 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 99 (6.06%) | 4 / 37 (10.81%) | 12 / 99 (12.12%) |
| occurrences (all) | 7 | 4 | 13 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 2 / 37 (5.41%) | 2 / 99 (2.02%) |
| occurrences (all) | 0 | 2 | 2 |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 37 (5.41%) | 4 / 99 (4.04%) |
| occurrences (all) | 1 | 2 | 4 |
| Influenza | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 3 / 37 (8.11%) | 6 / 99 (6.06%) |
| occurrences (all) | 1 | 3 | 7 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 1 / 37 (2.70%) | 8 / 99 (8.08%) |
| occurrences (all) | 5 | 1 | 8 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 2 / 37 (5.41%) | 3 / 99 (3.03%) |
| occurrences (all) | 1 | 2 | 3 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 3 / 37 (8.11%) | 5 / 99 (5.05%) |
| occurrences (all) | 2 | 3 | 6 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 8 / 37 (21.62%) | 10 / 99 (10.10%) |
| occurrences (all) | 0 | 9 | 11 |
| Urinary tract infection | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 99 (0.00%) 0 | 0 / 37 (0.00%) 0 | 2 / 99 (2.02%) 2 |
| Viral infection subjects affected / exposed occurrences (all) | 2 / 99 (2.02%) 3 | 4 / 37 (10.81%) 4 | 9 / 99 (9.09%) 12 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 4 / 99 (4.04%) 4 | 3 / 37 (8.11%) 3 | 8 / 99 (8.08%) 8 |

| | | | |
|---|-----------------------|--|--|
| Non-serious adverse events | Maintenance High-Dose | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 27 / 35 (77.14%) | | |
| Investigations C-reactive protein increased subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 3 | | |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Ligament sprain subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 35 (8.57%) 4 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Injection site pain | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 6 / 35 (17.14%) | | |
| occurrences (all) | 36 | | |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 35 (25.71%) | | |
| occurrences (all) | 9 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 35 (11.43%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 3 | | |
| Anal inflammation | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences (all) | 1 | | |
| Crohn's disease | | | |
| subjects affected / exposed | 7 / 35 (20.00%) | | |
| occurrences (all) | 8 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | | |
| occurrences (all) | 7 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | | |
| occurrences (all) | 3 | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|-----------------------|--|--|
| Toothache subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 35 (17.14%) 10 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 5 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 | | |
| Rash subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| Infections and infestations Ear infection subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 1 | | |
| Influenza | | | |

| | | | |
|------------------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 3 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | | |
| occurrences (all) | 2 | | |
| Viral infection | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | | |
| occurrences (all) | 5 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 14 April 2009 | <p>No subjects had been enrolled in the study at the time of this amendment. This amendment:</p> <ul style="list-style-type: none">- Identified a new Sponsor Clinical Program Director and Clinical Research Physician- Corrected an inconsistency in definition of positive and negative purified Protein derivative (PPD) tests- Reduced the number of blood draws by consolidating laboratory tests and decreasing the number of PCDAI assessments- Required North American site to use the PPD test; Rest of World sites had the option of using the QuantiFERON®-TB GOLD (QFT-GOLD) if the PPD test was not available.- Generalized location of study sites- Removed C-reactive protein (CRP) from the standard clinical chemistry laboratory battery- Corrected an inconsistency in timing of chest x-ray- Changed the method and timing of the wrist x-ray used to calculate bone age- Removed the "up to the age of 14 years" restriction on the Work Productivity and Activity Impairment Questionnaire for CD (WPAI:CD)- Specified the WPAI:CD assessments obtained during reinduction- Clarified administration of WPAI:CD for children and WPAI:CD for working individuals- Revised the wording of some WPAI:CD questions and made minor format changes- Corrected definition of scores for height velocity on PCDAI- Clarified rationale for calculating the PCDAI- Changed "rescue medication" to "rescue therapy" throughout |
| 20 October 2009 | <p>At the time of this amendment, 4 subjects had been enrolled in the study. This amendment:</p> <ul style="list-style-type: none">- Updated fax number for UCB study physician- Specified the assessments used to determine the effect of treatment on the subject's CD (exploratory variable)- Added a provision to do the PK assessments on the 10 subjects who completed the Induction Period in 2 stages depending on rate of completion of the Induction Period in each age group- Modified inclusion criteria for duration of CD diagnosis (Inclusion #2), use of parenteral corticosteroids prior to Screening (Inclusion #8 and Exclusion #12), use of antibiotics (Inclusion #8), and exclusion criteria for prior use of anti-TNFα agents (Exclusion #9) to better correspond with clinical practice- Clarified Exclusion criteria #1 (regarding draining fistula) and #16 (regarding negative test results for immunoglobulin G (IgG) against Varicella zoster)- Clarified hormonal contraceptives, added duration of contraceptive use in after discontinuation of study treatment to reflect updates to company core data sheet, and reconciled an inconsistency in wording between text in the protocol summary section and Section 9.2 (Exclusion #26) |

| | |
|-----------------|---|
| 20 October 2009 | <ul style="list-style-type: none"> - Added Exclusion criterion #28 dealing with hypersensitivity or intolerance to CZP or polyethylene glycol (PEG) - Added visit windows to accommodate occasional scheduling difficulties with the understanding that study treatment cannot exceed a total of 60 weeks - Deleted the Week 13 visit (PK and immunologic blood sampling) to reduce the number of study visits - Updated number of clinical studies conducted and changed reference to "current" Investigator Brochure rather than specifying the version - Specified the corticosteroid dose that would be considered rescue therapy - Added a wrist x-ray at Week 60 in addition to Week 0 to assess growth over the course of treatment - Incorporated previous administrative amendment regarding timing of vital signs in relationship to dosing - Expanded use of QFT-Gold to North American sites (all sites can use either PPD or QFT-Gold) to facilitate TB testing at the sites - Corrected an error in location of TB questionnaire - Corrected an inconsistency in laboratory values used to calculate the Week 0 PCDAI score - Updated the entire AE section to reflect current standard operating procedures and template language - Added statistical analyses of Tanner stage |
|-----------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|---|--------------|
| 14 June 2011 | Enrollment was temporarily suspended on 14-Jun-2011, in agreement with the study's DSMB recommendation, due to a higher than expected number of premature withdrawals. Enrollment was permanently terminated in Apr2012 following discussion with the Food and Drug Administration (FDA). | - |

Notes:

Limitations and caveats

None reported