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 ≥ 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 ≥ 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 Low-Dose

Arm 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

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 ≥ 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	

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	± 2.67	± 2.41	± 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	46.5	45.67	50.35
standard deviation	± 12.565	± 14.638	± 18.569
Height			
Units: centimeter			
arithmetic mean	157.46	155.32	157.22
standard deviation	± 13.841	± 13.589	± 13.32
Body Mass Index (BMI)			
Units: kilogram per square meter			
arithmetic mean	18.39	18.51	19.79
standard deviation	± 2.504	± 3.531	± 4.897
Body Surface Area (BSA)			
Units: square meter			
arithmetic mean	1.42	1.39	1.47
standard deviation	± 0.25	± 0.272	± 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 paticipants				
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	2 / 99 (2.02%)	2 / 37 (5.41%)	4 / 99 (4.04%)
occurrences (all)	2	2	7
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 99 (0.00%)	2 / 37 (5.41%)	2 / 99 (2.02%)
occurrences (all)	0	2	2
Ligament sprain			
subjects affected / exposed	0 / 99 (0.00%)	2 / 37 (5.41%)	2 / 99 (2.02%)
occurrences (all)	0	2	2
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 99 (9.09%)	4 / 37 (10.81%)	12 / 99 (12.12%)
occurrences (all)	12	10	26
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 99 (3.03%)	3 / 37 (8.11%)	6 / 99 (6.06%)
occurrences (all)	3	4	7
Injection site pain			
subjects affected / exposed	22 / 99 (22.22%)	4 / 37 (10.81%)	22 / 99 (22.22%)
occurrences (all)	55	17	108
Pyrexia			
subjects affected / exposed	9 / 99 (9.09%)	6 / 37 (16.22%)	20 / 99 (20.20%)
occurrences (all)	15	7	31
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 99 (4.04%)	3 / 37 (8.11%)	10 / 99 (10.10%)
occurrences (all)	4	4	12
Abdominal pain upper			
subjects affected / exposed	4 / 99 (4.04%)	5 / 37 (13.51%)	9 / 99 (9.09%)
occurrences (all)	4	5	12
Anal inflammation			
subjects affected / exposed	0 / 99 (0.00%)	0 / 37 (0.00%)	2 / 99 (2.02%)
occurrences (all)	0	0	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	0 / 99 (0.00%)	1 / 37 (2.70%)	3 / 99 (3.03%)
occurrences (all)	0	1	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	0 / 99 (0.00%)	0 / 37 (0.00%)	2 / 99 (2.02%)
occurrences (all)	0	0	2
Viral infection			
subjects affected / exposed	2 / 99 (2.02%)	4 / 37 (10.81%)	9 / 99 (9.09%)
occurrences (all)	3	4	12
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 99 (4.04%)	3 / 37 (8.11%)	8 / 99 (8.08%)
occurrences (all)	4	3	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	2 / 35 (5.71%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	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	0 / 35 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	5		
Oropharyngeal pain			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	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	No subjects had been enrolled in the study at the time of this amendment. This amendment: - 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	At the time of this amendment, 4 subjects had been enrolled in the study. This amendment: - 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	- 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