Clinical trial results:
A Phase II, multi-center, double-blind, placebo-controlled, parallel-group, dose-response study to assess the safety and efficacy of CDP870/Certolizumab pegol, dosed subcutaneously in patients with active crohn's disease

Summary

EudraCT number	2014-004399-42
Trial protocol	Outside EU/EEA
Global end of trial date	08 November 2007

Results information

Result version number	v1
This version publication date	30 June 2016
First version publication date	11 June 2015

Trial information

Trial identification

Sponsor protocol code	C87037

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00291668
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Japan Co., Ltd
Sponsor organisation address	Shinjuku-ku, Tokyo, Japan, 160-0023
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	26 August 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to estimate the dose response in subjects with active Crohn's Disease (CD), and to evaluate the efficacy of certolizumab pegol in these subjects.

Protection of trial subjects:

Not applicable

Background therapy:

Steroids, immunosuppressants, antibacterial agents, 5-ASA derivatives, antidiarrheal drugs, topical ano-rectal treatments, and laxative drugs/enemas were allowed concomitantly with no change in dosage and administration from the start of the observation period to Week 6.

Evidence for comparator:

Not applicable

Actual start date of recruitment	02 March 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	9 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 94
Worldwide total number of subjects	94
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)	0
Adolescents (12-17 years)	6
Adults (18-64 years)	88

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study started to enroll subjects in March 2006.

Pre-assignment

Screening details:

20 Centers in Japan screened a total of 128 subjects of which 94 subjects were randomized.
Participant Flow refers to the Safety Population, including all randomized subjects who received at least one dose of study medication (Placebo or Certolizumab Pegol).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received two subcutaneous (sc) injections of Placebo on Weeks 0 (first dose), 2 and 4.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received two subcutaneous (sc) injections of Placebo on Weeks 0 (first dose), 2 and 4.

Arm title	Certolizumab pegol 200 mg

Arm description:

Subjects received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.

Arm type	Experimental
Investigational medicinal product name	Certolizumab Pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects in the CZP 200 mg arm received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.
Subjects in the CZP 400 mg arm received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.

Arm title	Certolizumab pegol 400 mg

Arm description:

Subjects received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.

Arm type	Experimental

Investigational medicinal product name	Certolizumab Pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects in the CZP 200 mg arm received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.
Subjects in the CZP 400 mg arm received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.

Number of subjects in period 1	Placebo	Certolizumab pegol 200 mg	Certolizumab pegol 400 mg
Started	32	30	32
Completed	28	29	31
Not completed	4	1	1
SAE, non-fatal + AE, non-serious, non-fatal	1	-	-
AE, non-serious, non-fatal	1	-	-
SAE, non-fatal	1	1	1
Lack of efficacy	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received two subcutaneous (sc) injections of Placebo on Weeks 0 (first dose), 2 and 4.	
Reporting group title	Certolizumab pegol 200 mg
Reporting group description:	
Subjects received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.	
Reporting group title	Certolizumab pegol 400 mg
Reporting group description:	
Subjects received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.	

Reporting group values	Placebo	Certolizumab pegol 200 mg	Certolizumab pegol 400 mg
Number of subjects	32	30	32
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	30.6	32.7	31.4
standard deviation	± 8.16	± 9.34	± 8.27
Gender Categorical Units: Subjects			
Male	26	22	25
Female	6	8	7
Age , Customized Units: Subjects			
16-29 years	14	11	12
30-39 years	15	12	15
40-64 years	3	7	5

Reporting group values	Total		
Number of subjects	94		
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Male	73		
Female	21		

Age , Customized Units: Subjects			
16-29 years	37		
30-39 years	42		
40-64 years	15		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received two subcutaneous (sc) injections of Placebo on Weeks 0 (first dose), 2 and 4.

Reporting group title	Certolizumab pegol 200 mg

Reporting group description:

Subjects received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.

Reporting group title	Certolizumab pegol 400 mg

Reporting group description:

Subjects received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.

Subject analysis set title	Full Analysis Set (Placebo treated subjects)
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as the subjects who were randomized and allocated to study medication, but excluded the following subjects as determined by data review prior to unblinding:
- Subjects with Good Clinical Practice (GCP) violations
- Subjects who were not diagnosed (definitely) with Crohn’s Disease
- Subjects who received no dose of study medication
- Subjects with no data after randomization

Subject analysis set title	Full Analysis Set (CZP 200 mg treated subjects)
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as the subjects who were randomized and allocated to study medication, but excluded the following subjects as determined by data review prior to unblinding:
- Subjects with Good Clinical Practice (GCP) violations
- Subjects who were not diagnosed (definitely) with Crohn’s Disease
- Subjects who received no dose of study medication
- Subjects with no data after randomization

Subject analysis set title	Full Analysis Set (CZP 400 mg treated subjects)
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as the subjects who were randomized and allocated to study medication, but excluded the following subjects as determined by data review prior to unblinding:
- Subjects with Good Clinical Practice (GCP) violations
- Subjects who were not diagnosed (definitely) with Crohn’s Disease
- Subjects who received no dose of study medication
- Subjects with no data after randomization

Primary: Crohn’s Disease Activity Index (CDAI) response (clinical response or remission) at Week 6

End point title	Crohn’s Disease Activity Index (CDAI) response (clinical response or remission) at Week 6[1]

End point description:

Percentage of subjects in clinical response at Week 6 or clinical remission at Week 6 based on CDAI score. Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 6) – (CDAI score at Week 0). Remission is defined as a CDAI score of ≤ 150 points.

End point type	Primary

End point timeframe:

Week 6

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	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	25 (10 to 40)	43.3 (25.6 to 61.1)	48.4 (30.8 to 66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Crohn’s Disease Activity Index (CDAI) score at Week 2

End point title	Crohn’s Disease Activity Index (CDAI) score at Week 2

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	29	31	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	255.9 (± 68.02)	214.2 (± 83.51)	224.9 (± 85.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Crohn’s Disease Activity Index (CDAI) score at Week 4

End point title	Crohn’s Disease Activity Index (CDAI) score at Week 4

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	243.1 (± 68.57)	199.7 (± 91.25)	204.6 (± 75.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Crohn’s Disease Activity Index (CDAI) score at Week 6

End point title	Crohn’s Disease Activity Index (CDAI) score at Week 6

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	232.4 (± 89.28)	211 (± 99.91)	198.1 (± 87.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve CDAI response at Week 2

End point title	Percentage of subjects who achieve CDAI response at Week 2

End point description:

CDAI Response at Week 2 is defined as clinical response at Week 2 or remission at Week 2. Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 2) – (CDAI score at Week 0). Remission is defined as a CDAI score of ≤ 150 points.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	15.6 (3 to 28.2)	40 (22.5 to 57.5)	32.3 (15.8 to 48.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve CDAI response at Week 4

End point title	Percentage of subjects who achieve CDAI response at Week 4

End point description:

CDAI Response at Week 4 is defined as clinical response at Week 4 or remission at Week 4. Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 4) – (CDAI score at Week 0). Remission is defined as a CDAI score of ≤ 150 points.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	21.9 (7.6 to 36.2)	46.7 (28.8 to 64.5)	38.7 (21.6 to 55.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 2

End point title	Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 2

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	28.1 (12.5 to 43.7)	46.7 (28.8 to 64.5)	45.2 (27.6 to 62.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 4

End point title	Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 4

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's

Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	25 (10 to 40)	56.7 (38.9 to 74.4)	54.8 (37.3 to 72.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 6

End point title	Percentage of subjects who achieve a reduction in CDAI scores of at least 70 points at Week 6

End point description:

The Crohn's Disease Activity Index (CDAI) is used to quantify the symptoms of subjects with Crohn's Disease. A score of 150 or below indicates disease remission and a score above 450 indicates extremely severe disease. A decrease in CDAI over time indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	43.8 (26.6 to 60.9)	53.3 (35.5 to 71.2)	61.3 (44.1 to 78.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve remission (CDAI <= 150) at Week 2

End point title	Percentage of subjects who achieve remission (CDAI <= 150) at Week 2

End point description:

Remission at Week 2 is defined as a CDAI score <= 150 points at Week 2.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	3.1 (0 to 9.2)	20 (5.7 to 34.3)	16.1 (3.2 to 29.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve remission (CDAI <= 150) at Week 4

End point title	Percentage of subjects who achieve remission (CDAI <= 150) at Week 4

End point description:

Remission at Week 4 is defined as a CDAI score <= 150 points at Week 4.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	6.3 (0 to 14.6)	26.7 (10.8 to 42.5)	22.6 (7.9 to 37.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve remission (CDAI <= 150) at Week 6

End point title	Percentage of subjects who achieve remission (CDAI <= 150) at Week 6

End point description:

Remission at Week 6 is defined as a CDAI score <= 150 points at Week 6.

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	15.6 (3 to 28.2)	26.7 (10.8 to 42.5)	32.3 (15.8 to 48.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 2

End point title	Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 2

End point description:

Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 2) – (CDAI score at Week 0).

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	15.6 (3 to 28.2)	36.7 (19.4 to 53.9)	29 (13.1 to 45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 4

End point title	Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 4

End point description:

Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 4) – (CDAI score at Week 0).

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	18.8 (5.2 to 32.3)	36.7 (19.4 to 53.9)	32.3 (15.8 to 48.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 6

End point title	Percentage of subjects who achieve clinical response (reduction in CDAI scores of at least 100 points) at Week 6

End point description:

Clinical response is defined as at least a 100-point decrease from the Week 0 CDAI score, where change = (CDAI score at Week 6) – (CDAI score at Week 0).

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects (95 % CI)	21.9 (7.6 to 36.2)	36.7 (19.4 to 53.9)	41.9 (24.6 to 59.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 2

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 2

End point description:

The IBDQ global score is calculated as the sum of the responses (each ranging from 1 to 7) to all 32 questions on the IBDQ and can therefore range from 32 to 224. A higher score indicates a better quality of life.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	29	31	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	171.3 (± 22.45)	166.1 (± 22.14)	169.7 (± 23.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 4

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 4

End point description:

The IBDQ global score is calculated as the sum of the responses (each ranging from 1 to 7) to all 32 questions on the IBDQ and can therefore range from 32 to 224. A higher score indicates a better quality of life.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	172.6 (± 24.04)	169.4 (± 21.75)	170.3 (± 23.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 6

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) global score at Week 6

End point description:

The IBDQ global score is calculated as the sum of the responses (each ranging from 1 to 7) to all 32 questions on the IBDQ and can therefore range from 32 to 224. A higher score indicates a better quality of life.

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: units on a scale				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	173.1 (± 25.49)	165.6 (± 23.25)	170.8 (± 24.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 2

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 2

End point description:

The total IBDQ score consists of 32 questions, each ranging from 1 to 7, with higher scores indicating a better quality of life.
There are 4 IBDQ Domain Scores:
- Bowel Symptoms Domain Score, ranging from 10 to 70 (10 questions ranging from 1 to 7)
- Systemic Symptoms Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)
- Emotional Function Domain Score, ranging from 12 to 84 (12 questions ranging from 1 to 7)
- Social Function Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: units on a scale				
arithmetic mean (standard deviation)				
Bowel Symptoms Domain Score (n=29, 29, 31)	54.4 (± 7.17)	53.4 (± 8.18)	54.7 (± 8.77)	
Systemic Symptoms Domain Score (n=29, 29, 31)	22.4 (± 5.01)	22.4 (± 5.17)	22.7 (± 4.51)	
Emotional Function Domain Score (n=29, 29, 31)	65.3 (± 8.91)	62.3 (± 9.54)	63.3 (± 8.53)	
Social Function Domain Score (n=28, 29, 31)	29.4 (± 5.64)	28 (± 4.33)	29 (± 5.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 4

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 4

End point description:

The total IBDQ score consists of 32 questions, each ranging from 1 to 7, with higher scores indicating a better quality of life.
There are 4 IBDQ Domain Scores:
- Bowel Symptoms Domain Score, ranging from 10 to 70 (10 questions ranging from 1 to 7)
- Systemic Symptoms Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)
- Emotional Function Domain Score, ranging from 12 to 84 (12 questions ranging from 1 to 7)
- Social Function Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: units on a scale				
arithmetic mean (standard deviation)				
Bowel Symptoms Domain Score (n=28, 27, 30)	55.4 (± 7.22)	54 (± 9)	55.5 (± 8.04)	
Systemic Symptoms Domain Score (n=28, 27, 30)	23.3 (± 5.49)	23.4 (± 4.21)	22.9 (± 4.44)	
Emotional Function Domain Score (n=28, 27, 30)	65.3 (± 8.85)	63.1 (± 8.9)	63.2 (± 9.55)	
Social Function Domain Score (n=27, 27, 30)	28.8 (± 6.73)	28.9 (± 4.82)	28.7 (± 5.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 6

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) domain scores at Week 6

End point description:

The total IBDQ score consists of 32 questions, each ranging from 1 to 7, with higher scores indicating a better quality of life.
There are 4 IBDQ Domain Scores:
- Bowel Symptoms Domain Score, ranging from 10 to 70 (10 questions ranging from 1 to 7)
- Systemic Symptoms Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)
- Emotional Function Domain Score, ranging from 12 to 84 (12 questions ranging from 1 to 7)
- Social Function Domain Score, ranging from 5 to 35 (5 questions ranging from 1 to 7)

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	30	31	
Units: units on a scale				
arithmetic mean (standard deviation)				
Bowel Symptoms Domain Score (n=28, 27, 30)	55.4 (± 7.77)	51.8 (± 8.44)	55.8 (± 8.43)	
Systemic Symptoms Domain Score (n= 28, 27, 30)	23.3 (± 6.74)	22.4 (± 4.49)	23.4 (± 4.62)	
Emotional Function Domain Score (n= 28, 27, 30)	65.3 (± 8.76)	63.2 (± 9.45)	62.1 (± 10.43)	
Social Function Domain Score (n= 27, 27, 30)	29.2 (± 6.48)	28.1 (± 5.69)	29.5 (± 5.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) value at Week 2

End point title	C-reactive protein (CRP) value at Week 2

End point description:

CRP data for subjects receiving rescue medication were excluded.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	29	31	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	22.15 (15.43 to 31.8)	13.58 (9.45 to 19.52)	13.86 (9.11 to 21.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) value at Week 4

End point title	C-reactive protein (CRP) value at Week 4

End point description:

CRP data for subjects receiving rescue medication were excluded.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	23.47 (16.02 to 34.4)	12.87 (8.56 to 19.36)	12.02 (8.68 to 16.65)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) value at Week 6

End point title	C-reactive protein (CRP) value at Week 6

End point description:

CRP data for subjects receiving rescue medication were excluded.

End point type	Secondary

End point timeframe:

Week 6

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	23.32 (16.95 to 32.07)	15.1 (9.46 to 24.11)	12.62 (8.79 to 18.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) Ratio to Baseline at Week 2

End point title	C-reactive protein (CRP) Ratio to Baseline at Week 2

End point description:

CRP data for subjects receiving rescue medication were excluded.

End point type	Secondary

End point timeframe:

Week 2

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	29	31	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	0.85 (0.64 to 1.13)	0.58 (0.42 to 0.8)	0.5 (0.35 to 0.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) Ratio to Baseline at Week 4

End point title	C-reactive protein (CRP) Ratio to Baseline at Week 4

End point description:

CRP data for subjects receiving rescue medication were excluded.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	1.04 (0.83 to 1.31)	0.53 (0.37 to 0.76)	0.44 (0.32 to 0.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive protein (CRP) Ratio to Baseline at Week 6

End point title	C-reactive protein (CRP) Ratio to Baseline at Week 6
End point description:	
CRP data for subjects receiving rescue medication were excluded.	
End point type	Secondary
End point timeframe:	
Week 6	

End point values	Full Analysis Set (Placebo treated subjects)	Full Analysis Set (CZP 200 mg treated subjects)	Full Analysis Set (CZP 400 mg treated subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	27	30	
Units: mg/L				
geometric mean (confidence interval 95%)				
Geometric Mean (95% CI)	1.03 (0.85 to 1.25)	0.63 (0.4 to 0.98)	0.46 (0.32 to 0.66)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events were collected from the time of signing the informed consent through the last Observation (up to 28 weeks).	
Adverse event reporting additional description:	
Adverse Events refer to the Safety Population, including all randomized subjects who received at least one dose of study medication (Placebo or Certolizumab Pegol).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received two subcutaneous (sc) injections of Placebo on Weeks 0 (first dose), 2 and 4.	
Reporting group title	Certolizumab pegol 400 mg
Reporting group description:	
Subjects received two subcutaneous (sc) injections of 200 mg CZP on Weeks 0 (first dose), 2 and 4.	
Reporting group title	Certolizumab pegol 200 mg
Reporting group description:	
Subjects received one subcutaneous (sc) injection of 200 mg CZP and one injection of Placebo to maintain the study blind on Weeks 0 (first dose), 2 and 4.	

Serious adverse events	Placebo	Certolizumab pegol 400 mg	Certolizumab pegol 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 32 (9.38%)	3 / 32 (9.38%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Crohn's disease			
subjects affected / exposed	3 / 32 (9.38%)	0 / 32 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Certolizumab pegol 400 mg	Certolizumab pegol 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 32 (50.00%)	14 / 32 (43.75%)	11 / 30 (36.67%)
Investigations			

White blood cell count decreased			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	2	1	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	2 / 30 (6.67%)
occurrences (all)	1	2	3
Vomiting			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	3
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Pharynx discomfort			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Comedone			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	10 / 32 (31.25%) 11	7 / 32 (21.88%) 9	7 / 30 (23.33%) 8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported