Clinical trial results:
A Phase IIIb, Multinational, Open-label, follow-on Trial to C87085 Designed to Assess the Long-term Safety of Certolizumab Pegol, a Pegylated Fab' Fragment of a Humanized Anti-TNF-alpha Monoclonal Antibody, Administered at Weeks 0, 2 and 4, and Then Every 4 Weeks Thereafter, in Subjects With Moderately to Severely Active Crohn's Disease Who Have Participated in Study C87085

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

Summary

EudraCT number	2007-002716-26
Trial protocol	BE FI HU LV EE IT CZ AT
Global end of trial date	22 December 2014

Results information

Result version number	v1 (current)
This version publication date	29 January 2016
First version publication date	29 January 2016

Trial information

Trial identification

Sponsor protocol code	C87088

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00552344
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES GmbH
Sponsor organisation address	Alfred-Nobel-Str. 10, Monheim, Germany, 40789
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical study was to assess the safety of long-term therapy with Certolizumab Pegol (CZP) in those subjects who participated in C87085.

Protection of trial subjects:

No specific additional measurements to minimise pain and distress were required, the safety of the subjects was closely followed as usual.

Background therapy:

Background therapy was not required, but it was allowed if subjects entered the study on stable dose of e.g. immunosuppressants, corticosteroids, 5-ASA analogues (see inclusion criteria of feeder study C87085) and kept this throughout the study.

Evidence for comparator:

Not applicable

Actual start date of recruitment	19 May 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 60
Country: Number of subjects enrolled	United States: 77
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Czech Republic: 20
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Hungary: 47
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Latvia: 7
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Ukraine: 19
Country: Number of subjects enrolled	Australia: 17

Country: Number of subjects enrolled	Brazil: 25
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	New Zealand: 19
Worldwide total number of subjects	402
EEA total number of subjects	153

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	393
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in May 2008 and concluded in Dec 2014.
Participant Flow refers to the Safety Population including all enrolled subjects who received at least 1 open-label injection of study medication.

Pre-assignment

Screening details:

406 subjects were screened: 3 subjects were considered as screen failures and were not enrolled. 403 subjects entered the study from C87085. 1 subject was enrolled in this study, but did not receive any open-label study medication and was withdrawn from the study; this subject was, therefore, not included in any of the analyses.

Period 1

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

Arms

Arm title	Certolizumab Pegol

Arm description:

Certolizumab Pegol 200 mg/vial; 400 mg subcutaneously at Week 0, 2 and 4, thereafter 400 mg subcutaneously at every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Cimzia
Investigational medicinal product code	CDP870
Other name	CZP
Pharmaceutical forms	Solution for injection in pre-filled syringe, Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

• Active substance: Certolizumab Pegol
• Pharmaceutical form:first reconstituted, lyophilized powder formulation of CZP and after implementation of Amendment 2 (after 401 subjects were enrolled) prefilled syringe
• Concentration: 200 mg/ml
• Route of Administration: Subcutaneous use

Number of subjects in period 1	Certolizumab Pegol
Started	402
Completed	87
Not completed	315
Consent withdrawn by subject	48
SAE, fatal + AE, non-serious non-fatal	1
Loss of efficacy	75
AE, non-serious non-fatal	38
Other Reason	22
Lost to follow-up	8

SAE, non-fatal	6
Lack of efficacy	55
SAE, non-fatal + AE, non-serious non-fatal	62

Baseline characteristics

Reporting groups	
Reporting group title	Certolizumab Pegol
Reporting group description:	
Certolizumab Pegol 200 mg/vial; 400 mg subcutaneously at Week 0, 2 and 4, thereafter 400 mg subcutaneously at every 4 weeks.	

Reporting group values	Certolizumab Pegol	Total	
Number of subjects	402	402	
Age Categorical Units: Subjects			
18 - < 65 years	393	393	
65 - < 85 years	9	9	
>= 85 years	0	0	
Age Continuous Units: years			
arithmetic mean	37.3		
standard deviation	± 12.68	-	
Gender Categorical Units: Subjects			
Male	181	181	
Female	221	221	

End points

End points reporting groups

Reporting group title	Certolizumab Pegol

Reporting group description:

Certolizumab Pegol 200 mg/vial; 400 mg subcutaneously at Week 0, 2 and 4, thereafter 400 mg subcutaneously at every 4 weeks.

Subject analysis set title	Certolizumab Pegol (Intention-to-Treat)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Certolizumab Pegol 200 mg/vial; 400 mg subcutaneously at Week 0, 2 and 4, thereafter 400 mg subcutaneously at every 4 weeks.
The ITT Population includes all enrolled subjects irrespective of any protocol deviations who received at least 1 open-label injection of study treatment and who had at least 1 efficacy measurement after the first open-label injection.

Primary: Percentage of Subjects With at Least One Adverse Event (AE) During the Duration of the Study C87088 (up to 272 weeks)

End point title	Percentage of Subjects With at Least One Adverse Event (AE) During the Duration of the Study C87088 (up to 272 weeks)[1]

End point description:

An AE is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

End point type	Primary

End point timeframe:

From study start to the end of the Safety Follow-up Period (up to 272 weeks)

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 end point. Results were summarized in tables as descriptive statistics only.

End point values	Certolizumab Pegol			
Subject group type	Reporting group			
Number of subjects analysed	402			
Units: percentage of subjects				
number (not applicable)				
percentage of subjects	89.6			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least One Serious Adverse Event (SAE) During the Duration of the Study C87088 (up to 272 weeks)

End point title	Percentage of Subjects With at Least One Serious Adverse Event (SAE) During the Duration of the Study C87088 (up to 272 weeks)[2]

End point description:

An SAE is defined as any untoward medical occurrence that occurs at any dose which results in death, is life threatening, requires hospitalization, results in persistent/significant disability/incapacity, is an

infection that requires parenteral antibiotics, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Primary

End point timeframe:

From study start to the end of the Safety Follow-up Period (up to 272 weeks)

Notes:

[2] - 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 end point. Results were summarized in tables as descriptive statistics only.

End point values	Certolizumab Pegol			
Subject group type	Reporting group			
Number of subjects analysed	402			
Units: percentage of subjects				
number (not applicable)				
percentage of subjects	37.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Harvey Bradshaw Index (HBI) Remission (HBI ≤ 4) at Study Completion Visit (Week 262)

End point title	Percentage of Subjects Achieving Harvey Bradshaw Index (HBI) Remission (HBI ≤ 4) at Study Completion Visit (Week 262)

End point description:

HBI remission is defined as total HBI score of 4 points or less. HBI score consists of clinical parameters of general well-being (0 to 4), abdominal pain (0 to 3), number of liquid stools per day, abdominal mass (0 to 3), and complications (8 items, score 1 per item) lower scores indicating better well being. The first three parameters are scored for the previous day.

End point type	Secondary

End point timeframe:

Week 262

End point values	Certolizumab Pegol (Intention-to-Treat)			
Subject group type	Subject analysis set			
Number of subjects analysed	397			
Units: percentage of subjects				
number (confidence interval 95%)				
percentage of subjects (95 % CI)	11.6 (8.4 to 14.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Inflamatory Bowel Disease Questionnaire (IBDQ) Remission (IBDQ ≥ 170) at Study Completion Visit (Week 262)

End point title	Percentage of Subjects Achieving Inflamatory Bowel Disease Questionnaire (IBDQ) Remission (IBDQ ≥ 170) at Study Completion Visit (Week 262)

End point description:

IBDQ remission is defined as having a total IBDQ score of 170 points or greater. IBDQ score consists of 32 questions eaching having a score of 1 to 7. Overall scores range from 32 to 224.

End point type	Secondary

End point timeframe:

Week 262

End point values	Certolizumab Pegol (Intention-to-Treat)			
Subject group type	Subject analysis set			
Number of subjects analysed	397			
Units: percentage of subjects				
number (confidence interval 95%)				
percentage of subjects (95 % CI)	7.8 (5.2 to 10.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Certolizumab Pegol after 1 year (Week 52)

End point title	Plasma Concentration of Certolizumab Pegol after 1 year (Week 52)

End point description:

Plasma samples for determination of Certolizumab Pegol were taken prior to Certolizumab Pegol administration.

End point type	Secondary

End point timeframe:

Week 52

End point values	Certolizumab Pegol			
Subject group type	Reporting group			
Number of subjects analysed	402			
Units: µg/mL				
geometric mean (confidence interval 95%)				
geometric mean (95 % CI)	6.317 (5.407 to 7.381)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Positive Anti-CZP Anti-body Status at Any Time From Week 0 of the Feeder Study C87085 to the Study Completion Visit in C87088

End point title	Percentage of Subjects With Positive Anti-CZP Anti-body Status at Any Time From Week 0 of the Feeder Study C87085 to the Study Completion Visit in C87088

End point description:

Subjects are counted as antibody positive to Certolizumab Pegol if they have at least one positive result from Week 0 in the previous study C87085 [NCT00552058] to the Last Visit in this study. A positive result is defined as Anti-CZP antibody levels > 2.4 units/mL.

End point type	Secondary

End point timeframe:

From Week 0 of study C87085 [NCT00552058] to Study Completion Visit (Week 262) of C87088 (up to 268 weeks)

End point values	Certolizumab Pegol			
Subject group type	Reporting group			
Number of subjects analysed	402			
Units: percentage of subjects				
number (not applicable)				
percentage of subjects	10.2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events presented below where collected from the Final Visit in Feeder study C87085 (Week 0) over the whole study period until the Safety-Follow-Up Visit (up to 274 weeks).

Adverse event reporting additional description:

Adverse Events refer to the Safety Population including all enrolled subjects who received at least 1 open-label injection of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Certolizumab Pegol

Reporting group description:

Certolizumab Pegol 200 mg/vial; 400 mg subcutaneously at Week 0, 2 and 4, thereafter 400 mg subcutaneously at every 4 weeks.

Serious adverse events	Certolizumab Pegol		
Total subjects affected by serious adverse events			
subjects affected / exposed	149 / 402 (37.06%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal cancer			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteritis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypotension			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicose vein			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pregnancy				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pregnancy on contraceptive				
subjects affected / exposed	5 / 402 (1.24%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Incarcerated hernia				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mass				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Unevaluable event				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Social circumstances			
Physical assault			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social stay hospitalisation			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Victim of abuse			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Menstrual disorder			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic prolapse			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vaginal inflammation			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary artery thrombosis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary mass				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary vasculitis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Acute psychosis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	3 / 402 (0.75%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Depression suicidal				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				

Colonoscopy				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigation				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Abdominal wound dehiscence				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anastomotic haemorrhage				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Alcohol poisoning				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal anastomosis complication				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Joint injury			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural inflammation			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion-related acute lung injury			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Carpal tunnel syndrome			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Demyelination			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 402 (0.25%)		
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	3 / 402 (0.75%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Coagulopathy			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Iron deficiency anaemia			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal artery occlusion			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 402 (1.49%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Abdominal distension			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Anorectal disorder			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon dysplasia			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			

subjects affected / exposed	51 / 402 (12.69%)		
occurrences causally related to treatment / all	8 / 59		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocolonic fistula			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Enterocutaneous fistula			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Enterovesical fistula			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal inflammation			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal mucosal disorder			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileal stenosis				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ileal fistula				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal fistula				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	11 / 402 (2.74%)			
occurrences causally related to treatment / all	2 / 11			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal stenosis				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Large intestinal ulcer				

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Irritable bowel syndrome				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mechanical ileus				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal perforation				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal prolapse				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				

subjects affected / exposed	6 / 402 (1.49%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic necrosis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal and urinary disorders				
Calculus urinary				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Calculus ureteric				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage urinary tract				

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	5 / 402 (1.24%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Ureteric obstruction				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Goitre				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fistula				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Spinal osteoarthritis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tenosynovitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Abdominal sepsis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal wall abscess			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dengue fever				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear infection				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal viral infection				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis externa				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mastoiditis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psoas abscess				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subdiaphragmatic abscess			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	5 / 402 (1.24%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Certolizumab Pegol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	351 / 402 (87.31%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	28 / 402 (6.97%)		
occurrences (all)	30		
Nervous system disorders			
Headache			
subjects affected / exposed	45 / 402 (11.19%)		
occurrences (all)	58		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	34 / 402 (8.46%)		
occurrences (all)	45		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	54 / 402 (13.43%)		
occurrences (all)	106		
Influenza like illness			
subjects affected / exposed	23 / 402 (5.72%)		
occurrences (all)	40		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	127 / 402 (31.59%)		
occurrences (all)	191		
Diarrhoea			
subjects affected / exposed	61 / 402 (15.17%)		
occurrences (all)	93		
Abdominal pain			
subjects affected / exposed	75 / 402 (18.66%)		
occurrences (all)	122		
Nausea			

subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all)	46 / 402 (11.44%) 63 43 / 402 (10.70%) 60 32 / 402 (7.96%) 37 24 / 402 (5.97%) 28		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	 23 / 402 (5.72%) 27 39 / 402 (9.70%) 49		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 27 / 402 (6.72%) 39		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 57 / 402 (14.18%) 79 36 / 402 (8.96%) 40		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 63 / 402 (15.67%) 99 46 / 402 (11.44%) 88		

Influenza			
subjects affected / exposed	30 / 402 (7.46%)		
occurrences (all)	35		
Sinusitis			
subjects affected / exposed	29 / 402 (7.21%)		
occurrences (all)	48		
Urinary tract infection			
subjects affected / exposed	25 / 402 (6.22%)		
occurrences (all)	31		
Bronchitis			
subjects affected / exposed	21 / 402 (5.22%)		
occurrences (all)	32		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2008	Protocol Amendment 1, dated 31 Jul 2008, was implemented after 37 subjects were enrolled in the study. The protocol was amended: - To change the planned study period from a Treatment Period of 50 weeks (plus Safety Follow-up (SFU)) to 262 weeks (plus SFU) to allow for up to 5 years of treatment with Certolizumab Pegol (CZP). - To amend the inclusion criteria to allow enrollment of subjects only if they had completed the Treatment Period of C87085 prior to enrolling into C87088. - To correct typographical errors and to clarify further inconsistencies.
28 May 2010	Protocol Amendment 2, dated 28 May 2010, was implemented after 401 subjects were enrolled in the study. The protocol was amended: - To initiate implementation of the switch from administration of the reconstituted, lyophilized powder formulation of CZP to the bioequivalent, liquid formulation supplied in the prefilled syringe (PFS).To change the name and contact information for the Study Physician and Clinical Project Manager to reflect recent personnel changes at UCB. - To update the phone numbers for serious adverse event (SAE) reporting. - To update the List of Abbreviations to reflect the changes to the protocol. - To adapt recruitment numbers to reflect the actual recruitment status at the time of the amendment. - To correct information on autoantibody samples that were previously mistakenly labeled in the protocol as plasma samples but were actually serum samples. As per the laboratory manual used for this study, these samples were drawn and processed as serum samples since the beginning of the study. Due to an oversight, this information was not changed from “plasma” to “serum” samples in Protocol Amendment 1. - To revise the schedule of assessments to include instructions for switching subjects from CZP lyophilized powder to PFS, and to change “plasma”-autoantibodies to “serum”-autoantibodies. - To update the protocol with information on the clinical supply of CZP PFS (description, packaging, and labeling) to be used in the switch from the lyophilized formulation to PFS. - To update the protocol with details of the switch from the lyophilized powder formulation of CZP to the PFS. - To add updates and clarifications to the definitions, reporting procedures, and follow up for adverse events (AEs), pregnancies, and SAEs, and to add a subsection to the protocol on AEs of special interest. - To correct Financial Disclosure responsibilities to comply with UCB's current Standard Operating Procedures (SOPs). - To make administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported