C87059* / RPCE06G2013**, 2006-003870-88

CLINICAL STUDY REPORT SYNOPSIS

This synopsis is provided for informational purposes only and is not intended or recommended as a substitute for professional medical advice.

This synopsis may include approved and non-approved uses, formulations or treatment regimens. The results from a single study may not reflect the overall results for the specific product. Prescribing decisions should be made by healthcare professionals based on the approved labeling information for the specific product in the respective country.

Personal information has been removed to protect the privacy of patients and the individuals named in the synopsis.

Sponsor:

UCB Pharma SA
Allée de la Recherche 60
1070 Anderlecht (Brussels)
Belgium

Official study title:

A Phase IIIb multi-center, double-blind, placebo-controlled, randomized trial to examine the corticosteroid-sparing effect of certolizumab pegol in patients with moderate to severe Crohn's disease (COSPAR I)

* Sponsor´s study number

** Sponsor´s protocol code: Study has been registered on EudraCT under this protocol code

CLINICAL STUDY REPORT SYNOPSIS: C87059

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

Title of study: A Phase IIIb multi-center, double-blind, placebo-controlled, randomized trial to examine the corticosteroid-sparing effect of certolizumab pegol in patients with moderate to severe Crohn's disease (COSPAR I)

Investigator(s): This was a multicenter study; 62 investigators enrolled subjects in this study.

Study site(s): This was a multicenter study conducted at 110 centers in the [redacted] of which 62 sites enrolled subjects.

Publication(s) (reference[s]): none

Studied period: The total duration of study was a maximum of 54 weeks per subject. **First subject enrolled:** 01 Nov 2006 **Last subject completed:** 06 Jul 2009	**Phase of development:** Phase 3b

Objective(s): The primary objective of this study was to compare certolizumab pegol (CZP) 400mg and placebo treatments for the proportion of subjects who had been successfully withdrawn from prednisone or prednisolone according to the tapering schedule of the protocol and had remained off corticosteroids and were in disease remission (Crohn's Disease Activity Index [CDAI] ≤150 points) at Week 38 of treatment.

Methodology: This was a multicenter, parallel-group, randomized, placebo-controlled (38 weeks), double-blind, study of induction dosing (11 doses of CZP 400mg versus placebo given subcutaneously at Weeks 0, 2, 4, 8, 12, 16, 20, 24, 28, 32, and 36). Following assessment and confirmation of eligibility (up to a 6-week Run-In Period), subjects who presented with a flare of moderate to severe Crohn's disease (CD) (CDAI of ≥220 to ≤450 points), were not on maintenance corticosteroid treatment, had not received treatment with corticosteroids within the previous 1 month, and were candidates for corticosteroid treatment were randomized to CZP 400mg or placebo in a 1:1 ratio. There was a Safety Follow-Up Period of 10 weeks following the 38-week Double-Blind Treatment Period. Subjects who completed this study had the opportunity to continue into the open-label extension study (C87065).

Number of subjects (planned and analyzed): A total of 352 subjects (176 subjects per group) were planned to be enrolled in this study. Ultimately, 174 subjects were enrolled (87 subjects per group). Recruitment was stopped prior to reaching the planned sample size

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

of 352 subjects due to slower than expected enrollment.

Diagnosis and main criteria for inclusion: Subjects enrolled were males or females, 18 years or older who presented with a flare of moderate to severe CD (CDAI of ≥220 to ≤450), were not on maintenance corticosteroid treatment, had not received treatment with corticosteroids within the previous 1 month, and were candidates for corticosteroid treatment. Subjects could have been on immunosuppressant or 5- aminosalicylates (ASA) therapy if the dose had been stable for 8 weeks or 4 weeks, respectively.

Test product, dose(s) and mode of administration, batch number(s): Certolizumab pegol, an anti-tumour necrosis factor alpha (anti-TNFα) humanized antibody Fab' fragment–polyethylene glycol (PEG) conjugate, was provided as a solution for injection in 10mM sodium acetate buffer and 125mM sodium chloride, pH 4.7. It was supplied in 3mL vials with a fill of 1.4mL (for an extractable volume of 1mL corresponding to a dose of 200mg). CZP 400mg, was administered as 2 subcutaneous injections of 1mL at 2 distinct sites (lateral abdominal wall; upper, outer thigh; or upper arm) using separate syringes and needles at each injection site. Batch numbers: [redacted]

Duration of treatment: The treatment period was 38 weeks, which included a total of 11 injections of study medication administered at Weeks 0, 2, 4, 8, 12, 16, 20, 24, 28, 32, and 36.

Reference therapy, dose(s) and mode of administration, batch number(s): Placebo was a commercially available sodium chloride 0.9% (preservative free). Batch numbers: [redacted]

Criteria for evaluation:

Efficacy: The primary efficacy variable was the proportion of subjects who had been withdrawn from prednisone or prednisolone therapy according to the corticosteroid-tapering schedule and had remained off corticosteroids and were in disease remission (CDAI ≤150 points) at Week 38.

The secondary and exploratory efficacy variables were:

- Proportion of subjects with remission (CDAI ≤150 points) and off steroids at each visit
- Proportion of subjects with continuous remission (CDAI ≤150 points) and off steroids at each visit

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

- Cumulative proportion of subjects with relapse/treatment failure at each study visit after Week 0, with relapse/treatment failure defined as a CDAI>150 points and an increase in CDAI of ≥70 points vs Week 0
- Time to relapse/treatment failure
- Per-subject median weekly dose and cumulative dose of corticosteroids over the duration of the study, and change from Baseline in the median weekly dose
- CDAI scores at each visit and changes from Baseline
- Change from Baseline in the HRQOL as assessed by the IBDQ total score at Week 38
- Direct cost parameters: number of concomitant medications, healthcare provider consultations not foreseen by the protocol, medical procedures, emergency room visits, and hospitalizations

The safety variables were:

- Adverse events
- Laboratory evaluations
- Vital signs
- Weight
- Physical examinations
- Chest x-ray
- PPD skin test

Statistical methods: All randomized subjects who received at least 1 injection of study medication were included in the intention-to-treat (ITT) population. All randomized subjects who received at least 1 injection of study medication, excluding subjects who were not in remission (CDAI>150 points) at Visit 2 (Week 0), were included in the conditional ITT (CITT) population. The per-protocol (PP) population was defined as a subset of the ITT population, consisting of subjects who did not have any major protocol deviations as identified by a blinded review of the data and confirmed prior to database lock. Baseline was defined as the last non-missing value collected prior to the first injection of the randomized double-blind treatment. Summary statistics are provided for all efficacy, safety, and Baseline/demographic variables. Summary statistics consist of frequency tables for

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

categorical variables. For continuous variables, descriptive statistics (number of available observations, mean, median, standard deviation, minimum, maximum, and 25th and 75th percentiles) were tabulated. Data from individual study centers were not pooled or analyzed by individual study center.

At the time the recruitment was stopped the planned sample size was not reached. Therefore, the study was not adequately powered for formal statistical comparison. All analyses are considered to be exploratory.

The primary efficacy variable was the proportion of subjects who had been withdrawn from prednisone or prednisolone therapy according to the corticosteroid-tapering schedule and had remained off corticosteroids and were in disease remission (CDAI $\leq$150) at Week 38. This superiority study was to have been considered positive if the null hypothesis of no difference between the treatments (CZP 400mg vs placebo) for the primary efficacy variable was rejected in order to conclude CZP 400mg is superior to placebo. A logistic regression model was used to compare the treatment groups for the proportion of subjects who were in disease remission and off corticosteroids at Week 38, with factors for treatment, immunosuppressant use at study entry, prior infliximab use, and country as covariates in the model. The 95% confidence intervals (CIs) were calculated for the odds ratios. Withdrawal subjects were considered as failures at Week 38. The primary efficacy variable was analyzed using the ITT (primary) and CITT populations. If more than 15% of the ITT population was excluded from the PP population, the analysis was performed on the PP population. A sensitivity analysis was performed by calculating the remission rate off corticosteroids excluding subjects with a CDAI score missing or who withdrew before the assessment from the analysis population. A complementary analysis was performed using the last observation carried forward (LOCF) approach for the missing CDAI scores.

Secondary efficacy variables were analyzed using the ITT (excluding relapse/treatment failure and time to relapse) and CITT populations. Summary statistics are presented for continuous remission, as well as the chi-square test to compare the treatment groups at Weeks 16, 24, and 38. The cumulative proportion of subjects with relapse/treatment failure was summarized by treatment group for each visit after Week 0, and 95% CIs were calculated for the differences between the 2 treatment groups at Weeks 16, 24 and 38. The time to relapse was summarized by Kaplan-Meier plots. Median weekly and cumulative corticosteroid doses and CDAI score and change from Baseline in CDAI score are presented and summarized using descriptive statistics. Treatment difference for the mean change from Baseline of the IBDQ total score was assessed using an analysis of covariance (ANCOVA) model (Baseline IBDQ score and treatment group as covariate) at Weeks 16,

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

24, and at last visit on or before Week 38.

For the exploratory outcome research variables, summary statistics were provided for each direct cost parameter as well as information on the frequency distribution of the parameter (number of subjects by number of medical resources used) on the ITT and CITT populations, by period of onset and treatment group.

The primary efficacy variable of disease remission and the secondary efficacy variables of continuous remission and off corticosteroids, and treatment failure/relapses at Week 38 were also investigated in subgroup analyses by CRP status, immunosuppressant use at Screening, CD duration, history of resections, CDAI score, and time to remission during the Run-In Period. Comparisons of placebo and CDP870-treated groups were made using a logistic regression model to compare the treatment groups with factors for treatment, immunosuppressant use at study entry, prior infliximab use, and country as covariates in the model. The 95% CIs were calculated for the odds ratios. P-values were for information purposes only. Analyses were performed on the ITT and/or CITT populations.

Safety was monitored by adverse events, laboratory parameters, vital signs, presence of auto-antibodies, weight, physical examination and chest x-ray. Adverse events and laboratory data were presented separately for each study period and were summarized by treatment group.

Summary and conclusions:

Subject disposition: A total of 279 subjects were screened for the study and 174 subjects were randomized (87 subjects to CZP 400mg and 87 subjects to placebo). Of the randomized subjects, 28 subjects (32.2%) in the CZP 400mg group and 23 subjects (26.4%) in the placebo group completed the study. The most common reasons for early discontinuation were lack/loss of efficacy in both groups (37 subjects [42.5%] in the CZP 400mg group and 42 subjects [48.3%] in the placebo group), followed by AE (8 subjects [9.2%] in the CZP 400mg group and 12 subjects [13.8%] in the placebo group).

Efficacy results: The primary efficacy endpoint of this study (to compare CZP 400mg and placebo treatments for the proportion of subjects who had been successfully withdrawn from prednisone or prednisolone according to the tapering schedule of the protocol and had remained off corticosteroids and were in disease remission [CDAI ≤150 points] at Week 38 of treatment) did not meet statistical significance, although a numerically greater proportion of subjects were in disease remission (CDAI≤150 points) and off corticosteroids at Week 38 in the CZP 400mg group (26.4%) compared with the placebo group (21.8%; p=0.578). Secondary variables also did not show a statistically significant difference

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

between CZP 400mg treatment and placebo with regard to the proportion of subjects in disease remission at each study visit, continuous remission at study endpoint, or relapse/treatment failure at study endpoint. The proportion of subjects in disease remission, continuous remission, or with relapse/treatment failure were unaffected by CRP level at Screening and Baseline, use of immunosuppressant at Screening, CD duration, number of resections, or CDAI score at Baseline; whereas, CDAI score at Screening and time to remission affected these outcomes. Subjects with a CDAI score ≥ median at Screening treated with CZP 400mg had a higher occurrence of disease remission at Week 38 (p=0.028) and continuous remission at Week 38 (p=0.048) suggesting that subjects with more pronounced CD symptoms are more likely to respond to treatment; there was not a statistically significant difference between treatment groups observed for the cumulative proportion of subjects with relapse/treatment failure at Week 38. Subjects who achieved disease remission within ≥2 to <4 weeks during the Run-In Period treated with CZP 400mg had a higher occurrence of relapse/treatment failure compared with the placebo group (p=0.040). No statistically significant differences between treatment groups were observed for the proportion of subjects in disease remission or in continuous remission at Week 38 by time to remission during the Run-In Period.

There was no statistically significant difference between treatment groups in the secondary efficacy variables of corticosteroid use, CDAI scores, or HRQOL as assessed by the IBDQ scores. The majority of subjects in the CZP 400mg and placebo groups did not start any medications potentially affecting CD during the Double-Blind Treatment Period, including anti-TNFα (95.4% and 98.9%, respectively), immunosuppressants (75.9% and 87.4%, respectively), corticosteroids (50.6% and 59.8%, respectively), 5-ASA (77.0% and 80.5%, respectively), and antibiotics (64.4% and 63.2%, respectively).Low resource utilizations were observed during the Double-Blind Treatment period with the majority of the subjects having no emergency room visits, hospital stays, or medical procedures and 1 or fewer healthcare provider consultations. Similar findings were reported between the 2 treatment groups.

Caution must be taken when interpreting the p-values for the efficacy analyses as these tests are un-powered due to the reduced sample size.

Safety results: A total of 93.1% of subjects in the CZP 400mg group and 98.9% of subjects in the placebo group experienced at least 1 TEAE during the Double-Blind Treatment and Safety-Follow-Up Periods combined. Severe TEAEs were reported in 23% of subjects in both groups. In 50.6% of subjects in the CZP 400mg group and 44.8% of subjects in the placebo group, the TEAEs were described by the Investigator as related to

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

study medication (ie, possibly, probably, or highly probably related). Adverse events leading to permanent study medication discontinuation were reported in 8.0% of subjects in the CZP 400mg group and 13.8% of subjects in the placebo group. Serious adverse events were reported in 10.3% of subjects in the CZP 400mg group and 9.2% of subjects in the placebo group. One subject in the placebo group died due to an AE of acute respiratory and renal failure during the Safety Follow-Up Period that was considered to be unlikely related to study medication.

The majority of TEAEs in both groups (77% each) were mild or moderate in severity. The most commonly reported TEAEs (reported in ≥10% in either treatment group) that occurred at a higher incidence in the CZP 400mg group compared with the placebo group were vomiting (11.5% vs 5.7%), muscle spasms (10.3% vs 5.7%), and headache (21.8% vs 14.9%).

Most common adverse events reported during the DBT + SFU Periods

Preferred term	Placebo (N=87) n (%)	CZP 400mg (N=87) n (%)
Crohn's disease	44 (50.6)	35 (40.2)
Headache	13 (14.9)	19 (21.8)
Nasopharyngitis	13 (14.9)	12 (13.8)
Arthralgia	9 (10.3)	12 (13.8)
Vomiting	5 (5.7)	10 (11.5)
Nausea	8 (9.2)	9 (10.3)
Muscle spasms	5 (5.7)	9 (10.3)
Abdominal pain	11 (12.6)	8 (9.2)

CZP=certolizumab pegol; DBT=Double-Blind Treatment; SFU=Safety Follow-Up

Note: Events are listed by decreasing order of frequency in the CZP 400mg group.

The only treatment-emergent SAEs reported in more than 1 subject in either treatment group were exacerbation of CD (0 subjects in the CZP 400mg group vs 5 subjects [5.7%] in the placebo group) and non-cardiac chest pain (2 subjects [2.3%] in the CZP 400mg group vs 0 subjects in the placebo group). Musculokseletal and connective tissue disorders occurred more frequently in CZP 400mg-treated subjects compared with placebo-treated subjects, including arthralgia (13.8% vs 10.3%), muscle spasms (10.3% vs 5.7%), and

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

myalgia (4.6% vs 0). Two subjects reported malignancies during the Double-Blind Treatment Period that resulted in discontinuation from the study, 1 subject in the CZP 400mg group (basal cell carcinoma) and 1 subject in the placebo group (squamous cell carcinoma); neither event was considered to be an SAE. No TB infections were reported.

An AE was determined by the Investigator as an injection reaction and further categorized as: 1) an injection site reaction; 2) an acute systemic injection reaction; or 3) a delayed systemic injection reaction. As presented in the following table by the specific injection site reaction events, a higher proportion of subjects in the CZP 400mg group reported at least 1 injection site reaction (22 subjects [25.3%] with 38 events) compared with the placebo group (4 subjects [4.6%] with 5 events), the majority of which were considered to be related to study medication (21.8% in the CZP 400mg group and 3.4% in the placebo group).

	Placebo (N=87)	**CZP 400mg (N=87)**
Subjects with at least 1 injection site reaction, n (%)	**4 (4.6)**	**22 (25.3)**
Injection site reaction	1 (1.1)	5 (5.7)
Injection site discolouration	0	3 (3.4)
Injection site bruising	1 (1.1)	3 (3.4)
Injection site erythema	0	2 (2.3)
Injection site pain	0	2 (2.3)
Injection site swelling	0	2 (2.3)
Injection site irritation	1 (1.1)	1 (1.1)
Injection site pruritus	1 (1.1)	1 (1.1)
Injection site discomfort	0	1 (1.1)
Injection site rash	0	1 (1.1)
Injection site vesicles	0	1 (1.1)

Data source: Table 1.3.1:10 and Table 1.3.1:11

Few hypersensitivity-like events other than injection site reactions were observed. Acute systemic injection reactions were reported in 1 subject (1.1%) with 1 event in the CZP 400mg group (vasovagal syncope) and 3 subjects (3.4%) with 7 events in the placebo group (flushing [2 events], dry mouth, dysgeusia, hyperhidrosis, nausea, and rhinitis). Four subjects (4.6%) in the CZP 400mg group reported a total of 6 delayed systemic injection reactions (face edema, urticaria, arthralgia, rash, rash maculo-papular, and flushing)

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

compared with no such events in the placebo group. All acute and delayed systemic reactions were considered related to study medication by the Investigator with the exception of one acute systemic reaction event reported by a CZP 400mg-treated subject. Two subjects permanently discontinued study medication due to delayed systemic injection reactions. None of the injection reactions were considered severe or serious.

Transient changes in hematology and chemistry parameters considered to be clinically relevant were noted in a small number of subjects in both treatment groups. These findings were generally reported as TEAEs. No reports of leukopenia, neutropenia, thrombocytopenia, or pancytopenia were reported in this study. Markedly abnormal (Grade 3 or Grade 4) chemistry values were observed for 3 subjects (1 placebo subject and 2 CZP 400mg subjects) during the Double-Blind Treatment Period or Safety Follow-Up Period. One placebo-treated subject and 1 CZP 400mg-treated subject had a markedly abnormal low (Grade 3) value for potassium during the study, and 1 CZP 400mg-treated subject [redacted] had a markedly abnormal high (Grade 3) value for GGT during the Safety Follow-Up Period. No indications of hepatotoxicity were observed. No markedly abnormal hematology values were observed. No clinically relevant changes were noted in urinalysis examinations.

None of the small changes in SBP, DBP, heart rate, or weight were considered clinically meaningful, either within or between treatment groups.

Conclusions: The primary efficacy endpoint of this study (to compare CZP 400mg and placebo treatments for the proportion of subjects who had been successfully withdrawn from prednisone or prednisolone according to the tapering schedule of the protocol and had remained off corticosteroids and were in disease remission [CDAI≤150 points] at Week 38 of treatment) did not meet statistical significance. Secondary efficacy endpoints to support the primary analysis also did not meet statistical significance. Caution must be taken when interpreting the p-values for these analyses as these tests were un-powered due to the reduced sample size. The data from this study support the following conclusions:

- A numerically greater proportion of subjects were in disease remission (CDAI≤150 points) and off corticosteroids at Week 38 in the CZP 400mg group (26.4%) compared with the placebo group (21.8%) and at each study visit (with the exception of Weeks 2, 4, and 12).
- The proportion of subjects with continuous remission (CDAI≤150 points) and off corticosteroids was generally similar between treatment groups at Week 38 and all

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

visits.

- The cumulative proportions of subjects with relapse/treatment failure (defined as CDAI>150 points and an increase in CDAI≥70 points vs Week 0) were generally similar between the CZP 400mg and placebo groups at Week 38 and each study visit. Times to relapse/treatment failure were also similar between treatment groups.
- Corticosteroid use was similar between groups over the study period.
- CDAI scores at each study visit and changes from Baseline were variable; however, a general trend towards a decrease from baseline over time was observed in both the CZP 400mg and placebo groups. The mean CDAI score for both treatment groups was <150 points at each time point beyond Week 0.
- Meaningful improvement in IBDQ total score (defined as mean change of ≥16 points from Baseline) was not observed for either treatment group at Week 38. However, subjects treated with CZP 400mg indicated statistically significant improvement in emotional function compared with placebo-treated subjects (p=0.046).
- Resource use was generally similar between CZP 400mg-treated subjects and placebo subjects:
    - The majority of subjects in the CZP 400mg and placebo groups did not start any medications potentially affecting CD during the Double-Blind Treatment Period, including anti-TNFα (95.4% and 98.9%, respectively), immunosuppressants (75.9% and 87.4%, respectively), corticosteroids (50.6% and 59.8%), 5-ASA (77.0% and 80.5%, respectively), and antibiotics (64.4% and 63.2%, respectively).
    - A higher proportion of CZP 400mg-treated subjects were using multiple general concomitant medications (excluding medications potentially influencing CD) compared with placebo-treated subjects (at least 1 medication: 78.2% vs 65.5%).
    - Low resource utilizations were observed during the Double-Blind Treatment Period with the majority of subjects having no emergency room visits, hospital stays, or medical procedures, and having 1 or 0 unforeseen healthcare provider consultations. Similar findings were reported between the 2 treatment groups.

The results of subgroup analyses of subjects in disease remission and off corticosteroids at Week 38, in continuous remission and off corticosteroids at Week 38, or with relapse/treatment failure at Week 38 are summarized below. Caution must be taken when

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

interpreting the p-values for these analyses as these tests were un-powered due to the small number of subjects in each group at Week 38.

- The proportion of subjects in disease remission or in continuous disease remission were unaffected by CD duration, number of resections, or time to remission during the Run-In Period. Both disease remission and continuous remission were experienced by a numerically greater proportion of subjects in the CZP 400mg group compared with the placebo group for subjects with a CRP level <5mg/L at Screening and Baseline, using immunosuppressants at Screening, or a CDAI score ≥ median at Baseline.
  - A significantly greater proportion of subjects with a CDAI score ≥ median at Screening were in disease remission at Week 38 in the CZP 400mg group (25.6%) compared with the placebo group (8.3%; p=0.028) and in continuous remission at Week 38 in the CZP 400mg group (20.5%) compared with the placebo group (6.3%; p=0.048).
  - A significantly greater proportion of subjects with a CDAI score ≥ median at Screening were in continuous remission at Week 38 in the CZP 400mg group (20.5%) compared with the placebo group (6.3%; p=0.048).
- The proportion of subjects with relapse/treatment failure at Week 38 were unaffected by CD duration, number of resections, or CDAI score at Screening or Baseline. Relapse/treatment failure was experienced by a numerically smaller proportion of subjects in the CZP 400mg group with a CRP level <5mg/L at Screening and Baseline and a numerically greater proportion of subjects in the CZP 400mg group who were using immunosuppressants.
  - The cumulative proportion of subjects with relapse/treatment failure was significantly greater in the CZP 400mg group (65.6%) compared with the placebo group (43.3%) for subjects who achieved disease remission within ≥2 to <4 weeks during the Run-In Period (p=0.040).

Safety conclusions include the following:

- The mean duration of exposure to study medication was approximately 175 days for the CZP 400mg group and 162 days for the placebo group. Subjects in both the CZP 400mg and placebo groups received on average approximately 6 of the 11 planned doses of study medication. A total of 29.9% of subjects in the CZP 400mg group and 25.3% of subjects in the placebo group received 11 or more of the planned study medication doses.

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

- Overall, the incidence and pattern of AEs were similar between the CZP 400mg and placebo groups. The most commonly reported TEAE was exacerbation of CD, which was reported at a lower incidence in the CZP 400mg group (40.2%) compared with the placebo group (50.6%). Of the most common TEAEs (reported in ≥10% in either treatment group), vomiting (11.5% vs 5.7%), muscle spasms (10.3% vs 5.7%), and headache (21.8% vs 14.9%) were reported at a higher incidence in the CZP 400mg group compared with the placebo group.The majority of TEAEs in both groups (77% each) were mild or moderate in severity. The most common severe TEAEs reported during the combined Double-Blind Treatment and Safety Follow-Up Periods included exacerbation of CD (1.1% in the CZP 400mg group vs 13.8% in the placebo group), abdominal pain (4.6% vs 1.1%), headache (2.3% in both groups), and depression (2.3% vs 0).
- In nearly half of subjects in the CZP 400mg group (50.6%) and the placebo group (44.8%) TEAEs were described by the Investigator as related to study medication (ie, possibly, probably, or highly probably related). The most commonly reported drug-related TEAE was exacerbation of CD, which was reported at a lower incidence in the CZP 400mg group (4.6%) compared with the placebo group (16.1%). Of the most common drug-related TEAEs (reported in ≥5% in either treatment group), only injections site reaction was reported at a higher incidence in the CZP 400mg group compared with placebo (5.7% vs 1.1%).
- A similar proportion of subjects reported SAEs in the CZP 400mg group (10.3%) and the placebo group (9.2%). The only treatment-emergent SAEs reported in more than 1 subject in either treatment group were exacerbation of CD (0 subjects in the CZP 400mg group vs 5 subjects [5.7%] in the placebo group) and non-cardiac chest pain (2 subjects [2.3%] in the CZP 400mg group vs 0 subjects in the placebo group). One subject in the placebo treatment group [redacted] died during the Safety Follow-Up Period due to acute respiratory and renal failure, which the Investigator considered to be unlikely related to study medication.
- No malignancies were reported as SAEs. Two subjects discontinued from the study due to non-serious malignancies during the Double-Blind Treatment Period, 1 subject in the CZP 400mg group (basal cell carcinoma) and 1 subject in the placebo group (squamous cell carcinoma).
- Adverse events leading to permanent study medication discontinuation were reported in 8.0% of subjects in the CZP 400mg group and 13.8% of subjects in the placebo group.

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

The only TEAE leading to permanent study medication discontinuation in more than 1 subject in either treatment group was exacerbation of CD, all of which occurred in the placebo group (6 subjects [6.9%]). All other TEAEs leading to permanent study medication discontinuation were reported in only 1 subject in either treatment group.

- A higher proportion of subjects in the CZP 400mg group reported at least 1 injection site reaction (22 subjects [25.3%] with 38 events) compared with the placebo group (4 subjects [4.6%] with 5 events), the majority of which were considered to be related to study medication (21.8% and 3.4%, respectively). Few acute systemic injection reactions (1 subject [1.1%] CZP 400mg group and 3 subjects [3.4%] in the placebo group) and delayed systemic injection reactions (4 subjects (4.6%) in the CZP 400mg group) were reported in either treatment group. All acute and delayed systemic reactions were considered related to study medication by the Investigator with the exception of one acute systemic reaction event reported by a CZP-400 mg subject. Two subjects permanently discontinued study medication due to delayed systemic injection reactions (maculo-papular rash; rash and arthralgia). None of the injection reactions were considered severe or serious.
- Mean and median changes in hematology and chemistry parameters were generally small and not considered to be clinically relevant. Transient changes in hematology and chemistry parameters considered to be clinically relevant were noted in a small number of subjects in both treatment groups. Clinically relevant findings in post-Baseline hematology values during the Double-Blind Treatment Period were similar between the treatment groups (2 subjects each) and included elevated neutrophils (3 subjects), elevated leukocytes (2 subjects), decreased lymphocytes (2 subjects) and decreased hemoglobin (1 subjects). Clinically relevant findings in post-Baseline clinical chemistry values during the Double-Blind Treatment Period were observed in 4 CZP 400mg-treated subjects (elevated CRP [3 subjects]; and elevated ALT and AST [1 subject]) and 7 placebo-treated subjects (elevated ALT, AST, GGT, CRP, and creatinine [1 subject each]; and low potassium [2 subjects]). Markedly abnormal (Grade 3 or Grade 4) chemistry values during the Double-Blind Treatment Period or Safety Follow-Up Period were observed for 3 subjects: 1 placebo-treated subject and 1 CZP 400mg-treated subject with a low (Grade 3) value for potassium, and 1 CZP 400mg-treated subject [redacted] had a high (Grade 3) value for GGT during the Safety Follow-Up Period. No markedly abnormal hematology values were observed. Abnormal hematology and chemistry values were generally reported as TEAEs, none of which were severe. No clinically relevant changes were noted in urinalysis

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).

Name of company: UCB Pharma SA	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume:** Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

examinations.

- None of the small changes in SBP, DBP, heart rate, or weight were considered clinically meaningful, either within or between treatment groups. No TB infections were reported.

Report date: 14 Oct 2010

1: On EudraCT this study is registered under the following sponsor´s protcol code: RPCE06G2013. The sponsor´s study number is: C87059 (subsequently explanation added on 19th of May 2015).