C87040/ CDP 870-040, 2005-002141-39
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 S.A. – Pharma Sector
Chemin du Foriest
1420 Braine-l'Alleud
Belgium

Official study title:

Multicentre, dose response, randomized, double-blind, parallel, 3 arms, placebo-controlled clinical study to evaluate the efficacy and the safety of subcutaneous CDP870 (certolizumab pegol) at 2 different 12 weeks dose regimens (400 mg initial dose at week 0 with 200 mg every 2 weeks thereafter and 400 mg every 2 weeks), followed by a minimum of 12 weeks of follow-up without treatment (or until relapse) in subjects suffering from moderate to severe chronic plaque psoriasis who are candidates for systemic therapy and/or phototherapy and/or Photochemotherapy

Study Title on EudraCT:
Multicenter, dose response, randomized, double blind, parallel, 3 arms, placebo controlled clinical trial to evaluate the efficacy and the safety of subcutaneous CDP870 (certolizumab pegol) at 2 different 12 weeks dose regimens followed by a minimum of 12 wks of follow-up without treatment (or until relapse) in subjects suffering from moderate- to-severe chronic plaque psoriasis who are candidates for systemic therapy and/or phototherapy and/or photochemotherapy

2. SYNOPSIS

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

Title of Study: **

Multicentre, dose response, randomized, double-blind, parallel, 3 arms, placebo-controlled clinical study to evaluate the efficacy and the safety of subcutaneous CDP870 (certolizumab pegol) at 2 different 12 weeks dose regimens (400 mg initial dose at week 0 with 200 mg every 2 weeks thereafter and 400 mg every 2 weeks), followed by a minimum of 12 weeks of follow-up without treatment (or until relapse) in subjects suffering from moderate to severe chronic plaque psoriasis who are candidates for systemic therapy and/or phototherapy and/or photochemotherapy.

Investigator(s):

15 investigators were involved in the study.

Study Centre(s):

The study was conducted at 15 centres in total. Five centres were in [redacted], and 10 centres were in [redacted].

Publications:

JP Ortonne, C Tasset, K Reich, W Sterry, Safety and Efficacy of Subcutaneous Certolizumab Pegol, a New Anti-TNFα monoclonal Antibody, in Patients with Moderate-to-Severe Chronic Plaque Psoriasis: Preliminary Results from a Double-blind, Placebo-controlled Trial. Journal of American academy of dermatology 2007;56(Suppl2):21.

JP Ortonne, C Tasset, K Reich, Efficacy of certolizumab pegol, a PEGylated Fab' fragment of an anti-TNFα monoclonal antibody, in patients previously exposed to biologicals: preliminary results of a randomised, placebo-controlled, Phase II clinical trial in psoriasis, EADV meeting, Vienna 2007.

K Reich , C Tasset , JP Ortonne, Efficacy and safety of Certolizumab Pegol, in patients with chronic plaque psoriasis: preliminary results of a randomized, double-blind, placebo-controlled trial. Ann Rheum Dis 2007;66(Suppl II):251.

JP Ortonne, W Sterry, C Tasset, K Reich, Certolizumab pegol, the first PEGylated Anti-TNFα, is effective and well tolerated in patients with moderate-to-severe chronic plaque psoriasis: preliminary data from a phase II study. Journal of the European Academy of dermatology and venerology 2007;21(supl1):26,ABS P031.

JP Ortonne, W Sterry, G Coteur, D Keininger, K Reich, Improved health-related quality of life in psoriasis patients following 10 weeks' treatment with Certolizumab Pegol: Data from a phase II study, 21st world congress of dermatology, Buenos Aires 2007.

K Reich , W Sterry, C Tasset, I Terpstra, JP Ortonne, Efficacy and time to relapse with Certolizumab Pegol, the first PEGylated anti- TNFα agent, in patients with moderate-to-severe chronic plaque psoriasis: Phase II study results, 21st world congress of dermatology, Buenos Aires 2007.

JP Ortonne, K Reich, D Keininger, Certolizumab pergola improved health-related quality of life in patients with psoriasis: data from a phase II study. Journal of American academy of dermatology 2008;58(2Suppl2):AB121.

JP Ortonne, K Reich, W Sterry, I Terpsta, Safety and efficacy (PASI90 and global evaluation) of subcutaneous certolizumab pegol in patients with moderate to severe chronic plaque psoriasis: results from a double-blind, placebo-controlled trial. Journal of American academy of dermatology 2008;58(2Suppl2):AB4

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

** Title of Study on EudraCT is different, for details please refer to the first page of this document (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	
Studied Period (years): From 2005 to 2006 [2]	**Phase of Development:** Phase IIb	

Objectives:
This study evaluated efficacy and safety of CDP870 (200 mg and 400 mg) versus placebo, administered subcutaneously (sc) every 2 weeks for 12 weeks, in subjects with moderate to severe chronic plaque psoriasis.

Methodology:
This was a multicentre, dose response, randomized, double-blind, placebo-controlled, parallel group study. Subjects were randomized to one of three treatment groups: placebo (PBO), CDP870 200 mg, and CDP870 400 mg.

Randomization was stratified by study centre, severity of psoriasis at baseline and previous systemic treatment and/or phototherapy and/or photochemotherapy for psoriasis. The randomization was centralized, using a dynamic allocation procedure. This minimized the imbalance between treatment arms within the levels of the stratification factors.

The PBO treatment group received sc injections of placebo at week 0, and every 2 weeks until week 10.

The CDP870 200 mg treatment group received 400 mg CDP870 by sc injection at week 0, followed by 200 mg CDP870 by sc injection every 2 weeks until week 10.

The CDP870 400 mg treatment group received 400 mg CDP870 by sc injection at week 0, followed by 400 mg CDP870 by sc injection every 2 weeks until week 10.

At the end of the treatment period, subjects entered a follow-up period of 12 to 24 weeks.

At the end of the treatment period for all randomized subjects, the data base with the treatment period data was locked (first lock) and unblinded. The final primary efficacy results, secondary and exploratory endpoints over the treatment period, as well as interim safety results were produced. The outputs at this time point were created in such a way that the treatment code for individual subjects could not be revealed. All personnel (CDM, statistical programmer, statistician, etc.) who were unblinded at this stage of the study, ensured to keep the blind to the rest of the team until the data base lock of a subsequent re-treatment study (C87044). The final data base of study C87040 was locked (second lock) after the last follow-up visit of the last subject of study C87040 (11-Jan-2007). This data base contained all data from the treatment period as well as the follow-up period. At this point the analyses related to the follow-up were performed, and due to the addition of new data from the follow-up period, a final safety analysis was performed. All analyses already finalized at the time of the first database lock were re-run for the purpose of checking consistency of the data. The outputs of the C87040 study were only released after the database lock of the C87044 study (11-Jun-2007).
Results described in this study report are based on the analysis following the second lock. Relevant changes in the data base regarding the data from the first lock are described in this report.

Number of Subjects:
Planned: 150 subjects (50 in each treatment group) were to be randomized, in a maximum of 18 centers.
Participated: 176 subjects were randomized to three treatment groups: PBO (59 subjects), CDP870 200 mg (59 subjects), and CDP870 400 mg (58 subjects). Fifteen centers randomized subjects.

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)
[2] 17-Oct-2005 to 14-Nov-2006 (this note was added for clarification purposes afterwards)
* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

Diagnosis and Main Criteria for Inclusion:
Adult men and women > 18 years.
Subjects with chronic plaque psoriasis that was stable for at least 3 months and was moderate to severe for at least 6 months.
Subjects with PASI ≥ 12 and BSA ≥ 10%.
Subjects who were candidates for systemic psoriasis therapy and/or phototherapy and/or chemophototherapy.
Subjects having a social security system (applicable for [redacted] only).

Test Product: CDP870	**Dose and Mode of Administration:** CDP870 (200 mg/mL) in saline (10 mM sodium acetate, 125 mM sodium chloride, pH 4.7) administered in dosages of 200 mg or 400 mg, by sc injection.	**Batch Number:** [redacted]

Duration of Treatment: 12 weeks

Reference Therapy: Placebo	**Dose and Mode of Administration:** Commercially available 0.9% saline (preservative free) solution of pharmacopoeial (USP/Phr. Eur.) quality, by sc injection.	**Batch Number:** [redacted]

Criteria for Evaluation:
Efficacy / Pharmacokinetics / HRQOL:

Efficacy
Primary efficacy parameters were proportion of subjects (responders) achieving at least a 75% decrease from baseline in the Psoriasis Area and Severity Index (PASI75) score at week 12, and proportion of subjects with a Psoriasis Global Assessment (PGA) rating of 'clear' or 'almost clear' at week 12. Subjects with a missing PASI or PGA score at week 12 were considered as non-responders for that parameter.

The following secondary efficacy parameters were based on PASI:

- Time to PASI50 and to PASI75, defined as the time elapsed between the start of the treatment period and the first occurrence of PASI50 and PASI75 respectively. This parameter applied only to those subjects who had achieved PASI75 at the end of the treatment period.
- Time to relapse, defined as the time elapsed between the last dose and when maximal improvement in PASI from baseline was reduced by > 50%. This parameter applied only to those subjects who had achieved PASI75 at the end of the treatment period.
- The proportion of subjects achieving ≥ 50% decrease from baseline in PASI (PASI50) and ≥ 90% decrease from baseline in PASI (PASI90) at the end of the 12 week treatment period.
- The proportion of subjects with a rebound effect, defined as worsening of psoriasis over baseline value (PASI>125%) or new pustular, erythrodermic or more inflammatory psoriasis occurring within two months after stopping therapy.

Other secondary efficacy parameters were:

- The body surface area (BSA) affected by psoriasis at week 12 and absolute change in BSA from baseline.
- The time to discontinuation from the treatment period due to lack of efficacy.

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)
* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

Exploratory efficacy parameters were:

- The evolution of PASI during the 12 week treatment period and the follow-up period.
- The evolution of PGA ratings during the 12 weeks treatment period and the follow-up period.
- The evolution of BSA (Body Surface Area) during the 12 week treatment period and the follow-up period.
- Health-related quality of life as assessed by the Dermatology Life Quality Index (DLQI).
- Subject's evaluation of change in disease activity as assessed by the Global Evaluation Scale (GES).
- VAS assessment of Psoriatic Arthritis during the 12 week treatment period and the follow-up period, in the subgroup of subjects with active psoriatic arthritis at baseline (defined as ≥ 3 swollen joints and ≥ 3 tender or painful joints).

Pharmacokinetics

Pharmacokinetic assessments were based on plasma concentrations of CDP870 and antibody formation.

Safety:

Safety was assessed by the following:

- Adverse event reporting
- Blood parameters (haematology, chemistry (included CRP) and hepatic enzymes).
- Urinary parameters evaluated by microscopy and dipstick.
- Level of auto-antibodies (anti-nuclear antibody (ANA), anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody, anti-cardiolipin IgG and anti-cardiolipin IgM antibodies).
- Vital signs
- ECG parameters
- Physical examination

Statistical Methods:

Summary statistics consisted of frequency tables for categorical variables. For continuous variables, descriptive statistics (number of available observations, mean, median, standard deviation, minimum and maximum) were tabulated.

All statistical tests were performed two-tailed at the 5% level of significance unless otherwise stated.

Primary Efficacy Analyses

Primary efficacy was analyzed on the ITT population. The two primary efficacy parameters were each analyzed using a logistic regression model including terms for treatment (three treatment groups), and severity of psoriasis at baseline (severe/moderate to severe). In order to limit the inflation of the overall Type I error rate, the global null hypothesis of equality between the three treatment groups was tested first. If the global treatment effect was significant at the 5% significance level, pair wise comparisons versus placebo were performed, each at 5% significance level. For each dose of CDP870, the odds ratio versus placebo was calculated with its 95% confidence intervals.

The study was declared successful if at least one of the two dose comparisons to placebo was statistically significant for PASI and PGA endpoints.

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

The primary efficacy parameters were also analyzed on the PP population. This PP analysis was considered as supportive of the primary efficacy analysis on the ITT population.

A sensitivity analysis of the primary efficacy parameters was performed using randomization-based statistical tests, in order to adequately reflect the randomization scheme. A sensitivity analysis was performed in order to verify the impact of missing values. An additional sensitivity analysis was performed where subjects who took forbidden concomitant antipsoriatic treatments were considered as non-responders.

Subgroup analyses were performed on the primary efficacy parameters in order to investigate the consistency of the treatment effect. Subgroups were based on age, gender, weight, BMI, baseline psoriasis severity, prior systemic treatment, centre, pooled centre, country, previous use of anti-TNF and presence of anti-CDP870 antibodies.

Secondary Efficacy Analyses
The following secondary efficacy parameters were analyzed using a logistic regression model including terms for treatment (three treatment groups), and severity of psoriasis at baseline (severe/moderate to severe):
PASI50 and PASI90 at week 12.

Time to PASI50 and to PASI75 and time to relapse were estimated and presented graphically for each treatment group using the Kaplan-Meier product-limit method. The median time and its two-sided 95% confidence interval were computed by treatment arm. Since this analysis was conditional upon the PASI75 response at week 12, no formal statistical comparisons were performed.

The BSA at week 12 and absolute change from baseline were summarized descriptively by treatment group. The absolute change from baseline was analyzed using an analysis of variance including terms for treatment, and severity of psoriasis at baseline. Pair wise comparisons between each active dose and placebo were performed using the difference in least square means with its 95% confidence intervals.

The time to withdrawal during the treatment period due to lack of efficacy was estimated and presented graphically for each treatment group using the Kaplan-Meier product-limit method. This parameter was analyzed using a Cox regression model stratified by severity of psoriasis at baseline. Pair wise comparisons between the active doses versus placebo were performed by estimating the hazards ratio with its 95% confidence interval.

Exploratory Efficacy Analyses
The exploratory efficacy parameters were summarized descriptively.

Evaluation of Safety
Clinical laboratory values, vital signs, ECGs and extent of exposure were presented descriptively by treatment group.

Adverse events were coded according to the Medical Dictionary for Regulatory Activities (MedDRA). Adverse events were summarized descriptively by treatment group, primary system organ class (SOC) and preferred term. Additional tables summarized adverse events by intensity and relationship to study drug, adverse events occurring within two hours of injection start, adverse events leading to withdrawal from the

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)
* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

study, and SAEs.

Pharmacokinetic Analyses
CDP870 plasma concentrations were summarized for each active treatment at Visits 1, 6, 8, 10, 11, 12, 13 and 13abc.

SUMMARY – CONCLUSIONS:
In total, 215 subjects were screened and 176 subjects were randomized to three treatment groups: PBO (59 subjects), CDP870 200 mg (59 subjects), and CDP870 400 mg (58 subjects). The 176 randomized subjects represented the ITT population.

The majority of subjects in each group completed the 12 week treatment period: 40 (67.8%) PBO subjects, 54 (91.5%) CDP870 200 mg subjects and 54 (93.1%) CDP870 400 mg subjects. Twenty eight subjects prematurely discontinued from the treatment period. The main reasons for discontinuation were lack or loss of efficacy (14 PBO subjects, 3 CDP870 200 mg subjects, and 1 CDP870 400 mg subject). Other reasons for discontinuing were adverse events (3 PBO subjects, 2 CDP870 200 mg subjects, and 3 CDP870 400 mg subjects), and lost to follow-up (2 PBO subjects).

Subjects in the ITT population entered a follow-up period lasting up to maximum 24 weeks after treatment. One hundred and twenty two (69.3%) subjects completed the follow-up period: 27 (45.8%) PBO subjects, 45 (76.3%) CDP870 200 mg subjects, and 50 (86.2%) CDP870 400 mg subjects. 54 subjects discontinued from the follow-up period. The main reasons for discontinuing from the follow-up period were lack or loss of efficacy (14 PBO subjects, and 7 CDP870 200 mg subjects), and unknown reasons (13 PBO subjects, 4 CDP870 200 mg subjects, and 4 CDP870 400 mg subjects).

Twenty six subjects (14.8%) in the ITT population had at least one major protocol deviation during the study (9 PBO subjects, 10 CDP870 200 mg subjects, and 7 CDP870 400 mg subjects).

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

The demographic and other baseline characteristics of subjects in the study were as follows:

Demographic and Other Baseline Characteristics – ITT Population

Characteristics	Descriptive statistics	PBO N = 59	CDP870 200 mg N = 59	CDP870 400 mg N = 58	Overall N = 176
Age (years)[a]	Mean (SD)	43.3 (12.78)	43.26 (10.12)	43.64 (12.36)	43.40 (11.74)
	Min - Max	20.1 – 73.3	18.8 – 70.1	21.9 – 72.8	18.8 – 73.3
Gender					
Male	n (%)	37 (62.7)	44 (74.6)	42 (72.4)	123 (69.9)
Female	n (%)	22 (37.3)	15 (25.4)	16 (27.6)	53 (30.1)
Race					
Caucasian	n (%)	57 (96.6)	57 (96.6)	58 (100.0)	172 (97.7)
Weight (kg)	Mean (SD)	79.16 (19.25)	84.40 (21.15)	83.12 (18.04)	82.22 (19.55)
	Min - Max	45.0 – 132.0	48.0 – 150.0	54.0 – 150.0	45.0 – 150.0
BMI (kg/m^2)	Mean (SD)	26.54 (4.99)	27.49 (5.91)	27.34 (5.45)	27.12 (5.45)
	Min - Max	16.7 – 39.9	18.1 – 55.8	19.0 – 53.8	16.7 – 55.8
Disease duration at screening (years)	Mean (SD)	19.66 (11.91)	20.95 (11.38)	19.56 (9.75)	20.06 (11.01)
	Min - Max	1.2 – 56.0	1.4 – 46.0	2.0 – 49.0	1.2 – 56.0
Severity of psoriasis at baseline[b]					
Moderate to severe	n (%)	22 (37.3)	26 (44.1)	20 (34.5)	68 (38.6)
Severe	n (%)	37 (62.7)	33 (55.9)	37 (63.8)	107 (60.8)
Missing	n (%)	0	0	1 (1.7)	1 (0.6)
PASI[c]	n	59	59	57	175
	Mean (SD)	22.55 (8.83)	21.36 (8.20)	21.95 (8.05)	21.95 (8.34)
	Min - Max	12.2 – 52.6	12.0 – 52.3	12.1 – 44.8	12.0 – 52.6
BSA[d]	n	59	59	57	175
	Mean (SD)	30.07 (17.65)	26.66 (16.46)	28.42 (14.28)	28.38 (16.18)
	Min - Max	10.0 – 70.0	10.0 – 70.0	10.0 – 78.0	10.0 – 78.0
PGA[e]					
Clear/almost clear/mild	n (%)	0	0	0	0
Moderate	n (%)	7 (11.9)	10 (16.9)	9 (15.5)	26 (14.8)
Moderate to severe	n (%)	31 (52.5)	28 (47.5)	31 (53.4)	90 (51.1)
Severe	n (%)	21 (35.6)	21 (35.6)	17 (29.3)	59 (33.5)
Missing	n (%)	0	0	1 (1.7)	1 (0.6)

[a] Age (years) at randomization visit
[b] Moderate to severe (12 ≤ PASI ≤ 20 and 10% ≤ BSA ≤ 20%), severe (PASI > 20 or BSA > 20%)
[c] PASI (Psoriasis Area and Severity Index) ranges from 0 – 72
[d] BSA (Body Surface Area), extent of skin involvement in psoriasis (%)
[e] PGA (Psoriasis Global Assessment)

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

EFFICACY / PHARMACOKINETIC / PHARMACODYNAMIC RESULTS:

EFFICACY

Primary efficacy parameters for this study were proportion of subjects (responders) achieving at least a 75% decrease from baseline in PASI score (PASI75) at week 12, and proportion of subjects with a PGA rating of 'clear' or 'almost clear' at week 12.

Comparison of the PASI75 and PGA Responder Rate at Week 12 (V10) – ITT Population

Parameter Treatment	Responder n (%)	Non-responder n (%)	Odds ratio: CDP870 / PBO[(a)] Estimate [95% CI]	Treatment effect p-value[(b)] Global vs PBO
PASI75 response at week 12[(c)]				< 0.001
PBO (N = 59)	4 (6.8)	55 (93.2)		
CDP870 200 mg (N = 59)	44 (74.6)	15 (25.4)	40.2 [13.7, 150.3]	< 0.001
CDP870 400 mg (N = 58)	48 (82.8)	10 (17.2)	73.4 [23.5, 292.6]	< 0.001
PGA response at week 12[(d)]				< 0.001
PBO (N = 59)	1 (1.7)	58 (98.3)		
CDP870 200 mg (N = 59)	31 (52.5)	28 (47.5)	64.1 [12.7, 1169.1]	< 0.001
CDP870 400 mg (N = 58)	42 (72.4)	16 (27.6)	162.6 [31.4, 2999.2]	< 0.001

Subjects with a missing PASI or PGA score at week 12 (V10) were considered as non-responders for that parameter.
[(a)] Logistic regression with treatment and baseline severity of psoriasis as factors. Confidence limits are based on likelihood ratio statistics.
[(b)] Likelihood ratio p-value for the global treatment effect and, if significant at 5%, for the pair wise comparison of each active treatment versus placebo.
[(c)] PASI75 response is defined as a decrease in PASI score at week 12 (V10) from baseline of at least 75%.
[(d)] PGA response is defined as a PGA rating at week 12 (V10) of 'clear' or 'almost clear'.

A PASI75 response at week 12 was observed in 6.8% (4) PBO subjects, 74.6% (44) CDP870 200 mg subjects, and 82.8% (48) CDP870 400 mg subjects.

A PGA response at week 12 was observed in 1.7% (1) PBO subject, 52.5% (31) CDP870 200 mg subjects, and 72.4% (42) CDP870 400 mg subjects.

Both CDP870 doses were statistically and clinically different from placebo for both co-primary efficacy endpoints.

The PP analysis confirmed the analysis on the ITT population.

A sensitivity analysis for missing data using a worst case scenario approach still confirmed the primary efficacy results. In this sensitivity analysis, subjects with missing scores for PASI or PGA at week 12 were considered as non-responders for that parameter for the active treatment groups, and considered as responders for the PBO group.

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

The conclusions of the primary efficacy analysis was also confirmed by both the sensitivity analysis using randomization based tests to reflect the randomization scheme, and the sensitivity analysis taking into account the intake of forbidden concomitant antipsoriatic treatment.

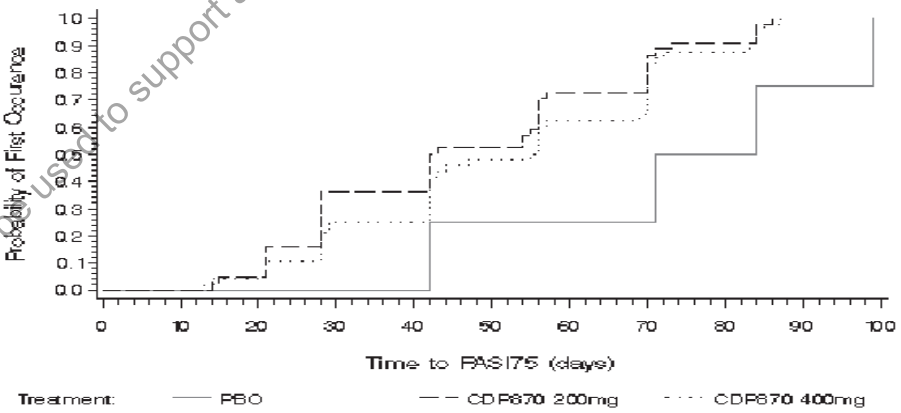
Subgroup analyses were performed on the primary efficacy parameters in order to investigate the consistency of the treatment effect. These results should be interpreted with caution due to the small overall sample size. Subgroups were based on age, gender, weight, BMI, baseline psoriasis severity, prior systemic treatment, centre, pooled centre, country, previous use of anti-TNF and presence of anti-CDP870 antibodies.

One interaction with treatment was found to be significant at the 10% significance level. The interaction between BMI and treatment was significant for PASI75 responders at week 12. Subjects with BMI less than 25 had higher response rates to treatment with CDP870 200 mg than subjects with BMI of 25 or greater.

The interaction between baseline psoriasis severity ('moderate to severe psoriasis' or 'severe psoriasis') and treatment was not significant for PASI75 (p = 0.441) and PGA (p = 0.608) responders at week 12.

The following secondary efficacy parameters were analyzed: time to treatment response, time to relapse, PASI50 and PASI90 responder rates, body surface area (BSA) affected by psoriasis, and time to withdrawal from treatment due to lack of efficacy.

In the subgroup of subjects with PASI75 response at week 12, the Kaplan-Meier estimate of the median time to PASI75 was 77.5 d (95% CI: 42.0, 99.0) for the PBO group, 42.50 d (95% CI: 28.0, 56.0) for the CDP870 200 mg group, and 55.5 d (95% CI: 42.0, 69.0) for the CDP870 400 mg group.
In the same subgroup, the median time to PASI50 was 56.5 d (95% CI: 14.0, 99.0) for the PBO group, 21.0 d (95% CI: 20.0, 28.0) for the CDP870 200 mg group, and 22.0 d (95% CI: 21.0, 30.0) for the CDP870 400 mg group.

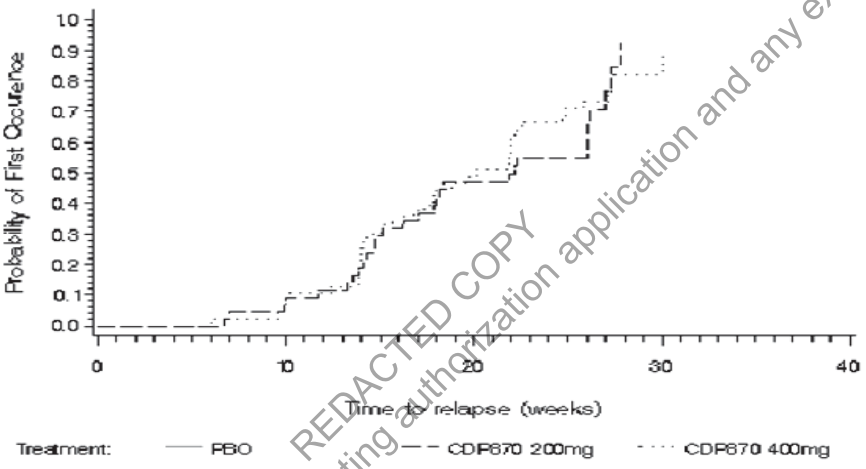


[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

For subjects that were PASI75 responders at week 12, the median time to relapse was 22.14 weeks (95% CI: 17.00, 26.00) for the CDP870 200 mg group (30 subjects), and 20.14 weeks (95% CI: 17.00, 22.29) for the CDP870 400 mg group (38 subjects). In this subgroup, 68.2% CDP870 200 mg subjects and 79.2% CDP870 400 mg subjects relapsed.
None of the PBO responders relapsed.



Within two months of stopping treatment 2 (1.7%) CDP870 treated subjects (1 in the 200 mg group, 1 in the 400 mg group) rebounded. Both subjects showed an increase from baseline in PASI >125%, and both were non-responders to treatment.

A PASI50 response at week 12 was observed in 7 (11.9%) PBO subjects, 51 (86.4%) CDP870 200 mg subjects, and 54 (93.1%) CDP870 400 mg subjects ($p < 0.001$ for the comparison of each CDP870 dose versus PBO).

At week 12, a PASI90 response was observed in 1 (1.7%) PBO subject, 23 (39.0%) CDP870 200 mg subjects, and 27 (46.6%) CDP870 400 mg subjects ($p < 0.001$ for the comparison of each CDP870 dose versus PBO).

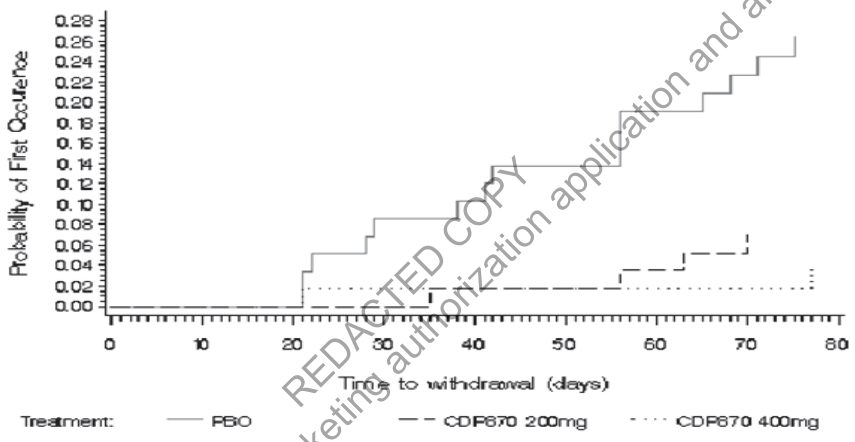
[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

The adjusted mean difference in BSA change from baseline during treatment with CDP870 versus PBO was 17.79 ($p < 0.001$; 95% CI: 12.57, 23.00) for the CDP870 200 mg group, and 20.29 ($p < 0.001$; 95% CI: 15.14, 25.43) for the CDP870 400 mg group.

During the study, 15 (25.4%) PBO subjects, 4 (6.8%) CDP870 200 mg subjects, and 2 (3.4%) CDP870 400 mg subjects withdrew from treatment period due to lack of efficacy or for worsening/exacerbation of psoriasis. For these subjects withdrawn the median time to withdrawal was 42.00 d for the PBO group, 59.50 d for the CDP870 200 mg group, and 49.00 d for the CDP870 400 mg group.



The hazard ratio for withdrawal from treatment with CDP870 versus PBO was 0.225 ($p = 0.008$; 95% CI 0.07, 0.68) for the CDP870 200 mg group, and 0.117 ($p = 0.004$; 95% CI: 0.03, 0.51) for the CDP870 400 mg group. This indicates that subjects treated with PBO were statistically more likely to withdraw from treatment with PBO than from treatment with CDP870.

Mean DLQI total scores decreased below the level of remission (i.e. 5 points) for both CDP870 treatment groups in contrast to the PBO group during the treatment period. This indicates that CDP870 treated subjects had clinically meaningful improvements in their HRQOL. Psoriasis had little or no impact on their lives at the end of the treatment period. During the follow-up period there was a gradual increase in mean DLQI total scores for both CDP870 treatment groups. Mean DLQI total scores for CDP870 treatment groups remained numerically lower (i.e. better) than scores for the PBO group until at least 24 weeks from treatment start.

A global evaluation of psoriasis using GES was made for each subject at week 12. The results did not take into consideration the premature discontinuations from treatment. According to the GES, a marked or moderate improvement was seen in 10 out of 37 (27.0%) PBO subjects, 47 out of 52 (90.4%) CDP870 200 mg subjects, and 50 out of 51 (98.0%) CDP870 400 mg subjects.

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

PHARMACOKINETICS

Geometric mean values (CV%) for plasma concentrations in the CDP870 200 mg treatment group were as follows: 25.05 µg/mL (42.6%) at week 4, 21.22 µg/mL (40.6%) at week 12, and 3.21 µg/mL (75.5%) at week 16 (week 4 of the follow-up period).

In the CDP870 400 mg treatment group, geometric mean values (CV%) for plasma concentrations were 39.98 µg/mL (41.9%) at week 4, 39.98 µg/mL (47.0%) at week 12, and 7.49 µg/mL (110.3%) at week 16 (week 4 of the follow-up period).

During the 12-week treatment period, 3 (5.0%) CDP870 200 mg subjects and 2 (3.5%) CDP870 400 mg subjects were anti-CDP870 antibody positive (at least one sample > 2.4 units/mL). During the overall study (including the follow-up period), 17 (28.3%) of CDP870 200 mg subjects and 18 (31.6%) CDP870 400 mg subjects were antibody positive. At the last follow-up visit, 10 (18.2%) CDP870 200 mg subjects and 13 (25.0%) CDP870 400 mg subjects were positive for anti-CDP870 antibodies.

Overall, the subjects who tested positive in the screening ELISA, the majority had no neutralizing antibody activity. Only 32.3% screening ELISA Ab positive subjects tested had antibodies showing activity in the neutralizing antibody assay.

SAFETY RESULTS:

The treatment-emergent adverse events (TEAEs) reported during the study are summarized as follows:

Overall Summary of Treatment-Emergent Adverse Events – Safety Population

	PBO (N = 58) n (%)	CDP870 200 mg (N = 60) n (%)	CDP870 400 mg (N = 57) n (%)	Overall (N = 175) n (%)
Total number of AEs	133	156	125	414
Any adverse events	41 (70.7)	43 (71.7)	40 (70.2)	124 (70.9)
AEs related to study drug	14 (24.1)	21 (35.0)	15 (26.3)	50 (28.6)
Serious adverse events	1 (1.7)	2 (3.3)	5 (8.8)[(a)]	8 (4.6)
AEs leading to death	0	0	0	0
AEs leading to permanent discontinuation	3 (5.2)	2 (3.3)	2 (3.5)	7 (4.0)

Treatment-emergent adverse events are defined in Appendix 16.1.9 of the report. TEAEs have an onset date between first study drug administration and 12 weeks after last study drug administration.
AEs with missing relationship are counted as 'Related'.
Drug-related AEs are described by the Investigator as possibly, probably or highly probably related to study drug.
[(a)] Two subjects reported a pregnancy with abortion as SAEs.

There were no clinically meaningful differences between treatment groups in the incidence of TEAEs reported.
More than two-thirds of subjects in each group reported at least one TEAE. The most frequently reported TEAEs according to primary SOC were infections and infestations (67 subjects, 38.3%), nervous system disorders (40 subjects, 22.9%), and general disorders and administration site conditions (37 subjects, 21.1%).

There were no clinically meaningful differences between groups in the profile of infections and infestations,

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

nervous system disorders, and general disorders and administration site conditions reported.
According to preferred term, nasopharyngitis was the most commonly reported infection and infestation. 10 (17.2%) PBO subjects, 4 (6.7%) CDP870 200 mg subjects, and 12 (21.1%) CDP870 400 mg subjects reported nasopharyngitis.

Headache was the most common nervous system disorder and was reported by 9 (15.5%) PBO subjects, 13 (21.7%) CDP870 200 mg subjects, and 8 (14.0%) CDP870 400 mg subjects.
Asthenia was the most common general disorder and administration site condition, and was reported by 3 (5.2%) PBO subjects, 3 (5.0%) CDP870 200 mg subjects, and 3 (5.3%) CDP870 400 mg subjects.
AEs occurring within 2 h of injection start were reported by 9 subjects: 1 PBO subject, 4 CDP870 200 mg subjects, and 2 CDP870 400 mg subjects. For 28 subjects (9 PBO subjects, 11 CDP870 200 mg subjects, and 8 CDP870 400 mg subjects), AEs were reported on the day of injection which potentially could have started within 2 h of injection start.

The majority of TEAEs reported were mild or moderate in intensity. Severe AEs were reported by 7 (12.1%) PBO subjects, 4 (6.7%) CDP870 200 mg subjects, and 4 (7.0%) CDP870 400 mg subjects. There was no consistent pattern in the severe AEs reported each treatment group. According to primary SOC, the most commonly reported severe AEs in the PBO group and CDP870 200 mg group were musculoskeletal and connective tissue disorders. Two subjects in the CDP870 400 mg group became pregnant during the study and their condition was reported as severe TEAEs. These pregnancies were also reported as SAEs.

Drug-related TEAEs were reported by 14 (24.1%) PBO subjects, 21 (35.0%) CDP870 200 mg subjects, and 15 (26.3%) CDP870 400 mg subjects. The most frequently reported TEAEs according to primary SOC were general disorders and administration site conditions (17 subjects, 9.7%), infections and infestations (16 subjects, 9.1%), and nervous system disorders (14 subjects, 8.0%). According to preferred term, headache was the most common drug-related disorder and was reported by 4 (6.9%) PBO subjects, 5 (8.3%) CDP870 200 mg subjects, and 2 (3.5%) CDP870 400 mg subjects.

There were no deaths during the study.

At least one treatment emergent SAE was reported by 1 (1.7%) PBO subject, 2 (3.3%) CDP870 200 mg subjects, and 5 (8.8%) CDP870 400 mg subjects. In the PBO group, 1 subject reported diarrhoea haemorrhagic as an SAE. In the CDP870 200 mg group, 3 SAEs were reported in 2 subjects (contusion, and urinary tract infection and gastroenteritis). In the CDP870 400 mg group, 7 SAEs were reported by 5 subjects (pregnancy [twice], disseminated tuberculosis, pregnancy, anxiety [twice] and gastroenteritis, and psoriasis). The SAE of pregnancy was reported twice by one subject, once during the treatment period and once post-treatment.

The incidence of TEAEs leading to permanent discontinuation from treatment was similar for each group. Three (5.2%) PBO subjects, 2 (3.3%) CDP870 200 mg subjects, and 2 (3.5%) CDP870 400 mg subjects permanently discontinued from treatment due to TEAEs. Four subjects were permanently discontinued from study medication due to the following SAEs: haemorrhagic diarrhoea (PBO group), urinary tract infection and gastroenteritis (CDP870 200 mg group), pregnancy (CDP870 400 mg group), and psoriasis (CDP870 400 mg group). 3 subjects permanently discontinued treatment due to TEAEs which were not reported as SAEs. These TEAEs were psoriasis (PBO group), vertigo (PBO group), and psoriasis

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)
* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)

Name of Sponsor/Company: UCB Pharma SA	Individual Study Table Referring to Module 5.3.5.1	*(For National Authority Use only)*
Name of Finished Product: Not applicable [1]	Volume:	
Name of Active Ingredient: CDP870	Page:	

(CDP870 200 mg group).

Subjects treated with CDP870 had no clinically meaningful differences in haematology, biochemistry, urinalysis, auto-antibody levels, vital signs or use of concomitant medications from subjects treated with PBO.

CONCLUSIONS:

CDP870 showed significant improvement of psoriasis symptoms in subjects suffering from moderate to severe chronic plaque psoriasis. Treatment with both doses of CDP870 (200 mg EOW after a loading dose of 400 mg and 400 mg EOW) significantly increased the PASI75 and PGA rating 'clear' or 'almost clear' response rates after 12 weeks of treatment compared to treatment with placebo.

Significant improvements were also shown for both active doses versus placebo on PASI50 and PASI90 response rates, on BSA affected by psoriasis and on the withdrawal from the treatment due to lack of efficacy. For half of the subjects who had responded to CDP870, relapse occurred later than 5 months after the stop of treatment. The onset of action for treatment responders appeared to be quicker in both CDP870 treatment groups compared to placebo. Within two months of stopping treatment, 2 CDP870 subjects experienced a rebound reaction (increase of ≥125% PASI score from baseline). Both subjects were non-responders to treatment.

The majority of the subjects treated with CDP870 reported moderate or marked improvements in their disease activity and had clinically meaningful improvements in HRQOL beyond remission levels, in contrast to PBO treated subjects. No consistent changes from baseline were found for mean VAS of psoriatic arthritis for any treatment group during the study. The VAS of psoriatic arthritis should be interpreted with caution due to the low number of subjects with psoriatic arthritis at baseline (13 [22.0%] PBO subjects, 15 [25.4%] CDP870 200 mg subjects, and 10 [17.2%] CDP870 400 mg subjects).

There were no deaths during the study. At least one SAE was reported by 1 (1.7%) PBO subject, 2 (3.3%) CDP870 200 mg subjects, and 5 (8.8%) CDP870 400 mg subjects. In the PBO group, one subject developed diarrhea hemorrhagic as an SAE. In the CDP870 200 mg group, one subject reported contusion, and one subject reported gastroenteritis and urinary tract infection as SAEs. In the CDP870 400 mg group, 7 SAEs were reported by 5 subjects: pregnancy (twice), disseminated tuberculosis, pregnancy, anxiety (twice) and gastroenteritis, and psoriasis.

Immunogenicity was low during the treatment phase (< 5%) but increased incidence as CDP870 cleared from the plasma.

Comparing with other anti-TNF treatments available, no unexpected safety signals were observed with CDP870. The two doses of CDP870 showed a similar safety profile.

Report Date:
22 April 2008

[1] Approved as Cimzia 200 mg solution for injection since October 2009 (this note was added for clarification purposes afterwards)

* Study has been registered as CDP 870-040 on EudraCT (subsequently addition of information on 19th of May 2015)