UCB reference No.: RXCE08B2006

Approved by UCB 16-Jun-2008

Clinical Study Summary (CSS)

DEV/SGE/01813.2008

CT Registry ID#: NCT00329303
Study No.: C87044

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Based on Clinical Study Report document reference code: RRCE06D1017

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Cimzia® Liquid Formulation	Certolizumab Pegol	Moderate to severe chronic plaque psoriasis

Name of Sponsor/Company: UCB Pharma SA

Title of Study: Follow-up of study C87040: Multicentre, double-blind study to describe the efficacy and safety of re-treatment with CDP870 (certolizumab pegol) subcutaneous at 2 different dose regimens (400 mg initial dose at week 0 with 200 mg every 2 weeks thereafter and 400 mg every 2 weeks) or placebo for 12 weeks, in subjects suffering from moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy and/or phototherapy and/or photochemotherapy, having responded to treatment in study C87040 and having subsequently relapsed.

Investigator(s) (number only): 11

Study Center(s) (number only): 12

Length of Study:
Date first patient enrolled: 02-May-2006
Date last patient completed: 09-May-2007

Phase of Development: Phase II

Abstract:
The primary objective of the study was to assess the difference in Psoriasis Area and Severity Index (PASI) scores between week 12 score of the first study C87040 and week 12 score of re-treatment study C87044. The primary efficacy variable was the difference in PASI scores between week 12 score of the C87040 study and week 12 score of re-treatment study C87044. For a subject with a missing PASI score at week 12 of re-treatment, the last PASI score under re-treatment was used (last observation carried forward). Safety assessments included the monitoring of adverse events (AEs) over the whole duration of studies C87040 and C87044, clinical laboratory tests, levels of auto-antibodies, vital signs, ECG parameters and physical examinations. Subjects were to be ≥18 years old, had responded to treatment at week 12 in study C87040 (having shown an improvement of ≥75% from baseline PASI score) and then relapsed during the follow-up period of study C87040 (in the 24 weeks after the end of the study treatment). Relapse was defined as a reduction by more than 50% of the maximal improvement in PASI score from baseline during the treatment period of study C87040. Subjects had to have a social security system (applicable for France only). Study C87044 consisted of a 12-week treatment period with CDP870 400 mg subcutaneously (sc) at week 0 followed by CDP870 200 mg, CDP870 400 mg or placebo sc every 2 weeks. Subjects received the same treatment as in study C87040. At the end of the treatment period, subjects entered a safety follow-up period of 12 weeks. Primary efficacy parameters were analyzed on the ITT population. Baseline characteristics for the ITT population were summarized descriptively. Evaluations used the baseline values from study C87040 (first treatment baseline) and the baseline from study C87044 (re-treatment baseline). No inferential analyses were performed to compare treatment groups in the C87044 study. Treatment groups were not directly comparable since the C87044 study population (34 subjects, 200 mg; 37 subjects, 400 mg; 0 subjects, placebo) consisted of responders that relapsed in the C87040 study and were not re-randomized.

CT Registry ID#: NCT00329303
Study No.: C87044

Number of Subjects:	**CDP870 200mg**	**CDP870 400mg**	**Overall**
Planned, N:			75
Participated, N:	34	37	71
Completed treatment, n (%):	32 (94.1)	35 (94.6)	67 (94.4)
Number of Subjects Withdrawn, n (%):	2 (5.9)	2 (5.4)	4 (5.6)
Withdrawn for Lack of Efficacy, n (%):	1 (2.9)	0	1 (1.4)
Other reasons [(a)], n (%):	1 (2.9)	2 (5.4)	3 (4.2)

[(a)] Other reasons for discontinuing from the treatment period were subject not available/working abroad, movement to another place, and non-compliant for visit/decision of Sponsor.

Demography:	**CDP870 200mg (N=34)**	**CDP870 400mg (N=37)**	**Overall (N=71)**
Gender (Females/Males):	11/23	10/27	21/50
Age (years), mean (SD):	44.2 (8.6)	44.6 (12.5)	44.4 (10.7)
Race, n (%):			
Caucasian:	34 (100.0)	37 (100.0)	71 (100.0)

Safety Outcomes:

- Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:

Overall, there were fewer subjects reporting TEAEs during the re-treatment period (study C87044) (32 subjects, 45.1%) than during the first treatment period (study C87040) (47 subjects, 66.2%). The most commonly reported class of TEAEs during the first treatment and re-treatment periods were infections and infestations (29.6% and 21.1%, respectively), nervous system disorders (19.7% and 12.7%, respectively), general disorders and administration site conditions (19.7% and 2.8%, respectively), and skin and subcutaneous tissue disorders (15.5% and 11.3%, respectively). TEAEs considered to be drug-related by the Investigator were reported by 26.8% and 16.9% subjects during the first treatment and re-treatment periods, respectively. Two subjects (5.4%) reported serious AEs (pregnancy, and anxiety and gastroenteritis) during the first treatment period. During the re-treatment period, no subjects reported SAEs or permanently discontinued from treatment due to adverse events. No deaths were reported during the first treatment or re-treatment periods. There were no clinically meaningful differences between the first treatment and the re-treatment periods with respect to laboratory parameters for haematology, biochemistry and shifts in ECG abnormalities. During both treatment periods, the majority of subjects showed no changes from baseline for the following antibodies: ANA, anti-dsDNA antibody, and anti-cardiolipin IgG and IgM antibodies.

CT Registry ID#: NCT00329303 **Study No.:** C87044		
Treatment Emergent AEs (TEAEs):	**First treatment period (C87040)**	**Re-treatment period (C87044)**
CDP870 200mg (N=34)		
Subjects with at least one TEAE, n (%):	23 (67.6)	14 (41.2)
MedDRA Primary System Organ Class with an incidence of ≥ 15%	*n (%) [n considered drug-related by the investigator]*	
Infections and infestations	6 (17.6) [1]	9 (26.5) [6]
Nervous system disorders	9 (26.5) [3]	3 (8.8) [0]
Respiratory, thoracic and mediastinal disorders	8 (23.5) [3]	3 (8.8) [0]
Skin and subcutaneous tissue disorders	5 (14.7) [1]	6 (17.6) [1]
General disorders and administration site conditions	10 (29.4) [8]	0
Gastrointestinal disorders	6 (17.6) [4]	4 (11.8) [0]
Musculoskeletal and connective tissue disorders	7 (20.6) [0]	2 (5.9) [2]
CDP870 400mg (N=37)		
Subjects with at least one TEAE, n (%):	24 (64.9)	18 (48.6)
MedDRA Primary System Organ Class with an incidence of ≥ 15%	*n (%) [n considered drug-related by the investigator]*	
Infections and infestations	15 (40.5) [3]	6 (16.2) [2]
Nervous system disorders	5 (13.5) [1]	6 (16.2) [2]
Skin and subcutaneous tissue disorders	6 (16.2) [1]	2 (5.4) [1]

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CT Registry ID#: NCT00329303
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Primary Outcomes:
The median PASI score was 1.60 at first treatment week 12 and 3.35 at re-treatment week 12 for the CDP870 200 mg group, and the median difference in PASI scores was 1.25 (95% CI: 0.10, 4.40). For the CDP870 400 mg group, the median PASI score was 1.80 at first treatment week 12 and 2.00 at re-treatment week 12, and median difference in PASI scores was 0.20 (95% CI: 0.00, 0.70). The mean and median differences in PASI scores between first treatment week 12 and re-treatment week 12 were not clinically significant for any of the treatment groups. This observation follows that of other TNF-α antagonists in re-treatment studies.

PASI score (ITT population):	**First treatment week 12 (C87040)**	**Re-treatment week 12 (C87044)**	**Difference[(a)]**
CDP780 200mg (N=34)			
Mean (SD) [95% CI]	1.96 (1.74) [1.35, 2.56]	5.62 (6.36) [3.40, 7.84]	3.66 (6.12) [1.53, 5.80]
Median [95% CI]	1.60 [0.90, 2.70]	3.35 [1.40, 6.30]	1.25 [0.10, 4.40]
Min-Max	0.0-6.6	0.0-25.4	-3.6-21.9
CDP780 400mg (N=37)			
Mean (SD) [95% CI]	1.85 (1.41) [1.38, 2.32]	3.14 (4.47) [1.65, 4.63]	1.29 (4.00) [-0.05, 2.62]
Median [95% CI]	1.80 [1.20, 2.60]	2.00 [0.60, 3.30]	0.20 [0.00, 0.70]
Min-Max	0.0-4.7	0.0-23.6	-3.0-19.2

For subjects with a missing PASI score at week 12 of re-treatment, the last PASI score under re-treatment was used (last observation carried forward). Subjects were not re-randomized, therefore treatment groups may not be comparable.
[(a)] Difference in 'PASI score at Re-Treatment Week 12' minus 'PASI score at First Treatment Week 12'.

Publication References based on the study: None

Date of report: 16-Jun-2008