UCB reference No.: RXCE08B2005

Approved by UCB 29-May-2008

Clinical Study Summary (CSS)

DEV/SGE/01434.2008

CT Registry ID#: NCT00245765
Study No.: C87040

These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert.

Based on Clinical Study Report document reference code: RRCE06D1016

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: Multicentre, 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 (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) (number only): 15

Study Center(s) (number only): 15

Length of Study:
Date first patient enrolled: 17-Oct-2005
Date last patient completed: 14-Nov-2006

Phase of Development: Phase IIb

Abstract:
The primary objective of the study was to assess the efficacy of certolizumab pegol (CDP870 or CZP) (200 mg and 400 mg) versus placebo (PBO). The primary efficacy variables were the proportion of subjects (reponders) achieving ≥75% decrease from baseline in the Psoriasis Area and Severity Index score (PASI75), and the proportion of subjects with a Psoriasis Global Assessment (PGA) rating 'clear' or 'almost clear' at the end of the 12-week treatment period. Safety assessments included the monitoring of adverse events (AEs), clinical laboratory tests, levels of auto-antibodies, vital signs, ECG parameters and physical examinations. Subjects had to be at least 18 years old, had chronic plaque psoriasis which was stable for ≥ 3 months with a moderate to severe severity for ≥ 6 months, had a PASI ≥ 12, had a Body Surface Area (BSA) ≥ 10%, were candidates for systemic psoriasis therapy and/or phototherapy and/or chemotherapy, and had a social security system (only applicable for France). The trial consisted of a 12-week treatment period with either PBO every 2 weeks, or CZP 400 mg at week 0 followed by CZP 200 mg or CZP 400 mg every 2 weeks. At the end of the treatment period, subjects entered a follow-up period for a maximum of 24 weeks. Subjects who responded at Week 12 and relapsed during the follow-up period were eligible to enter the re-treatment study C87044. Primary efficacy parameters were analyzed on the ITT population 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 CZP, 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.

CT Registry ID#: NCT00245765
Study No.: C87040

Number of Subjects:	**PBO**	**CZP 200 mg**	**CZP 400 mg**
Planned, N:	50	50	50
Randomized, N:	59	59	58
Completed treatment period, n (%):	40 (67.8)	54 (91.5)	54 (93.1)
Number of Subjects Withdrawn, n (%):	19 (32.2)	5 (8.5)	4 (6.9)
Withdrawn due to Adverse Events, n (%):	3 (5.1)	2 (3.4)	3 (5.2)[a]
Withdrawn for Lack of Efficacy, n (%):	14 (23.7)	3 (5.1)	1 (1.7)
Lost to follow-up, n (%):	2 (3.4)	0	0

[a] One subject discontinued the treatment period due to an AE after having received all of the protocol planned CZP injections.

Demography:	**PBO (N=59)**	**CZP 200 mg (N=59)**	**CZP 400 mg (N=58)**
Gender (Females/Males):	22/37	15/44	16/42
Age (years), mean (SD):	43.3 (12.78)	43.26 (10.12)	43.64 (12.36)
Race, n (%):			
Caucasian:	57 (96.6)	57 (96.6)	58 (100)
African-American:	0	1 (1.7)	0
Asian/Pacific Islander:	1 (1.7)	0	0
Hispanic:	0	1 (1.7)	0
Indian/Pakistani:	1 (1.7)	0	0

Safety Outcomes:

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

Overall, 71.7% and 70.2% of the subjects in the CZP 200 mg and CZP 400 mg, respectively, reported treatment-emergent (TE) AEs versus 70.7% of the PBO subjects. The most commonly reported class of TEAEs in the CZP 200 mg, CZP 400 mg and the PBO groups were infections and infestations (26.7%, 47.4%, and 41.4% of the subjects, respectively), nervous system disorders (28.3%, 19.3%, and 20.7% of the subjects, respectively), and general disorders and administration site conditions (26.7%, 19.3%, and 17.2% of the subjects, respectively).
TEAEs considered to be drug-related by the Investigator were reported for 35.0% and 26.3% of the CZP 200 mg and CZP 400 mg subjects, respectively, versus 24.1% of the PBO subjects.
There were no deaths during this study. Serious AEs (SAEs) were reported by 8 subjects: 2 CZP 200 mg subjects, 5 CZP 400 mg subjects and 1 PBO subject. Two subjects in the CZP 400 mg group reported pregnancy as SAE.
Two subjects in each CZP group reported a TEAE leading to permanent drug discontinuation versus 3 subjects in the PBO group. One additional subject in the CZP 400 mg group discontinued the treatment period due to an AE after having received all of the protocol planned CZP injections.
Subjects treated with CZP had no clinically meaningful differences in haematology, biochemistry, urinalysis, auto-antibody levels, or vital signs from subjects treated with PBO.

Treatment Emergent AEs (TEAEs):	**PBO (N=58)[a]**	**CZP 200 mg (N=60)[a]**	**CZP 400 mg (N=57)[b]**
Subjects with at least one TEAE, n (%):	41 (70.7)	43 (71.7)	40 (70.2)
MedDRA Primary System Organ Class with an incidence of ≥15% in any group	*n (%) [n considered drug-related by the investigator]*		
Infections and infestations	24 (41.4) [5]	16 (26.7) [5]	27 (47.4) [6]
Nervous system disorders	12 (20.7) [5]	17 (28.3) [6]	11 (19.3) [3]
General disorders and administration site conditions	10 (17.2) [3]	16 (26.7) [10]	11 (19.3) [4]
Musculoskeletal and connective tissue disorders	10 (17.2) [1]	14 (23.3) [2]	6 (10.5) [0]
Skin and subcutaneous tissue disorders	8 (13.8) [3]	12 (20.0) [5]	8 (14.0) [1]
Gastrointestinal disorders	12 (20.7) [5]	8 (13.3) [2]	7 (12.3) [1]

[a] One PBO subject received 1 dose of CZP 200 mg and was considered in the CZP 200 mg group for the safety analysis.
[b] One subject was randomized by mistake in the CZP 400 mg group and did not receive study medication.

CT Registry ID#: NCT00245765
Study No.: C87040

Death and other SAEs:	**PBO (N=58)**	**CZP 200 mg (N=60)**	**CZP 400 mg (N=57)**
Death	0	0	0
Subjects with SAEs, n (%):	1 (1.7)	2 (3.3)	5 (8.8)
MedDRA Primary System Organ Class	*n (%) [n considered drug-related by the investigator]*		
Infections and infestations	0	1 (1.7) [1]	2 (3.5) [2]
Pregnancy, puerperium and perinatal conditions	0	0	2 (3.5) [0]
Psychiatric disorders	0	0	1 (1.8) [0]
Injury, poisoning and procedural complications	0	1 (1.7) [0]	0
Gastrointestinal disorders	1 (1.7) [1]	0	0
Skin and subcutaneous tissue disorders	0	0	1 (1.8) [0]

Primary Outcomes:
A PASI75 response at week 12 was observed in 74.6% of the CZP 200 mg subjects and 82.8% of the CZP 400 mg subjects versus 6.8% of the PBO subjects. The odds ratio for response to treatment with CZP versus PBO was 40.2 ($p<0.001$; [95% CI: 13.7, 150.3]) for the CZP 200 mg group and 73.4 ($p<0.001$; [95% CI: 23.5, 292.6]) for the CZP 400 mg group. A PGA response at week 12 was observed in 52.5% of the CZP 200 mg subjects and 72.4% of the CZP 400 mg subjects versus 1.7% of the PBO subjects. The odds ratio for response to treatment with CZP versus PBO was 64.1 ($p<0.001$; [95% CI: 12.7, 1169.1]) for the CZP 200 mg group and 162.6 ($p<0.001$; [95% CI: 31.4, 2999.2]) for the CZP 400 mg group.

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

Subjects with a missing PASI or PGA score at Week 12 (V10) are considered as non-responders for that parameter.

Publication References based on the study:
Ortonne et al., JAAD 2007;56(Suppl2):21 - Ortonne et al., EADV meeting, Vienna 2007 - Reich et al., Ann Rheum Dis 2007;66(SupplII):251 - Ortonne et al., JEADV 2007;21(Suppl1):26 - Ortonne et al., 21st world congress of dermatology, Buenos Aires 2007 - Reich et al., 21st world congress of dermatology, Buenos Aires 2007 - Ortonne et al., JAAD 2008; 58(2Suppl2):AB121 and AB4.

Date of report: 29-May-2008