Clinical Study Summary (CSS)

DEV/SGE/01676.2008

CT Registry ID#: NCT00548834
Study No.: CDP870-011

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Based on Clinical Study Report document reference code: RRCE06C1440

Proprietary Drug Name	**INN**	**Therapeutic area and indication**
CIMZIA® liquid formulation	Certolizumab Pegol	Rheumatoid Arthritis

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
Efficacy and safety of CDP870 400 mg subcutaneously versus placebo in the treatment of the signs and symptoms of patients with rheumatoid arthritis who have previously failed at least one DMARD

Investigator(s) (number only): 36

Study Center(s) (number only): 36

Length of Study:
Date first patient enrolled: 13-Jun-2003
Date last patient completed: 12-Jul-2004

Phase of Development: Phase III

Abstract:
The primary objective was to compare the efficacy of certolizumab pegol (CDP870 or CZP) 400 mg every 4 weeks to placebo (PBO) in treating the signs and symptoms of subjects with rheumatoid arthritis. The primary efficacy variable was the American College of Rheumatology (ACR)20 responder rate at Week 24. A responder was defined as at least 20% improvement from baseline in the number of tender/painful and swollen joints as well as at least 20% improvement in at least 3 of the following 5 assessments: physician's global, subject's global, subject's assessment of arthritis pain, C-reactive protein, or Health Assessment Questionnaire-Disability Index. Safety measurements included assessment of adverse events (AEs), clinical laboratory tests, vital signs, physical examinations, electrocardiograms and chest X-rays, Purified Protein Derivative (PPD) skin test (at screening), and the presence of autoantibodies. Subjects had to be 18 to 75 years of age, inclusive, diagnosed with adult-onset rheumatoid arthritis (RA) of at least 6 months duration as defined by the 1987 ACR classification criteria, to have failed at least one disease modifying antirheumatic drug (DMARD), and to have discontinued all DMARD therapy at least 28 days prior to the first dose of study drug. The subjects could be on a stable dose of prednisone (or equivalent) ≤ 10 mg/day and nonsteroidal anti-inflammatory drugs. Each subject received CZP 400 mg or PBO subcutaneously every 4 weeks for a total of 6 injections. Subjects who completed the study or withdrew on or after Week 12 visit were eligible to participate in the open-label safety study (CDP870-015), unless they were withdrawn from the current study due to non-compliance or a possible study drug related AE. The frequency of ACR20 responders/non-responders at Week 24 was compared using Cochran-Mantel-Haenszel (CMH) test controlling for country.

Number of Subjects:	**PBO**	**CZP 400 mg**
Planned, N:	100	100
Enrolled, N:	109	111
Completed, n (%):	28 (25.7)	76 (68.5)
Number of Subjects Withdrawn, n (%):	81 (74.3)	35 (31.5)
Withdrawn due to Adverse Events, n (%):	2 (1.8)	5 (4.5)
Lack of efficacy, n (%)	75 (68.8)	24 (21.6)
Withdrawn for Other Reasons, n (%):	4 (3.7)	6 (5.4)

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Demography:	**PBO (N=109)**	**CZP 400 mg (N=111)**
Gender (Females/Males):	97/12	87/24
Age (years), mean (SD):	54.9 (11.61)	52.7 (12.71)
Race, n (%):		
Asian	1 (0.9)	2 (1.8)
Black	8 (7.3)	13 (11.7)
White	87 (79.8)	90 (81.1)
Not listed	13 (11.9)	6 (5.4)

Safety Outcomes:

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

Overall, 75.7% of the subjects in the CZP 400 mg group experienced at least 1 treatment-emergent (TE)AE versus 57.8% of the subjects in the PBO group. The most commonly reported class of TEAEs in the PBO and CZP 400 mg group were infections and infestations (14.7% and 29.7% of the subjects, respectively), general disorders and administration site conditions (26.6% and 12.6% of the subjects, respectively), and respiratory, thoracic and mediastinal disorders (16.5% and 19.8% of the subjects, respectively). TEAEs considered to be drug-related were reported in 22.0% and 24.3% of the subjects in the PBO and CZP 400 mg group, respectively.

There were no deaths during the trial. Serious AEs were reported by 3 subjects (2.8%) in the PBO group and 8 subjects (7.2%) in the CZP 400 mg group. Two subjects (1.8%) and 5 subjects (4.5%) in the PBO and CZP 400 mg group, respectively, had a TEAE leading to permanent study drug discontinuation.

Vital signs and physical findings remained generally unchanged from Baseline in each of the 2 treatment groups. Although the differences in changes from Baseline between the 2 treatment groups were statistically significant for many tests, there were no patterns to suggest a clinically relevant effect of study drug on the clinical laboratory values.

Treatment Emergent AEs (TEAE):	**PBO (N=109)**	**CZP 400 mg (N=111)**
Subjects with at least one TEAE, n (%):	63 (57.8)	84 (75.7)
MedDRA Primary System Organ Class with an incidence of ≥ 15% in any group	*n (%) [n considered drug-related by the Investigator]*	
Gastrointestinal disorders	15 (13.8) [4]	19 (17.1) [3]
General disorders and administration site conditions	29 (26.6) [17]	14 (12.6) [5]
Infection and infestations	16 (14.7) [2]	33 (29.7) [5]
Musculoskeletal and connective tissue disorders	8 (7.3) [1]	17 (15.3) [1]
Nervous system disorders	15 (13.8) [4]	22 (19.8) [7]
Respiratory, thoracic and mediastinal disorders	18 (16.5) [1]	22 (19.8) [4]
Death and other SAEs:	**PBO (N=109)**	**CZP 400 mg (N=111)**
Subjects with SAEs, n (%):	3 (2.8)	8 (7.2)
Deaths	0	0
MedDRA Primary System Organ Class with an incidence of ≥ 1.5% in any group	*n (%) [n considered drug-related by the Investigator]*	
Infections and infestation	0	2 (1.8) [1]
Musculoskeletal and connective tissue disorders	0	2 (1.8) [0]
Nervous system disorders	0	2 (1.8) [0]

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Primary Outcomes:
At Week 24, a total of 10 (9.3%) subjects receiving PBO were considered to be ACR20 responders compared to 50 (45.5%) subjects receiving CZP 400 mg, which was a statistically significant and meaningful difference ($p < 0.001$).

ACR20 Response at Week 24 (modified Intent-To-Treat population, mITT)	**PBO (N=109)**	**CZP 400 mg (N=111)**
Total, n (%)[(a)]	108 (100.0)	110 (100.0)
Responder, n (%)	10 (9.3)	50 (45.5)
p-value	< 0.001	

[(a)] One subject in each treatment group was excluded from the mITT population for the primary efficacy analysis.

Publication Reference(s) based on the study: None

Date of report: 04-Jun-2008