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Clinical Study Summary (CSS)

DEV/SGE/01677.2008

CT Registry ID#: NCT00544154
Study No.: CDP870-014

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Based on Clinical Study Report document reference code: RRCE06C1441

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 in combination with methotrexate compared to methotrexate alone in the treatment of the signs and symptoms of patients with rheumatoid arthritis who are partial responders to methotrexate

Investigator(s) (number only): 43

Study Center(s) (number only): 43

Length of Study:
Date first patient enrolled: 23-Oct-2002
Date last patient completed: 12-Jan-2004

Phase of Development: III

Abstract:
The primary objective of this study was to compare the efficacy of certolizumab pegol (CDP870 or CZP) in combination with methotrexate (MTX) to MTX alone in treating the signs and symptoms of subjects with rheumatoid arthritis (RA) who are partial responders to MTX. The primary efficacy endpoint was the American College of rheumatology (ACR)20 responder rate at Week 24. A subject was considered an ACR20 responder if 20% or greater improvement in the number of swollen joints and tender joints and a 20% or greater improvement in 3 of the 5 remaining ACR core set measures (Subject's Assessment of Pain (VAS), Subject's Global Assessment of Arthritis, Physician's Global Assessment of Arthritis, Subject's Assessment of Physical function by Health Assessment Questionnaire - disability index (HAQ-DI), acute phase reactant value [only CRP for this study]) was observed. Safety assessments included the monitoring of adverse events (AEs), clinical laboratory tests, vital signs, chest X-ray, 12-lead electrocardiogram (ECG), and presence of autoantibodies. Subjects had to be 18 to 75 years of age, inclusive, be diagnosed with adult-onset RA of at least 6 months duration as defined by the 1987 ACR classification criteria for RA, have received MTX for at least 6 months with a stable dose of MTX of 15 to 25 mg/week for at least 8 weeks prior to the first dose of study medication (doses as low as 10 mg were permitted if reduced due to toxicity), 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 placebo (PBO) subcutaneously every 4 weeks for a total of 6 injections. MTX treatment continued during the study at the same dose taken prior to enrollment in the study. Subjects who completed the current study or who withdrew on or after the Week 12 visit were eligible to participate in the open-label safety study (CDP870-015), unless they were withdrawn from the study due to non-compliance or a possibly study drug-related AE. The ACR20 response was analyzed by the Cochran-Mantel-Haenszel (CMH) method stratified by country.

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Number of Subjects:	**PBO + MTX**	**CZP + MTX**
Planned, N:	125	125
Enrolled, N:	121[(a)]	126[(a)]
Completed, n (%):	65 (53.7)	98 (77.8)
Number of Subjects Withdrawn, n (%):	56 (46.3)	28 (22.2)
Withdrawn due to Adverse Events, n (%):	6 (5.0)	7 (5.6)
Withdrawn due to Lack of Efficacy, n (%):	45 (37.2)	16 (12.7)
Withdrawn for Other Reasons, n (%):	5 (4.1)	5 (4.0)

[(a)]Two subjects in each of the treatment groups did not take study medication.

Demography:	**PBO + MTX (N=121)**	**CZP + MTX (N=126)**
Gender (Females/Males/Unknown):	80/40/1	91/35/0
Age (years), mean (SD):	55.6 (11.69)[a]	53.0 (12.29)
Race, n (%):		
Asian	1 (0.8)	0
White	119 (98.3)	126 (100.0)
Unknown	1 (0.8)	0

[a] N=120

Safety Outcomes:

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

Treatment-emergent (TE) AEs were reported in 97 (78.2%) subjects in the CZP 400 mg plus MTX group versus 83 (69.7%) subjects receiving PBO plus MTX. The most commonly reported class of TEAEs during treatment with PBO plus MTX and CZP plus MTX group were general disorders and administration site conditions (28.6% and 17.7% of the subjects, respectively), infections and infestations (14.3% and 26.6% of the subjects, respectively), and respiratory, thoracic and mediastinal disorders (14.3% and 23.4% of the subjects, respectively). Study drug-related TEAEs were reported for 33 subjects (27.7%) in the PBO plus MTX group and 31 subjects (25.0%) in the CZP plus MTX group.

There were no deaths during the trial. Serious AEs (SAEs) were reported by 10.1% and 12.9% of the subjects in the PBO plus MTX and CZP plus MTX group, respectively. Six subjects (5.0%) in the PBO plus MTX group and 7 subjects (5.6%) in the CZP plus MTX group had an AE leading to permanent discontinuation. Vital signs 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. In subjects for whom data were available, there were no meaningful differences between PBO plus MTX and CZP 400 mg plus MTX with respect to changes in autoantibody status from Baseline through Week 24/early termination.

Treatment Emergent AEs (TEAE)	**PBO + MTX (N=119)**	**CZP + MTX (N=124)**
Subjects with at least one TEAE, n (%):	83 (69.7)	97 (78.2)
MedDRA Primary System Organ Class with an incidence of ≥ 15% in any group	*n (%) [n considered drug-related by the Investigator]*	
Gastrointestinal disorders	19 (16.0) [2]	22 (17.7) [2]
General disorders and administration site conditions	34 (28.6) [23]	22 (17.7) [8]
Infections and infestations	17 (14.3) [4]	33 (26.6) [8]
Musculoskeletal and connective tissue disorders	17 (14.3) [1]	22 (17.7) [0]
Nervous system disorders	18 (15.1) [1]	23 (18.5) [8]
Respiratory, thoracic and mediastinal disorders	17 (14.3) [4]	29 (23.4) [4]
Skin and subcutaneous tissue disorders	12 (10.1) [1]	22 (17.7) [10]

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Death and Other SAEs:	**PBO + MTX (N=119)**	**CZP + MTX (N=124)**
Death, n (%)	0	0
Subjects with SAEs, n (%):	12 (10.1)	16 (12.9)
MedDRA Primary System Organ Class with an incidence of ≥ 2% in any group	*n (%) [n considered drug-related by the Investigator]*	
Infections and infestations	2 (1.7) [1]	3 (2.4) [2]
Nervous system disorders	3 (2.5) [0]	2 (1.6) [1]
Skin and subcutaneous tissue disorders	0	3 (2.4) [3]
Primary Outcomes: At Week 24, at total of 27 (22.9%) subjects receiving PBO plus MTX were considered to be ACR20 responders compared to 56 (45.9%) subjects receiving CZP 400 mg plus MTX. This difference was statistically and clinically significant ($p < 0.001$).		
ACR20 Response at Week 24	**PBO + MTX (N=119)**	**CZP + MTX (N=124)**
Total	118 (100.0)	122 (100.0)
Responder	27 (22.9)	56 (45.9)
p-value	< 0.001	
Publication Reference(s) based on the study: None		
Date of report: 04-Jun-2008		