UCB reference No.: RXCE06E1658

Approved by UCB 08-Jun-2008

Clinical Study Summary (CSS)

DEV/SGE/01703.2008

CT Registry ID#: NCT00152490
Study No.: CDP870-031

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: RXCE07A1202

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
CIMZIA® Liquid formulation	Certolizumab pegol (CDP870)	Active Crohn's disease

Name of Sponsor/Company: UCB Pharma SA

Title of Study: A Phase III multi-national, multi-centre, double-blind placebo-controlled parallel group, 26 Week study to assess the safety and efficacy of the humanised anti-TNF PEG conjugate, CDP870 400 mg sc, (dosed at Weeks 0, 2, 4 then 4-weekly to Week 24), in the treatment of patients with active Crohn's disease

Investigator(s) (number only): Not specified in the CSR

Study Center(s) (number only): 171

Length of Study:
Date first patient enrolled: 10-Dec-2003
Date last patient completed: 31-May-2005

Phase of Development: Phase III

Abstract:

The primary objective of this study was to compare the efficacy of subcutaneous certolizumab pegol (CDP870 or CZP) 400 mg administration versus placebo (PBO) in the treatment of signs and symptoms of active Crohn's disease (Crohn's Disease Activity Index [CDAI] between 220 and 450, scored over the 7 days prior to the first dose of study drug and C-Reactive Protein [CRP] ≥10 mg/L at Baseline) over a 26 Week period. The primary efficacy variables were the percentage of subjects with clinical response at Week 6 and both at Week 6 and 26 in the stratum defined by CRP ≥10 mg/L at Baseline. Safety assessments included the monitoring of adverse events (AEs), clinical laboratory tests, physical examination, vital signs, chest X-ray, antibodies to CZP and auto-antibodies. Subjects were at least 18 years old, had a confirmed diagnosis of Crohn's disease for ≥ 3 months prior to study entry with a CDAI score between 220 and 450, inclusive, scored over the 7 days prior to the first dose of study drug. CZP 400 mg or PBO was administered at Weeks 0, 2, and 4, and then every 4 weeks to Week 24. The Intent-to-Treat population was the primary population for the analysis of efficacy. The 2 treatments were compared by means of logistic regression analysis (odds ratio, 95% confidence interval [CI] and p-values) with factors for treatment, steroid use at entry, immunosuppressant use at entry and geographical region.

Number of Subjects:	**PBO**	**CZP 400 mg**
Planned, N:	302	302
Enrolled, N:	329	331
Completed, n (%):	176 (53.5)	202 (61.0)
Number of Subjects Withdrawn, n (%):	153 (46.5)	129 (39.0)
Withdrawn due to Adverse Events, n (%):	39 (11.9)	37 (11.2)
Withdrawn for Other Reasons, n (%):	114 (34.7)	93 (28.1)

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Demography:	**PBO (N=329)**	**CZP 400 mg (N=331)**
Gender (Females/Males):	198/131	174/157
Age (years), mean (SD):	37.9 (12.02)	36.8 (11.83)
Race, n (%):		
Caucasian	314 (95.4)	313 (94.6)
Afro-Caribbean	0	5 (1.5)
Asian (Indian)	1 (0.3)	2 (0.6)
Asian (Oriental)	2 (0.6)	2 (0.6)
Other	12 (3.6)	9 (2.7)

Safety Outcomes:

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

Overall, 269 subjects (81.3%) reported treatment-emergent (TE) AEs in the CZP 400 mg group compared with 260 subjects (79.0%) in the PBO group. The most commonly reported class of TEAEs during treatment with CZP 400 mg and PBO were gastrointestinal disorders (42.0% and 42.6% of subjects, respectively) and infections and infestations (42.0% and 31.0% of subjects, respectively).

Drug-related AEs occurred in 32.6% and 36.5% of subjects and AEs leading to withdrawal occurred in 10.9% and 11.9% of subjects in the CZP 400 mg group and the PBO group, respectively.

Serious AEs (SAEs) occurred in 10.3% of subjects in the CZP 400 mg group compared to 7.0% of subjects in the PBO group. Three SAEs were recorded in relation to the death of a subject in the CZP 400 mg group that occurred more than 10 months after the subject was withdrawn, but none of the events was considered by the Investigator to be related to study drug.

No important trends or differences between the 2 treatment groups were noted in vital signs, physical examination, and chest X-ray. There was however, a trend for a larger decrease from Baseline in mean white blood cells, neutrophils and platelets in the CZP mg group and a larger increase from Baseline in lymphocytes and monocytes compared with the PBO group that showed smaller changes in either direction. Detection of auto-antibodies during the study was low. Auto-antibodies were not detected in any of the tested subjects who withdrew during the study.

Treatment Emergent AEs (TEAE)	**PBO (N=329)**	**CZP 400 mg (N=331)**
Subjects with at least one TEAE, n (%):	260 (79.0)	269 (81.3)
Primary System Organ Class with an incidence of ≥ 10% in any treatment group	*n (%) [n considered drug-related by the Investigator]*	
Gastrointestinal disorders	140 (42.6) [38]	139 (42.0) [45]
Infections and infestations	102 (31.0) [15]	139 (42.0) [27]
Nervous system disorders	69 (21.0) [19]	76 (23.0) [22]
General disorders and administration site conditions	96 (29.2) [61]	59 (17.8) [29]
Musculoskeletal and connective tissue disorders	54 (16.4) [9]	46 (13.9) [9]
Skin and subcutaneous tissue disorders	34 (10.3) [13]	45 (13.6) [18]
Death and Other SAEs	**PBO (N=329)**	**CZP 400 mg (N=331)**
Death, n (%):	0	1 (0.3)
Subjects with SAEs, n (%):	23 (7.0)	34 (10.3)
Primary System Organ Class with an incidence of ≥ 2% in any treatment group	*n (%) [n considered drug-related by the Investigator]*	
Gastrointestinal disorders	13 (4.0) [11]	20 (6.0) [13]
Infections and infestations	3 (0.9) [1]	7 (2.1) [1]

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Primary Outcomes:
The percentage of subjects with clinical response in the CRP ≥10 mg/L stratum at Baseline, defined as a decrease in CDAI Score of ≥100 points from Baseline at Week 6, was 37.2% and 26.0% (p=0.037) in the CZP 400 mg group and the PBO group, respectively. The percentage of subjects with clinical response at both Weeks 6 and 26 was 21.5% and 12.3% (p=0.045) in the CZP 400 mg group and the PBO group, respectively.

Subjects with Clinical Response at Week 6 in the CRP ≥10 mg/L Stratum at Baseline Intent-to-Treat population	**PBO (N=156)**	**CZP 400 mg (N=146)**
Number of subjects	154	145
Frequency (%)	40 (26.0)	54 (37.2)
95% CI for Percentage Response	[19.0, 32.9]	[29.4, 45.1]
Odds Ratio [95% CI]	1.70 [1.03, 2.80]	
p-value	0.037	

Subjects with Clinical Response at Week 6 and 26 in the CRP ≥10 mg/L Stratum at Baseline Intent-to-Treat population	**PBO (N=156)**	**CZP 400 mg (N=146)**
Number of subjects	154	144
Frequency (%)	19 (12.3)	31 (21.5)
95% CI for Percentage Response	[7.1, 17.5]	[14.8, 28.2]
Odds Ratio [95% CI]	1.91 [1.02, 3.57]	
p-value	0.045	

Publication Reference(s) based on the study: None

Date of report: 08-Jun-2008