Clinical Study Summary (CSS)

DEV/SGE/01704.2008

CT Registry ID#: NCT00152425
Study No.: CDP870-032

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See Drug Details page of this website for approved drug label.

Based on Clinical Study Report document reference code: RRCE05F2305

Proprietary Drug Name	**INN**	**Therapeutic area and indication**
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 maintenance of clinical response to humanised anti-TNF PEG conjugate, CDP870 400 mg sc, (dosed 4-weekly from Weeks 8 to 24), in the treatment of patients with active Crohn's disease who have responded to open induction therapy (dosed at Weeks 0, 2 and 4) with CDP870

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

Study Center(s) (number only): 147

Length of Study:
Date first patient enrolled: 18-Feb-2004
Date last patient completed: 06-May-2005

Phase of Development: Phase III

Abstract:
The primary objective was to compare the efficacy of repeated 4-weekly treatment with certolizumab pegol (CZP or CDP870) versus placebo (PBO) in subjects with 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), following successful open induction therapy with CZP, in the maintenance of clinical response over 26 weeks. The primary efficacy endpoint was the percentage of subjects with clinical response at Week 26 (CZP versus PBO), in the stratum defined by CRP ≥10 mg/L at Baseline. Clinical response was defined as a decrease in CDAI score of ≥100-points from Baseline. Safety assessments included the monitoring of adverse events (AEs), clinical laboratory tests, physical examination, vital signs, autoantibodies and antibodies to CZP. Subjects were at least 18 years old and 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 was administered for 6 weeks open induction therapy followed by 18 weeks of 4-weekly double-blind treatment. The intent-to-Treat population was the primary population for the analysis of efficacy. The 2 treatment groups were compared using logistic regression (odds ratio, 95% confidence interval [CI]) with factors for treatment, steroid use at entry, immunosuppressant use at entry and geographical region.

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Number of Subjects:	**Open-label**	**Double-blind Responders of Open-Label**	
	CZP 400 mg	**PBO**	**CZP 400 mg**
Planned, N:	712	196	196
Enrolled, N:	668	212	216
Completed, n (%):	445 (66.6)	109 (51.4)	151 (69.9)
Number of Subjects Withdrawn, n (%):	223 (33.4)	103 (48.6)	65 (30.1)
Withdrawn due to adverse events, n (%)[a]:	44 (6.6)	29 (13.7)	21 (9.7)
Withdrawn due to lack of improvement/disease deterioration, n (%)[a]:	159 (23.8)	75 (35.4)	46 (21.3)
Withdrawn due to subject decision, n (%)[a]:	21 (3.1)	13 (6.1)	14 (6.5)
Withdrawn due to clinical decision, n (%)[a]:	19 (2.8)	13 (6.1)	7 (3.2)
Withdrawn due to protocol non-compliance, n (%)[a]:	6 (0.9)	0	1 (0.5)
Withdrawn due to lost to follow-up, n (%)[a]:	4 (0.6)	2 (0.9)	1 (0.5)
Withdrawn for other reasons, n (%)[a]:	20 (3.0)	6 (2.8)	1 (0.5)

[a] More than 1 reason for withdrawal may be recorded for a subject.

Demography:	**Open-label phase Non-responders**	**Open-label phase Responders**	
	CZP 400 mg (N=240)	**PBO (N=212)**	**CZP 400 mg (N=216)**
Gender (Females/Males):	126/114	102/110	124/92
Age (years), mean (SD):	38.0 (12.12)	37.7 (12.09)	37.5 (11.20)
Race, n (%):			
Caucasian	229 (95.4)	193 (91.0)	203 (94.0)
Afro-Caribbean	3 (1.3)	3 (1.4)	2 (0.9)
Asian (Indian)	1 (0.4)	4 (1.9)	6 (2.8)
Asian (Oriental)	0	1 (0.5)	1 (0.5)
American Indian	0	1 (0.5)	0
Other	7 (2.9)	10 (4.7)	4 (1.9)

Safety Outcomes:

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

During the open-label phase, 67.9% of subjects who were non-responders to open-label induction, and 53.5% subjects who responded to open-label induction with CZP 400 mg reported at least 1 treatment-emergent (TE)AE. During the double-blind maintenance phase of the study, 64.8% of subjects in the CZP 400 mg group and 67.5% of subjects in the PBO group experienced TEAEs. The most common class of TEAE during open-label induction and double-label maintenance phase were gastrointestinal disorders (35.4% of non-responders and 13.6% of responders; 25.5% and 22.7% of subjects in the PBO and CZP 400 mg group, respectively) and infections and infestations (18.3% of non-responders and 20.6% of responders; 25.9% and 32.9% the subjects in the PBO and CZP 400 mg group, respectively). In the open-label induction phase, 31.7% of subjects of the non-responders had a drug-related AE compared to 19.9% of responders. In the double-blind maintenance phase, 27.4% subjects receiving PBO and 22.7% of subjects treated with CZP 400 mg experienced a drug-related AE.

One subject died during the open-label induction phase due to a fentanyl overdose, a serious AE (SAE) which was assessed as unlikely related to the study drug. In the open-label phase, 17.5% non-responders and 1.2% responders reported an SAE. In the double-blind phase, 6.6% subjects treated with PBO and 5.6% subjects treated with CZP 400 mg experienced an SAE. The incidence of AEs leading to permanent drug withdrawal in the open-label phase was higher for the non-responders (19.6%) compared to the responders (0.9%). In the double-blind phase, 13.2% of the PBO-treated subjects and 8.3% of the CZP 400 mg-treated

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subjects reported an AE leading to permanent discontinuation of the study drug.
There were no significant trends in the laboratory data or other safety parameters suggestive of a safety signal for CZP.

Treatment Emergent AEs (TEAE):	**Open-label induction**		**Double-blind maintenance**	
	Non-responder at Week 6 (N=240)	**Responder at Week 6 (N=428)**	**PBO (N=212)**	**CZP (N=216)**
Subjects with at least one TEAE, n (%):	163 (67.9)	229 (53.5)	143 (67.5)	140 (64.8)
Primary System Organ Class with an incidence of ≥10% in any group	*n (%) [n considered drug-related by the Investigator]*			
Gastrointestinal disorders	85 (35.4) [23]	58 (13.6) [14]	54 (25.5) [17]	49 (22.7) [7]
Infections and infestations	44 (18.3) [23]	88 (20.6) [20]	55 (25.9) [7]	71 (32.9) [24]
Nervous system disorders	38 (15.8) [15]	68 (15.9) [23]	18 (8.5) [4]	18 (8.3) [3]
General disorders and administration site conditions	39 (16.3) [24]	46 (10.7) [37]	47 (22.2) [35]	25 (11.6) [8]
Musculoskeletal and connective tissue disorders	23 (9.6) [3]	33 (7.7) [6]	32 (15.1) [4]	19 (8.8) [2]
Death and Other SAEs:	**Open-label induction**		**Double-blind maintenance**	
	Non-responder at Week 6 (N=240)	**Responder at Week 6 (N=428)**	**PBO (N=212)**	**CZP (N=216)**
Death, n (%):	1 (0.4)	0	0	0
Subjects with SAEs, n (%):	42 (17.5)	5 (1.2)	14 (6.6)	12 (5.6)
Primary System Organ Class with an incidence of ≥2% in any group	*n (%)[n considered drug-related by the Investigator]*			
Gastrointestinal disorders	28 (11.7) [4]	1 (0.2) [3]	9 (4.2) [3]	4 (1.9) [1]
Infections and infestations	11 (4.6) [4]	1 (0.2) [3]	2 (0.9) [1]	6 (2.8) [3]

Primary Outcomes:
The percentage of subjects with a clinical response at Week 26 in the stratum defined by CRP≥10 mg/L at baseline was statistically significant higher in the CZP 400 mg group compared to the PBO group in the Intent-To-Treat (ITT) population ($p < 0.001$). At Week 26, 69 subjects (61.6%) randomized to CZP 400 mg maintenance treatment were in clinical response, compared to 34 subjects (33.7%) randomized to PBO maintenance treatment.

Subjects with a clinical response at Week 26 ITT population	**PBO (N=101)**	**CZP 400 mg (N=112)**
Frequency, n (%)	34 (33.7)	69 (61.6)
95% CI for percentage response	[24.4, 42.9]	[52.6, 70.6]
Odds ratio [95% CI]	3.30 [1.83, 5.97]	
p-value	<0.001	

Publication Reference(s) based on the study: None

Date of report: 08-Jun-2008