Certolizumab Pegol for the Treatment of Chronic Plaque Psoriasis: DLQI and WPAI Patient-Reported Outcomes From an Ongoing Phase 3, Multicenter, Randomized, Active- and Placebo-Controlled Study (CIMPACT)

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INTRODUCTION

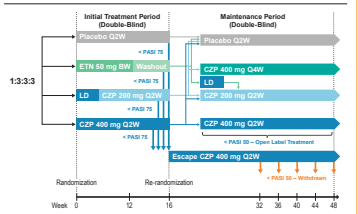
- Psoriasis affects ~3% of adults in the US[1,2] and ~2-6% of adults in Europe[3]; onset can begin at any age, though most patients develop the disease in the third decade of life[4]
- Psoriasis can have a significant negative impact on the physical, emotional, psychosocial, and economic well-being of affected patients[5,6]
  - In the US, over 80% of psoriasis patients report that the disease negatively affects their emotional state and their enjoyment of life[6]
  - Over 90% of unemployed US psoriasis patients report not working solely due to psoriasis or psoriatic arthritis, and almost half of working psoriasis patients regularly miss work due to the disease[6]
  - Quality of life instruments for psoriasis have been useful to assess the impact of psoriasis on patients lives and well-being[7,8]
- Certolizumab pegol (CZP) is the only PEGylated, Fc-free, anti-TNF biologic and is currently under investigation for the treatment of moderate-to-severe chronic plaque psoriasis
- Previously presented data through Week 16 of 3 ongoing, randomized, double-blind, placebo-controlled trials have demonstrated clinically meaningful efficacy and a safety profile consistent with anti-TNF therapy[9,10]
- CIMPACT (NCT02346240) is designed to assess the efficacy and safety of treatment with CZP compared with placebo and etanercept (ETN) in adult patients with moderate-to-severe chronic plaque psoriasis; results of patient-reported outcomes through Week 16 for all patients and results through Week 48 for patients initially treated with CZP are presented here

METHODS

Study Design

- CIMPACT is an ongoing phase 3, randomized, multinational, parallel-group, placebo- and active-controlled trial
- Patients were randomized 3:3:1:3 to CZP 400 mg every 2 weeks (Q2W), CZP 200 mg Q2W (after an initial loading dose of 400 mg at Weeks 0, 2 and 4), or placebo Q2W for 16 weeks or ETN twice weekly for 12 weeks (**Figure 1**)
- At Week 16, CZP- and ETN-treated PASI 75 responders were re-randomized and continued for 32 weeks of maintenance treatment:
  - From CZP 400 mg Q2W to 400 mg Q2W, 200 mg Q2W, or placebo Q2W
  - From CZP 200 mg Q2W to 400 mg every 4 weeks (Q4W), 200 mg Q2W, or placebo Q2W
  - From ETN to CZP 200 mg Q2W (after loading dose) or placebo Q2W
- At Week 16, placebo-treated PASI 75 responders continued placebo Q2W for 32 weeks of maintenance treatment
- At Week 16, PASI 75 nonresponders entered an Escape Arm for treatment with CZP 400 mg Q2W

Figure 1. Study Design



BW, twice weekly; CZP, certolizumab pegol; ETN, etanercept; LD, loading dose of CZP 400 mg at Weeks 0, 2, and 4 or Weeks 16, 18, and 20; PASI 50, ≥50% reduction in psoriasis area and severity index (PASI); PASI 75, ≥75% reduction in PASI; Q2W, every 2 weeks; Q4W, every 4 weeks

Patients

- Eligible patients were ≥18 years of age, had moderate-to-severe chronic plaque psoriasis for ≥6 months with a Baseline psoriasis area and severity index (PASI) ≥12, affected body surface area (BSA) ≥10%, and physician's global assessment (PGA; 5-point scale) ≥3
- Patients had to be candidates for systemic psoriasis therapy, phototherapy, and/or photochemotherapy
- Patients were excluded if they had erythrodermic, guttate, or generalized pustular forms of psoriasis; previous treatment with CZP, ETN, or >2 biologics (including anti-TNF); or history of primary failure to any biologic or secondary failure to >1 biologic

Patient-Reported Outcome Measures and Study Assessments

- Dermatology Life Quality Index (DLQI)
  - Validated, skin disease-specific questionnaire that assesses how disease symptoms/treatment affect patient health-related quality of life; higher scores indicate lower quality of life (numeric rating scale 0 to 30)
- Work Productivity and Activity Impairment–Specific Health Problem questionnaire (WPAI)
  - 6-item, self-reported survey that covers 4 domains of work/daily activity impairment, including:
    1. Absenteeism (work time missed)
    2. Presenteeism (reduced on-the-job effectiveness)
    3. Work productivity loss (overall work impairment)
    4. Activity impairment (impairment performing regular daily activities)
  - Questions related to the first 3 domains were to be completed only by patients who were employed at the time of the assessment; questions related to the last domain were to be completed by all patients
  - WPAI domain scores are impairment percentages; higher numbers indicate greater impairment and less productivity
- Assessments at Weeks 16 and 48
  - Change from Baseline (CfB) in DLQI
  - DLQI minimal clinically important difference (MCID; ≥4-point reduction[7]) responder rate
  - DLQI 0/1 (absolute score ≤1) responder rate
  - CfB in WPAI

Statistical Analysis

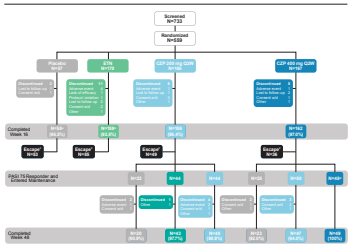
- Efficacy analyses at Week 16 were performed on the Randomized Set (all randomized patients)
- Efficacy analyses at Week 48 were performed on the Maintenance Set (patients completing the Week 16 visit with ≥1 efficacy measurement during the Maintenance Period)
- Inferential statistics for CfB in DLQI and WPAI at Week 16 were based on analysis of covariance (ANCOVA)
- Mean CfB values are presented for continuous variables, and percentages are presented for responder variables
- Last observation carried forward (LOCF) imputation was used to impute data for CfB in DLQI (Week 16 and 48) and WPAI (Week 16)
- Nonresponse imputation was used for DLQI MCID and DLQI 0/1 analyses
- Week 48 WPAI data was assessed based on observed cases

RESULTS

Patient Disposition, Demographics, and Baseline Characteristics

- A total of 167, 165, and 57 patients were randomized to CZP 400 mg Q2W, CZP 200 mg Q2W, or placebo, respectively (**Figure 2**)
- Patient demographics and Baseline characteristics were similar between groups (**Table 1**)

Figure 2. Patient Disposition



*Placebo-treated PASI 75 responders at Week 16 (N=2) continued placebo
†ETN-treated PASI 75 responders at Week 16 (N=74) were re-randomized to placebo (N=24) or CZP 200 mg Q2W (N=50)
‡PASI 75 nonresponders at Week 16 entered the Escape Arm for treatment with CZP 400 mg Q2W
§Two patients completed Week 16 but did not enter Maintenance Period (1 loss to follow-up; 1 consent withdrawn)
CZP 400 mg Q4W; BW, twice per week; CZP, certolizumab pegol; ETN, etanercept; PASI 75, ≥75% reduction in psoriasis area and severity index; Q2W, every 2 weeks; Q4W, every 4 weeks; wd, withdrawn

Table 1. Patient Demographics and Baseline Disease Characteristics

	Placebo (N=57)	CZP 200 mg Q2W (N=165)	CZP 400 mg Q2W (N=167)
Demographics			
Age (years), mean ± SD	46.5 ± 12.5	46.7 ± 13.5	45.4 ± 12.4
Male, n (%)	34 (59.6)	113 (68.5)	107 (64.1)
White, n (%)	57 (100)	158 (95.8)	162 (97.0)
Employed, n (%)	49 (86.0)	117 (70.9)	123 (73.7)
Geographic Region, n (%) North America Central/Eastern Europe Western Europe	10 (17.5) 36 (63.2) 11 (19.3)	26 (15.8) 107 (64.8) 32 (19.4)	27 (16.2) 109 (65.3) 31 (18.6)
Weight (kg) Mean ± SD Range	93.7 ± 29.7 55.0 – 198.5	89.7 ± 20.6 49.0 – 171.1	86.3 ± 20.0 41.8 – 152.0
BMI (kg/m²) Mean ± SD Range	31.2 ± 8.5 19.6 – 57.4	29.8 ± 6.1 18.3 – 53.0	28.9 ± 5.9 15.4 – 45.1
Baseline disease characteristics			
Duration of psoriasis at screening (years) Mean ± SD Range	18.9 ± 12.9 0.8 – 54.6	19.5 ± 13.2 0.5 – 63.7	17.8 ± 11.5 0.5 – 56.9
Concurrent psoriatic arthritis, n (%)	12 (21.1)	27 (16.4)	24 (14.4)
PASI Mean ± SD Range	19.1 ± 7.1 12.0 – 43.1	21.4 ± 8.8 12.0 – 55.5	20.8 ± 7.7 12.0 – 58.5
BSA (%), mean ± SD	24.3 ± 13.8	28.1 ± 16.7	27.6 ± 15.3
PGA, n (%) 3: moderate 4: severe	40 (70.2) 17 (29.8)	114 (69.1) 51 (30.9)	113 (67.7) 54 (32.3)
Prior biologic use,* n (%) anti-TNF anti-IL17	11 (19.3) 5 (8.8) 8 (14.0)	44 (26.7) 4 (2.4) 38 (23.0)	48 (28.7) 4 (2.4) 35 (21.0)
DLQI, mean ± SD	13.2 ± 7.6	12.8 ± 7.0	15.3 ± 7.3
WPAI domain scores, mean ± SD Absenteeism Presenteeism Work productivity loss Activity impairment	7.0 ± 24.1 18.4 ± 22.9 25.1 ± 29.7 26.1 ± 25.1	9.5 ± 24.9 21.1 ± 24.7 28.6 ± 31.2 29.8 ± 28.8	5.8 ± 16.6 28.4 ± 26.7 31.9 ± 29.5 35.1 ± 26.6

*Patients may have had exposure to >1 prior biologic but ≤2 per exclusion criteria
BMI, body mass index; BSA, body surface area; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; IL, interleukin; PASI, psoriasis area and severity index; PGA, physician's global assessment; Q2W, every 2 weeks; SD, standard deviation; TNF, tumor necrosis factor; WPAI, Work Productivity and Activity Impairment Questionnaire-Specific Health Problem

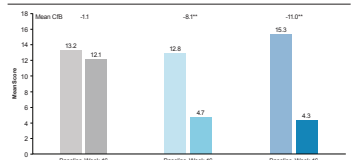
Patient-Reported Outcomes

DLQI

Baseline to Week 16

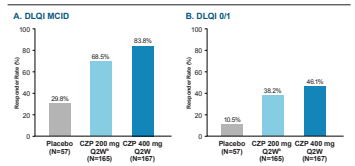
- At Week 16, patients treated with CZP 400 mg Q2W and CZP 200 mg Q2W demonstrated clinically meaningful improvements in DLQI vs placebo (**Figure 3**)
- At Week 16, CZP-treated patients demonstrated numerically greater improvement in both DLQI MCID (**Figure 4A**) and DLQI 0/1 (**Figure 4B**) responder rates compared with placebo-treated patients; the CZP 400 mg Q2W group had numerically greater improvement compared with the CZP 200 mg Q2W group

Figure 3. DLQI Mean Scores at Baseline and Week 16



**p<0.0001 vs placebo based on adjusted least squares mean difference from an ANCOVA model with treatment group, region, and prior biologic exposure (yes/no) as factors and Baseline DLQI score as a covariate using LOCF imputation
*CZP 200 mg Q2W patients received a loading dose of CZP 400 mg at Weeks 0, 2, and 4
†1 patient did not have DLQI mean score values
ANCOVA, analysis of covariance; CfB, change from Baseline; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; LOCF, last observation carried forward; Q2W, every 2 weeks

Figure 4. DLQI Minimal Clinically Important Difference[a] and DLQI 0/1 Responder Rates at Week 16

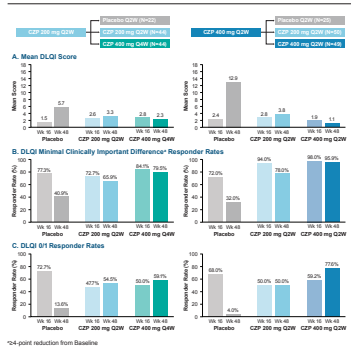


[a]4-point reduction from Baseline
*CZP 200 mg Q2W patients received a loading dose of CZP 400 mg at Weeks 0, 2, and 4
Based on nonresponse imputation
CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; LOCF, last observation carried forward; Q2W, every 2 weeks

Baseline to Week 48

- Better maintenance of response was observed at Week 48 for those patients re-randomized from CZP 400 mg Q2W or CZP 200 mg Q2W to either dose of CZP compared with placebo in DLQI (**Figure 5A**), DLQI MCID (**Figure 5B**), and DLQI 0/1 (**Figure 5C**); the greatest responses were noted in subjects treated with CZP 400 mg Q2W during both the Initial and Maintenance Periods

Figure 5. DLQI Scores and Responder Rates at Week 16 and Week 48



*24-point reduction from Baseline
Missing data handled using LOCF imputation and no statistical comparisons were performed at Week 48
CZP, certolizumab pegol; DLQI, Dermatology Quality of Life Index; LOCF, last observation carried forward; Q2W, every 2 weeks; Q4W, every 4 weeks

WPAI

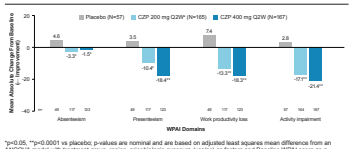
Baseline to Week 16

- As assessed by WPAI, patients receiving either CZP dose had improvements in absenteeism, presenteeism, work productivity loss, and activity impairment at Week 16 (**Figure 6**); greater improvements were generally observed in subjects receiving CZP 400 mg Q2W

Baseline to Week 48

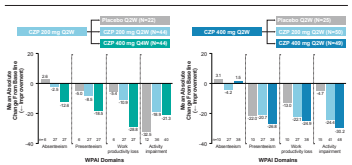
- Patients initially treated with CZP and re-randomized to the same or different dose of CZP maintained improvement across WPAI domains at Week 48 (**Figure 7**)

Figure 6. Mean Absolute Change from Baseline in WPAI Domain Scores at Week 16



*p<0.05, **p<0.0001 vs placebo; p-values are nominal and are based on adjusted least squares mean difference from an ANCOVA model with treatment group, region, prior biologic exposure (yes/no) as factors and Baseline WPAI score as a covariate using LOCF imputation
*CZP 200 mg Q2W patients received a loading dose of CZP 400 mg at Weeks 0, 2, and 4
ANCOVA, analysis of covariance; CZP, certolizumab pegol; LOCF, last observation carried forward; Q2W, every 2 weeks; WPAI, Work Productivity and Activity Impairment Questionnaire-Specific Health Problem

Figure 7. Mean Absolute Change from Baseline in WPAI Domain Scores at Week 48



Statistical comparisons not performed at Week 48
Based on observed cases
CZP, certolizumab pegol; Q2W, every 2 weeks; Q4W, every 4 weeks; WPAI, Work Productivity and Activity Impairment Questionnaire-Specific Health Problem

CONCLUSIONS

- In the Initial Treatment Period, CZP-treated patients had clinically meaningful improvements in DLQI, with a greater proportion of subjects achieving DLQI MCID and/or DLQI 0/1 compared with placebo
- Reduction in impairment while working and in daily activities, as assessed by WPAI, were improved in the CZP treatment groups at Week 16 compared with placebo
- Improvements in DLQI and WPAI were generally maintained through Week 48 in all CZP maintenance groups
  - DLQI 0/1 responder rates were maintained or improved throughout the Maintenance Treatment Period
  - Improvement in DLQI 0/1 responder rate and WPAI domains was most pronounced in the group that received CZP 400 mg Q2W in both the Initial and Maintenance Periods
- These results indicate that longer-term treatment with CZP has a positive impact on patient quality of life and functioning
- Given the substantial burden of disease experienced by patients with psoriasis, CZP has the potential to be an important new treatment option for patients with moderate-to-severe chronic plaque psoriasis

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