Certolizumab Pegol for the Treatment of Chronic Plaque Psoriasis: DLQI and WPAI Patient-Reported Outcomes From Two Ongoing Phase 3, Multicenter, Randomized, Placebo-Controlled Studies (CIMPASI-1 and CIMPASI-2)

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INTRODUCTION

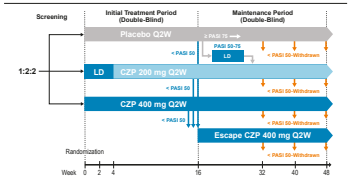
- Psoriasis affects ~3% of adults in the US and ~2-6% in Europe,[1-3] and most patients develop the disease in the third decade of life[4]
- The correlation between psoriasis and reduced quality of life has been well-documented,[5-7] with more severe forms of the disease associated with greater reduction in quality of life[5]
- Psoriasis is negatively correlated with work productivity, and patients with more severe disease experience increased productivity loss[8-10]
- Certolizumab pegol (CZP) is the only PEGylated, Fc-free, anti-tumor necrosis factor (TNF) biologic currently under development for the treatment of moderate-to-severe chronic plaque psoriasis and has demonstrated efficacy and safety in previous psoriasis trials[11,12]
- CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) are ongoing phase 3 trials designed to assess the efficacy and safety of CZP compared with placebo; patient-reported quality of life and work productivity from the first 48 weeks of these studies are presented here

METHODS

Study Design

- CIMPASI-1 and CIMPASI-2 are replicate, phase 3, randomized, double-blind, placebo-controlled, multicenter studies conducted in North America and Europe
- Patients were randomized 2:2:1 to CZP 400 mg every 2 weeks (Q2W), CZP 200 mg Q2W (following 400 mg loading dose at Weeks 0, 2, and 4), or placebo Q2W for 16 weeks (**Figure 1**)
- At Week 16, patients continued to receive treatment through Week 48 according to the following criteria:
  - CZP 400 mg Q2W- and CZP 200 mg Q2W-treated psoriasis area and severity index (PASI) 50 responders (≥50% reduction in PASI) continued to receive their initial blinded treatment
  - Placebo-treated Week 16 PASI 75 responders (≥75% reduction in PASI) continued blinded placebo treatment; PASI 50-75 responders (≥50% but <75% reduction in PASI) received CZP 200 mg Q2W (following 400 mg loading dose at Weeks 16, 18, 20)
  - Week 16 PASI 50 nonresponders entered the Escape Arm and received unblinded CZP 400 mg Q2W
- PASI 50 nonresponders at Week 32, 40, or 48 were withdrawn from the study

Figure 1. Study Design



CZP, certolizumab pegol; LD, CZP 400 mg loading dose at Weeks 0, 2, and 4 or Weeks 16, 18, and 20; PASI 50, ≥50% reduction in psoriasis area and severity index (PASI); PASI 50-75, ≥50% but <75% reduction in PASI; PASI 75, ≥75% reduction in PASI; Q2W, every 2 weeks

Patients

- Eligible patients were ≥18 years of age and had moderate-to-severe psoriasis for ≥6 months (PASI ≥12, affected body surface area [BSA] ≥10%, 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 previous treatment with CZP or with >2 biologics (including anti-TNF); had history of primary failure to any biologic or secondary failure to >1 biologic; had erythrodermic, guttate, or generalized pustular psoriasis types; or had history of current, chronic, or recurrent viral, bacterial, or fungal infections

Quality of Life and Work Productivity Assessments

- Mean change from Baseline (CfB) in Dermatology Life Quality Index (DLQI) at Week 16 (secondary endpoint) and Week 48 were assessed
- DLQI minimal clinically important difference (MCID; ≥4-point improvement[13]) responder rate, DLQI 0/1 (absolute score ≤1) responder rate, and CfB in Work Productivity and Activity Impairment Questionnaire-Specific Health Problem (WPAI) at Week 16 and Week 48 were also assessed
- Negative CfB values for DLQI and WPAI signify improvement

Statistical Analysis

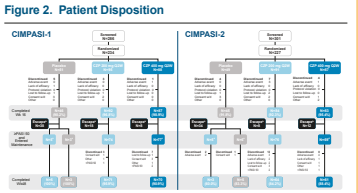
- Efficacy analyses were performed on the Randomized Set (all randomized patients)
- Inferential statistics for CfB in DLQI at Week 16 were based on an analysis of covariance (ANCOVA) model with treatment group, region, and prior biologic exposure (yes/no) as factors and Baseline DLQI score as a covariate; a similar ANCOVA model (substituting Baseline DLQI with Baseline WPAI score as a covariate) was used to calculate inferential statistics for CfB in WPAI at Week 16
- Mean CfB values are reported for continuous variables, and percentages are reported for responder variables
- Last observation carried forward (LOCF) was used to impute missing data for CfB in DLQI (Week 16 and Week 48) and WPAI (Week 16); nonresponse imputation was used for DLQI MCID and DLQI 0/1; CfB in WPAI at Week 48 was based on observed cases
- Week 16 PASI 50 nonresponders had Week 16 values carried forward to Week 48; all other missing data during the Maintenance Period were imputed using LOCF except for categorical endpoint data which were imputed as nonresponders

RESULTS

Patient Disposition, Demographics, and Baseline Characteristics

- In CIMPASI-1|CIMPASI-2, 88|87 patients were randomized to CZP 400 mg Q2W, 95|91 to CZP 200 mg Q2W, and 51|49 to placebo (**Figure 2**)
- In both studies, at least 90% of patients in each treatment arm completed Week 16 (**Figure 2**)
- Of those patients who entered the Maintenance Period in CIMPASI-1|CIMPASI-2, 90.9%|88.4% of CZP 400 Q2W patients and 95.9%|84.2% of CZP 200 mg Q2W patients completed Week 48 (**Figure 2**)
- Baseline DLQI scores were comparable across treatment groups for both studies while WPAI score trends varied slightly by study (**Table 1**)

Figure 2. Patient Disposition



*Upon entering Maintenance period, placebo-treated PASI 75 responders (≥75% reduction in PASI) continued blinded placebo treatment; PASI 50-75 responders (≥50% but <75% reduction in PASI) received CZP 200 mg Q2W
†PASI 50 nonresponders at Week 16 received open-label CZP 400 mg Q2W in the Escape Arm of the study
‡ 2 patients completed Week 16 but did not enter Maintenance Period due to adverse events
§2 patients completed Week 16 but did not enter Maintenance Period (1 loss to follow-up; 1 consent withdrawn)
CZP, certolizumab pegol; PASI 50, 50% reduction in psoriasis area and severity index (PASI); Q2W, every 2 weeks; wd, withdrawn

Table 1. Patient Demographics and Baseline Disease Characteristics

	CIMPASI-1			CIMPASI-2		
	Placebo (N=51)	CZP 200 mg Q2W (N=95)	CZP 400 mg Q2W (N=88)	Placebo (N=49)	CZP 200 mg Q2W (N=91)	CZP 400 mg Q2W (N=87)
Demographics						
Age (years), mean ± SD	47.9 ± 12.8	44.5 ± 13.1	43.6 ± 12.1	43.3 ± 14.5	46.7 ± 13.3	46.4 ± 13.5
Male, n (%)	35 (68.6)	67 (70.5)	60 (68.2)	26 (53.1)	58 (63.7)	43 (49.4)
White, n (%)	45 (88.2)	87 (91.6)	79 (89.8)	44 (89.8)	86 (94.5)	81 (93.1)
Geographic region, n (%) North America Europe	26 (51.0) 25 (49.0)	49 (51.6) 46 (48.4)	45 (51.1) 43 (48.9)	35 (71.4) 14 (28.6)	61 (67.0) 30 (33.0)	61 (70.1) 26 (29.9)
Weight (kg), mean ± SD	95.2 ± 19.5	92.6 ± 21.0	92.2 ± 21.7	87.1 ± 26.4	97.8 ± 25.6	91.8 ± 27.7
BMI (kg/m²), mean ± SD	32.2 ± 6.8	31.1 ± 7.3	30.7 ± 6.7	30.2 ± 8.0	32.8 ± 8.3	31.7 ± 8.9
Baseline Disease Characteristics						
Duration of psoriasis at screening (years), mean ± SD	18.5 ± 12.9	16.6 ± 12.3	18.4 ± 12.9	15.4 ± 12.2	18.8 ± 13.5	18.6 ± 12.4
Concurrent PsA (self-reported), n (%)	4 (7.8)	10 (10.5)	15 (17.0)	9 (18.4)	22 (24.2)	26 (29.9)
PASI score, mean ± SD	19.8 ± 7.5	20.1 ± 8.2	19.6 ± 7.9	17.3 ± 5.3	18.4 ± 5.9	19.5 ± 6.7
BSA affected (%), mean ± SD	26.1 ± 16.1	25.4 ± 16.9	24.1 ± 16.6	20.0 ± 9.5	21.4 ± 12.2	23.1 ± 11.6
Prior biologic use,* n (%) anti-TNF anti-IL17	15 (29.4) 10 (19.6) 3 (5.9)	30 (31.6) 19 (20.0) 8 (8.4)	29 (33.0) 17 (19.3) 4 (4.5)	14 (28.6) 9 (18.4) 2 (4.1)	32 (35.2) 22 (24.2) 8 (8.8)	30 (34.5) 22 (25.3) 4 (4.6)
DLQI, mean ± SD	13.9 ± 8.3	13.3 ± 7.4	13.1 ± 6.5	12.9 ± 7.3	15.2 ± 7.2	14.2 ± 7.2
WPAI domain scores, mean ± SD Absenteeism Presenteeism Work productivity loss Work activity impairment	5.2 ± 12.2 21.9 ± 25.5 24.5 ± 28.1 28.8 ± 25.1	2.3 ± 7.5 19.3 ± 25.6 20.6 ± 26.9 29.2 ± 28.0	5.2 ± 18.4 20.3 ± 25.0 24.4 ± 29.1 33.6 ± 28.8	2.5 ± 7.0 15.3 ± 17.4 16.8 ± 19.0 31.0 ± 29.6	7.0 ± 22.4 20.0 ± 25.8 25.9 ± 31.5 36.8 ± 32.7	1.3 ± 4.5 18.8 ± 19.8 19.3 ± 20.4 33.6 ± 28.9

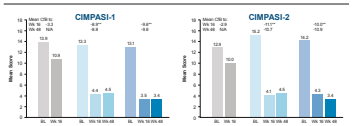
*Patients may have had exposure to >1 prior biologic but ≤2 per exclusion criteria
BMI, body mass index; BSA, body surface area; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; IL, interleukin; PASI, psoriasis area and severity index; PGA, physician's global assessment; PsA, psoriatic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

Patient-Reported Outcomes

DLQI

- At Week 16, mean CfB in DLQI demonstrated greater improvement for both CZP 400 mg Q2W and 200 mg Q2W vs placebo (**Figure 3**)
- Improvement was maintained with both CZP 400 mg Q2W and 200 mg Q2W at Week 48 (**Figure 3**)

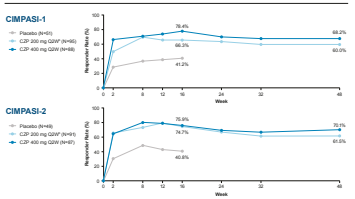
Figure 3. DLQI Mean Scores at Baseline, Week 16, and Week 48



**p<0.0001 vs placebo
*CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Statistical comparisons not performed at Week 48
P-values at Week 16 are based on adjusted least squares means 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
Week 16 PASI 50 nonresponders had Week 16 values carried forward to Week 48; all other missing data during the Maintenance Period were imputed using LOCF
ANCOVA, analysis of covariance; BL, Baseline; CfB, change from Baseline; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; LOCF, last observation carried forward; Q2W, every 2 weeks; Wk, week

- DLQI MCID responder rates were greater at Week 16 for CZP 400 mg Q2W and 200 mg Q2W vs placebo (**Figure 4**)
- Improvement was maintained for CZP 400 mg Q2W and 200 mg Q2W at Week 48 (**Figure 4**)

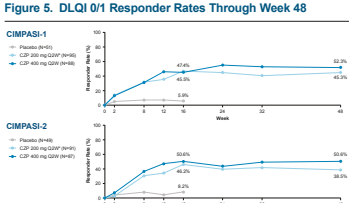
Figure 4. DLQI Minimal Clinically Important Difference[a] Responder Rates Through Week 48



[a]4-point improvement in DLQI
*CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Statistical comparisons not performed at Week 48
Week 16 PASI 50 nonresponders were imputed as nonresponders for all subsequent time points through Week 48; all other missing data were imputed via nonresponder imputation
CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; Q2W, every 2 weeks

- DLQI 0/1 responder rates were also greater at Week 16 for CZP 400 mg Q2W and 200 mg Q2W vs placebo (**Figure 5**)
- The rates were maintained for CZP 400 mg Q2W and 200 mg Q2W at Week 48 (**Figure 5**)

Figure 5. DLQI 0/1 Responder Rates Through Week 48

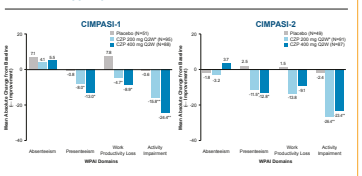


*CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Statistical comparisons not performed at Week 48
Week 16 PASI 50 nonresponders were imputed as nonresponders for all subsequent time points through Week 48; all other missing data were imputed via nonresponder imputation
CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; Q2W, every 2 weeks

WPAI

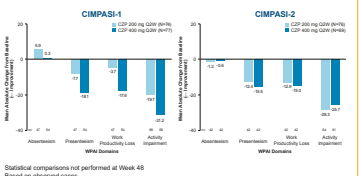
- Greater CfB to Week 16 was observed with both CZP doses compared with placebo in WPAI presenteeism (reduced work effectiveness), work productivity loss, and activity impairment domains (**Figure 6**)
- WPAI improvements for both CZP doses were maintained at Week 48 among completers (**Figure 7**)

Figure 6. Change From Baseline in WPAI Domain Scores at Week 16



*p<0.05, **p<0.0001 vs placebo
*CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
P-values are nominal and based on adjusted least squares means 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
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. 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; WPAI, Work Productivity and Activity Impairment Questionnaire–Specific Health Problem

CONCLUSIONS

- Treatment with CZP 400 mg Q2W or CZP 200 mg Q2W was associated with significant, clinically meaningful improvements in quality of life (DLQI) and work productivity (WPAI) versus placebo at Week 16
- Improvements in quality of life and work productivity were maintained through Week 48 with continued CZP 400 mg Q2W or CZP 200 mg Q2W treatment
- For most measures, improvements were numerically greater in patients receiving CZP 400 mg Q2W than in those receiving CZP 200 mg Q2W

References

1. Rachakonda et al. *J Am Acad Dermatol.* 2014;70(3):512-6. 2. Kurd et al. *J Am Acad Dermatol.* 2009;60(2):218-24. 3. Danielsen et al. *Br J Dermatol.* 2013;168(6):1303-10. 4. Farber et al. *Dermatologica.* 1974;148(1):1-18 5. Gelfand et al. *J Am Acad Dermatol.* 2004;51(5):704-8. 6. Reich et al. *Arch Dermatol Res.* 2008;300(10):537-44. 7. Revicki et al. *Dermatology.* 2008;216(3):260-70. 8. Armstrong et al. *PLoS One.* 2012;7(12):e52935. 9. Korman et al. *Dermatol Online J.* 2016;22(7):pii: 13030/qt4vb7q7hr. 10. Wu et al. *Am J Clin Dermatol.* 2009;10(6):407-10. 11. Reich et al. *Br J Dermatol.* 2012;167(1):180-90. 12. Gladman et al. *Arthritis Care Res (Hoboken).* 2014;66(7):1085-92. 13. Basra et al. *Dermatology.* 2015;230(1):27-33.

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