Durable Improvement in Patient Reported Outcomes across DLQI Subdomains Over 48 Weeks in Chronic Plaque Psoriasis Patients Treated with Certolizumab Pegol in Two Phase 3 Trials (CIMPASI-1 and CIMPASI-2)

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OBJECTIVE

- To assess the impact of certolizumab pegol on DLQI subdomains over 48 weeks' treatment in patients with moderate to severe plaque psoriasis.

BACKGROUND

- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease.
- PSO is associated with reduced health-related quality of life,[1] with a higher disease burden reported in female patients.[2]
- Certolizumab pegol (CZP) is a unique, Fc-free, PEGylated, anti-tumor necrosis factor biologic, approved by both the FDA and EMA for the treatment of moderate to severe PSO.[3,4]
- The clinical efficacy and safety of CZP in PSO has previously been reported, with durable improvements in signs and symptoms of disease over 48 weeks of treatment.[5,6]
- Here, we report the impact of CZP treatment on patient reported Dermatology Life Quality Index (DLQI) subdomains over 48 weeks.

METHODS

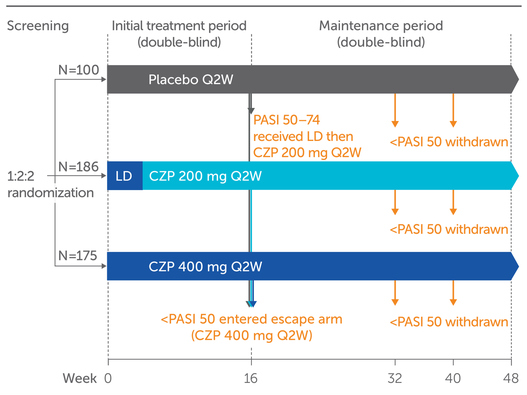
Study Design

- Patients enrolled in CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) received treatment according to the study diagram (Figure 1).

Patients

- ≥18 years of age with PSO for ≥6 months with Psoriasis Area Severity Index (PASI) ≥12, ≥10% body surface area affected, Physician's Global Assessment ≥3 on a 5-point scale.
- Candidates for systemic PSO therapy, phototherapy and/or photochemotherapy.
- Exclusion criteria: previous treatment with CZP or >2 biologics; history of primary failure to any biologic or secondary failure to >1 biologic; erythrodermic, guttate or generalized PSO types; history of current, chronic or recurrent viral, bacterial or fungal infections.

Figure 1. CIMPASI-1 and CIMPASI-2 study diagram



Only nine placebo randomized patients continued to receive placebo in the maintenance period.
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 from baseline in Psoriasis Area Severity Index; PASI 50–74: ≥50% but <75% reduction from baseline in Psoriasis Area Severity Index; Q2W: every two weeks.

Table 1. Demographics and baseline disease characteristics for all patients

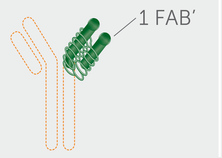
	CZP 400 mg Q2W (N=175)	CZP 200 mg Q2W[a] (N=186)	Placebo Q2W (N=100)
Age, years, mean (SD)	45.0 (12.9)	45.6 (13.2)	45.7 (13.8)
Male, n (%)	103 (58.9)	125 (67.2)	61 (61.0)
BMI, kg/m^2, mean (SD)	31.2 (7.9)	32.0 (7.8)	31.2 (7.4)
Prior biologic use, n (%)	59 (33.7)	62 (33.3)	29 (29.0)
Anti-TNF	39 (22.3)	44 (23.7)	19 (19.0)
Anti-IL-17	8 (4.6)	16 (8.6)	5 (5.0)
Anti-IL-12/IL-23	10 (5.7)	3 (1.6)	6 (6.0)
PSO duration, years, mean (SD)	18.5 (12.6)	17.7 (12.9)	17.0 (12.6)
PASI, mean (SD)	19.6 (7.3)	19.2 (7.2)	18.6 (6.6)
BSA affected, %, mean (SD)	23.6 (14.3)	23.5 (14.9)	23.1 (13.6)
PGA score, n (%)			
3 (moderate)	126 (72.0)	128 (68.8)	72 (72.0)
4 (severe)	49 (28.0)	58 (31.2)	28 (28.0)
DLQI, mean (SD)	13.7 (6.9)	14.2 (7.4)	13.4 (7.8)

[a]CZP 200 mg Q2W patients received CZP 400 mg Q2W at Weeks 0, 2 and 4. BMI: body mass index; BSA: body surface area; CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; IL: interleukin; PASI: Psoriasis Area Severity Index; PGA: Physician's Global Assessment; PSO: plaque psoriasis; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.

SUMMARY

We evaluated patient reported outcomes across DLQI subdomains for patients receiving certolizumab pegol dosed at 400 mg or 200 mg every two weeks for one year.

Certolizumab pegol (CZP)



After one year (48 weeks) of treatment with CZP 400 mg or 200 mg dosed every two weeks, mean DLQI score was improved by...

73% 62% Symptoms and feelings

78% 69% Daily activities

74% 65% Personal relationships

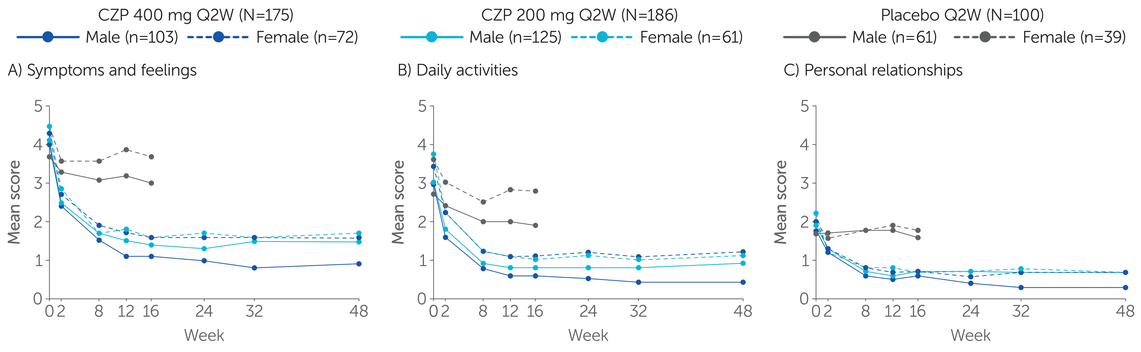
Certolizumab pegol rapidly reduced DLQI score across subdomains and response was durable to Week 48.

Table 2. Baseline DLQI subdomain scores for male and female patients

	CZP 400 mg Q2W			CZP 200 mg Q2W[a]			Placebo Q2W		
	All patients (N=175)	Male (n=103)	Female (n=72)	All patients (N=186)	Male (n=125)	Female (n=61)	All patients (N=100)	Male (n=61)	Female (n=39)
Mean score (SD)									
Symptoms and feelings	**4.1 (1.4)**	4.0 (1.3)	4.3 (1.5)	**4.2 (1.5)**	4.1 (1.6)	4.5 (1.4)	**4.0 (1.5)**	3.7 (1.4)	4.5 (1.6)
Daily activities	**3.2 (1.7)**	3.0 (1.6)	3.4 (1.8)	**3.2 (1.9)**	2.9 (1.9)	3.7 (1.7)	**3.1 (1.8)**	2.7 (1.8)	3.6 (1.6)
Leisure	**2.4 (1.9)**	2.4 (1.9)	2.5 (1.9)	**2.7 (2.0)**	2.5 (2.0)	2.9 (2.0)	**2.5 (2.2)**	2.1 (2.0)	2.9 (2.3)
Work and school	**0.9 (1.0)**	0.9 (0.9)	0.8 (1.0)	**0.9 (1.0)**	0.8 (1.0)	1.0 (1.1)	**0.9 (1.1)**	0.9 (1.0)	0.9 (1.1)
Personal relationships	**1.9 (1.9)**	1.8 (1.7)	2.0 (2.1)	**2.0 (1.9)**	1.9 (1.9)	2.2 (1.9)	**1.8 (2.1)**	1.7 (2.0)	2.0 (2.3)
Treatment	**1.2 (1.1)**	1.2 (1.0)	1.3 (1.1)	**1.3 (1.1)**	1.2 (1.1)	1.4 (1.1)	**1.2 (1.0)**	1.1 (1.1)	1.3 (1.0)

[a]CZP 200 mg Q2W patients received CZP 400 mg Q2W at Weeks 0, 2 and 4. Lower scores indicate greater quality of life. Symptoms and feelings: itchy/sore/painful stinging; embarrassed/self-conscious. Daily activities: interference with shopping/home/garden; influences clothes worn. Leisure: affects social/leisure activities; makes it difficult to do any sports. Personal relationships: problems with partners/friends/relatives; any sexual difficulties. Treatment: how much of a problem is treatment. CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; Q2W: every two weeks; SD: standard deviation.

Figure 2. DLQI subdomain mean scores through Weeks 0–48 for male and female patients



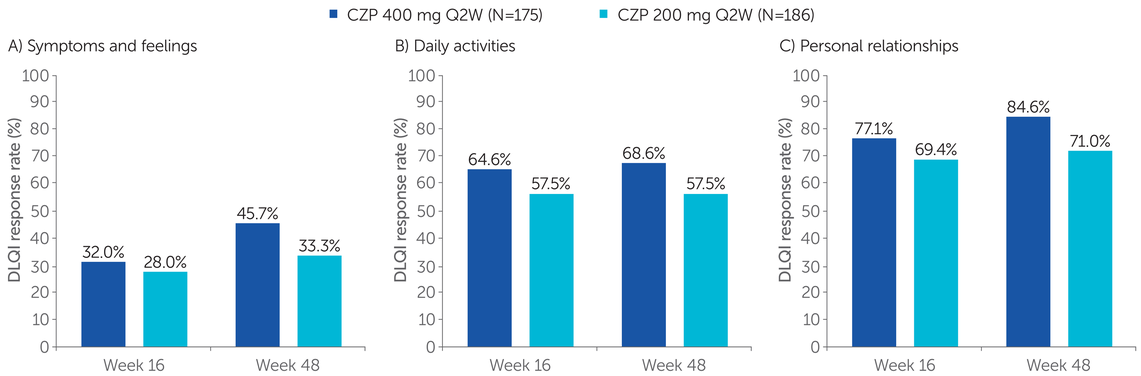
Mean score (SD)		CZP 400 mg Q2W	CZP 200 mg Q2W[a]	Placebo Q2W
Week 16	Male	1.1 (1.1)	1.4 (1.4)	3.0 (1.6)
	Female	1.6 (1.6)	1.6 (1.4)	3.7 (1.5)
	All patients	1.3 (1.4)	1.4 (1.4)	3.3 (1.6)
Week 48	Male	0.9 (1.2)	1.5 (1.7)	-
	Female	1.6 (1.8)	1.7 (1.7)	-
	All patients	1.2 (1.5)	1.6 (1.7)	-

Mean score (SD)		CZP 400 mg Q2W	CZP 200 mg Q2W[a]	Placebo Q2W
Week 16	Male	0.6 (1.1)	0.8 (1.3)	1.9 (1.6)
	Female	1.1 (1.7)	1.0 (1.2)	2.8 (1.3)
	All patients	0.8 (1.4)	0.8 (1.3)	2.2 (1.6)
Week 48	Male	0.4 (0.8)	0.9 (1.5)	-
	Female	1.2 (1.8)	1.1 (1.4)	-
	All patients	0.7 (1.4)	1.0 (1.4)	-

Mean score (SD)		CZP 400 mg Q2W	CZP 200 mg Q2W[a]	Placebo Q2W
Week 16	Male	0.6 (1.3)	0.7 (1.4)	1.6 (2.0)
	Female	0.7 (1.5)	0.7 (1.3)	1.8 (1.7)
	All patients	0.6 (1.4)	0.7 (1.3)	1.7 (1.9)
Week 48	Male	0.3 (1.0)	0.7 (1.4)	-
	Female	0.7 (1.7)	0.7 (1.3)	-
	All patients	0.5 (1.3)	0.7 (1.4)	-

LOCF imputation. Lower scores indicate greater quality of life. [a]CZP 200 mg Q2W patients received CZP 400 mg Q2W at Weeks 0, 2 and 4. CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; Q2W: every two weeks; SD: standard deviation.

Figure 3. Response rates for DLQI subdomains at Weeks 16 and 48 for all patients



Logistic regression with LOCF imputation. DLQI response rates were defined as a score of 0 (response of 'not at all' or 'not relevant'), indicating no impact of skin on that questionnaire item. Higher scores indicate greater quality of life.
CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; Q2W: every two weeks.

Study Assessments

- DLQI subdomains were assessed through Weeks 0–48:
  - Symptoms and feelings (itchy/sore/painful stinging; embarrassed/self-conscious)
  - Daily activities (interference with shopping/home/garden; influence on clothes worn)
  - Personal relationships (problems with partners/friends/relatives; any sexual difficulties)
  - Leisure (affects social/leisure activities; makes it difficult to do any sports)
  - Work and school (prevents or causes problems with work or studying)
  - Treatment (how much of a problem is treatment)
- DLQI response rates were defined as a score of 0 (response of 'not at all' or 'not relevant'), indicating no impact of skin on that questionnaire item.

Statistical Analyses

- Missing data were imputed as last observation carried forward (LOCF); patients who did not achieve at least a 50% improvement from baseline in PASI (PASI 50) at Weeks 16, 32 or 40 had their Week 16, 32 or 40 value carried forward to Week 48.
- DLQI response rates are the adjusted probabilities from a logistic regression model with factors for treatment group, region, study, prior biologic exposure, study x region, and study x prior biologic exposure.

RESULTS

Patient Disposition

- 175, 186, and 100 patients were randomized to CZP 400 mg every two weeks (Q2W), CZP 200 mg Q2W or placebo Q2W.
- Baseline demographics are shown in Table 1.
- At baseline, patients reported the greatest impact of disease on symptoms and feelings. Work and school was least affected (Table 2).
- Female patients reported higher baseline DLQI scores for symptoms and feelings, personal relationships and daily activities (Table 2).

DLQI Mean Score

- DLQI mean score reduced through Weeks 0–16 for CZP-treated patients compared to placebo, across subdomains (Figure 2).
- DLQI mean score was maintained, or further improved, through Weeks 16–48 for patients receiving CZP (Figure 2).
- At Week 48, the greatest change from baseline was reported in symptoms and feelings, followed by daily activities.
- Similar trends were also observed for leisure, work and school, and treatment.
- Change from baseline across all DLQI subdomains was similar between male and female patients.

DLQI Response Rates

- The largest improvements in response rate were observed for the subdomains shown in Figure 3. However, similar trends were also reported for leisure, work and school, and treatment.

CONCLUSIONS

- CZP dosed at both 400 mg Q2W and 200 mg Q2W was effective at reducing DLQI scores over the first 16 weeks of treatment.
- Responses were durable over a further 32 weeks of treatment to Week 48.
- Patients receiving CZP 400 mg Q2W consistently reported greater quality of life improvements across all subdomains.
- At baseline, female patients reported a greater burden of disease for symptoms and feelings, personal relationships and daily activities, indicated by higher mean baseline scores.

References: **1.** Kimball AB. *et al.* J Eur Acad Dermatol Venereol 2010;24:989–1004; **2.** Lesuis N. *et al.* BMC Medicine 2012;10:82. Available at: http://www.biomedcentral.com/1741-7015/10/82; **3.** Certolizumab Pegol Prescribing information. Available at http://www.accessdata.fda.gov; **4.** Certolizumab Pegol Summary of Product Characteristics. Available at http://www.ema.europa.eu/ema; **5.** Gottlieb AB. *et al.* J Am Acad Dermatol 2018;79:302–14.e6; **6.** Lebwohl M. *et al.* J Am Acad Dermatol 2018;79:266–76.e5.

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