Maintenance of Response With Certolizumab Pegol for the Treatment of Chronic Plaque Psoriasis: 48-Week Results From Two Ongoing Phase 3, Multicenter, Randomized, Placebo-Controlled Studies (CIMPASI-1 and CIMPASI-2)

Kristian Reich,[1] Andrew Blauvelt,[2] Diamant Thaçi,[3] Craig Leonardi,[4] Yves Poulin,[5] Daniel Burge,[6] Luke Peterson,[7] Janice Drew,[6] Catherine Arendt,[8] Alice B. Gottlieb[9]

[1]Dermatologikum Hamburg and SCIderm Research Institute, Hamburg, Germany; [2]Oregon Medical Research Center, Portland, OR; [3]University of Lübeck, Lübeck, Germany; [4]Central Dermatology and Saint Louis University School of Medicine, St. Louis, MO; [5]Centre de Recherche Dermatologique du Québec Métropolitain, Québec, Canada; [6]Dermira, Inc., Menlo Park, CA; [7]UCB BioSciences, Inc., Raleigh, NC; [8]UCB Pharma, Brussels, Belgium; [9]New York Medical College, Valhalla, NY

INTRODUCTION

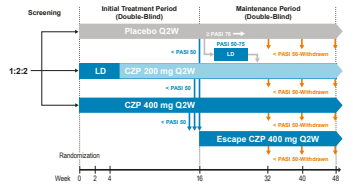
- Psoriasis affects ~3% of adults in the US[1,2] and ~2-6% in Europe,[3] and most patients develop the disease in the third decade of life[4]
- Therapy for patients with chronic plaque psoriasis varies per the severity of the disease, with topical therapies and/or phototherapy used to treat limited or mild psoriasis and photochemotherapy, cyclosporine, methotrexate, apremilast, or biologics such as tumor necrosis factor (TNF) inhibitors, anti-IL17s, and anti-IL12/23s used to treat moderate-to-severe forms
- Certolizumab pegol (CZP) is the only PEGylated, Fc-free, anti-TNF biologic currently under development for the treatment of moderate-to-severe chronic plaque psoriasis and has demonstrated positive results in previous psoriasis trials[5,6]
- CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) are ongoing phase 3 trials designed to assess the efficacy and safety of CZP compared with placebo; results from the first 48 weeks of the two studies are presented here

METHODS

Study Design

- CIMPASI-1 and CIMPASI-2 are replicate, phase 3, multicenter studies conducted in North America and Europe, consisting of randomized, double-blind, placebo-controlled periods for the first 48 weeks followed by 96 weeks of open-label observation
- 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, 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)
  - PASI 50 nonresponders at Week 16 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 chronic plaque 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 >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

Study Assessments

- Coprimary endpoints were PASI 75 and PGA 0/1 ('clear' or 'almost clear' with ≥2-category improvement) at Week 16
- Secondary endpoints reported here were PASI 90 at Week 16 and PASI 75 and PGA 0/1 at Week 48; PASI 90 at Week 48 was included as an additional endpoint
- Safety evaluation included assessment of treatment-emergent adverse events (TEAEs)

Statistical Analysis

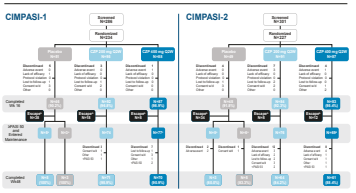
- All efficacy analyses were performed on the Randomized Set (all randomized patients)
- Logistic regression models with factors of treatment group, region, and prior biologic exposure (yes/no) were used to analyze PASI 75, PGA 0/1, and PASI 90 responder rates (Week 16)
  - The Markov chain Monte Carlo (MCMC) method for multiple imputation was used to account for missing data[7]
- Safety assessments were performed on the Safety Set, which included all randomized patients who received ≥1 dose of study medication

RESULTS

Patient Disposition, Demographics, and Baseline Characteristics

- In both studies, at least 90% of patients in each treatment arm completed Week 16, and the highest Week 16 completion rates were in the CZP 400 mg Q2W treatment group (**Figure 2**)
- Of those patients who entered the blinded Maintenance Period in CIMPASI-1|CIMPASI-2, 90.9%|88.4% of CZP 400 Q2W patients and 95.9%|84.2% CZP 200 mg Q2W patients completed Week 48 (**Figure 2**)
- Baseline PASI and PGA scores were comparable across treatment groups for both studies (**Table 1**)
- Roughly one-third of study participants reported prior biologic use, and the proportion across treatment arms was similar (**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 (not part of this report)
‡Two patients completed Week 16 but did not enter Maintenance Period due to adverse events
§Two 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=100)	CZP 400 mg Q2W (N=144)	Placebo (N=49)	CZP 200 mg Q2W (N=95)	CZP 400 mg Q2W (N=129)
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/m^2), 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,* 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
DLQI score, 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
BSA (%), 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
PGA score, n (%) 3: moderate 4: severe	35 (68.6) 16 (31.4)	62 (65.3) 33 (34.7)	65 (73.9) 23 (26.1)	37 (75.5) 12 (24.5)	66 (72.5) 25 (27.5)	61 (70.1) 26 (29.9)
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)
Any prior systemic psoriasis treatment, n (%)	36 (70.6)	66 (69.5)	61 (69.3)	36 (73.5)	65 (71.4)	63 (72.4)

*Presence of concurrent PsA was self-reported
†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

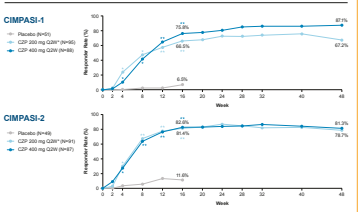
Coprimary Endpoints

- At Week 16, responder rates were greater for CZP 400 mg Q2W and 200 mg Q2W versus placebo for PASI 75 and PGA 0/1 (p<0.0001 for all) (**Figure 3**, **Figure 4**)

Secondary Endpoints

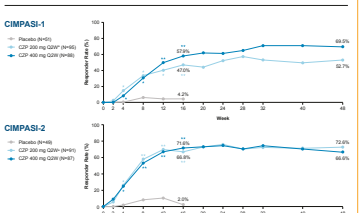
- CZP 400 mg Q2W and 200 mg Q2W PASI 75 responder rates were maintained to Week 48 (**Figure 3**)
- PGA 0/1 responder rates were also maintained to Week 48 for patients who continued to receive either dose of CZP during the Maintenance Period (**Figure 4**)
- At Week 16, PASI 90 responder rates were greater for CZP 400 mg Q2W and 200 mg Q2W versus placebo (p<0.0001 for both) (**Figure 5**)
- PASI 90 responder rates continued to improve beyond Week 16 and the difference between dose groups increased by Week 48 in CIMPASI-1 (**Figure 5**)

Figure 3. PASI 75 Responder Rates From Baseline to Week 48



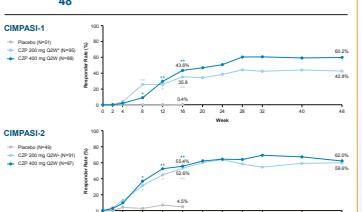
*p<0.05, **p<0.0001 versus placebo
•CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Based on logistic regression model with factors for treatment, region, and prior biologic exposure (yes/no)
Week 16 PASI 50 nonresponders were imputed as nonresponders throughout the Maintenance period; all other missing data were imputed via multiple imputation (MCMC method)
CZP, certolizumab pegol; MCMC, Markov chain Monte Carlo; PASI 75, ≥75% reduction in psoriasis area and severity index; Q2W, every 2 weeks

Figure 4. PGA 0/1 Responder Rates From Baseline to Week 48



*p<0.05, **p<0.0001 versus placebo
•CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Based on logistic regression model with factors for treatment, region, and prior biologic exposure (yes/no)
Week 16 PASI 50 nonresponders were imputed as nonresponders throughout the Maintenance period; all other missing data were imputed via multiple imputation (MCMC method)
CZP, certolizumab pegol; MCMC, Markov chain Monte Carlo; PGA 0/1, 'clear' or 'almost clear' with ≥2 category improvement (on 5-point scale) in physician's global assessment; Q2W, every 2 weeks

Figure 5. PASI 90 Responder Rates From Baseline to Week 48



*p<0.05, **p<0.0001 versus placebo
•CZP 200 mg Q2W patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4
Based on logistic regression model with factors for treatment, region, and prior biologic exposure (yes/no)
Week 16 PASI 50 nonresponders were imputed as nonresponders throughout the Maintenance period; all other missing data were imputed via multiple imputation (MCMC method)
CZP, certolizumab pegol; MCMC, Markov chain Monte Carlo; PASI 90, ≥90% reduction in psoriasis area and severity index; Q2W, every 2 weeks

Safety

- For CZP 400 mg Q2W and 200 mg Q2W vs placebo, TEAE|serious TEAE incidence rates per 100 patient-years from Baseline to Week 16 were 375.9|19.0 and 292.3|6.9 vs 297.1|6.8 in CIMPASI-1, and 405.7|15.3 and 308.7|7.4 vs 388.9/0 in CIMPASI-2
- For CZP 400 mg Q2W and 200 mg Q2W, TEAE|serious TEAE incidence rates per 100 patient-years was lower from Baseline to Week 48 compared with rates per 100 patient-years from Baseline to Week 16 (257.6|10.4 and 218.3|5.3 in CIMPASI-1, and 277.5|7.5 and 236.0|9.7 in CIMPASI-2) (**Table 2**)
- One serious infection was reported in the CZP 400 mg Q2W group in CIMPASI-1, and one in the CZP 400 mg Q2W group in CIMPASI-2; one death, due to motor vehicle accident, was reported in the CZP 400 mg Q2W group in CIMPASI-1 (**Table 2**)
- After 48 weeks of treatment, TEAEs occurring in >10% of all CZP-treated patients were nasopharyngitis and upper respiratory tract infection (**Table 3**)

Table 2. Adverse Events From Baseline to Week 48

	CIMPASI-1		CIMPASI-2	
	CZP 200 mg Q2W (N=100)[a]	CZP 400 mg Q2W (N=144)[a]	CZP 200 mg Q2W (N=95)[a]	CZP 400 mg Q2W (N=129)[a]
TEAEs, n (%) [incidence rate[a]]				
All	72 (72.0) [218.3]	111 (77.1) [257.6]	73 (76.8) [236.0]	103 (79.8) [277.5]
Serious	4 (4.0) [5.3]	11 (7.6) [10.4]	7 (7.4) [9.7]	7 (5.4) [7.5]
Discontinuations due to TEAE, n (%)[b]	0	5 (3.5)	8 (8.4)	8 (6.2)
Deaths, n (%)[b]	0	1 (0.7)	0	0
TEAEs of interest, n (%) [incidence rate[a]]				
Infections and infestations	50 (50.0) [102.5]	76 (52.8) [115.9]	48 (50.5) [98.1]	68 (52.7) [111.2]
Latent tuberculosis	0	1 (0.7) [0.9]	0	0
Active tuberculosis	0	0	0	0
Candida infections	1 (1.0) [1.3][c]	0	1 (1.1) [1.4][c]	2 (1.6) [2.1][c]
Oral fungal infection	0	0	0	1 (0.8) [1.0]
Fungal skin infection	0	1 (0.7) [0.9]	0	0
Herpes Zoster	0	0	1 (1.1) [1.4]	0
Herpes dermatitis	0	0	0	1 (0.8) [1.0]
Epstein-Barr viral infection	0	0	1 (1.1) [1.4]	0
Serious infections	0	1 (0.7) [0.9]	0	1 (0.8) [1.1]
Non-melanoma skin cancer[f]	0	1 (0.7) [0.9]	0	1 (0.8) [1.1]
Malignancy (excluding non-melanoma skin cancer)	0	0	0	0
IBD flare	0	0	0	0
Depression	0	2 (1.4) [1.8]	1 (1.1) [1.4]	2 (1.6) [2.1]

[a]Incidence of new cases per 100 subject-years
[b]Incidence rate not calculated
[c]Oral candidiasis
[d]Vulvovaginal candidiasis
[e]Nail Candida
[f]Both malignancies were basal cell carcinomas
[g]Patients who switched doses could have been counted in both CZP doses
Patients initially randomized to CZP 200 mg Q2W who received CZP 400 mg Q2W in the Escape Arm were counted in both CZP doses
CZP, certolizumab pegol; IBD, inflammatory bowel disease; TEAE, treatment-emergent adverse event

Table 3. Most Frequently Reported TEAEs (≥5% in Any Group): Baseline to Week 48

n (%), [incidence rate[a]]	CIMPASI-1 CZP 200 mg Q2W (n=100)[b]	CIMPASI-1 CZP 400 mg Q2W (N=144)[b]	n (%), [incidence rate[a]]	CIMPASI-2 CZP 200 mg Q2W (n=95)[b]	CIMPASI-2 CZP 400 mg Q2W (N=129)[b]
Nasopharyngitis	28 (28.0) [46.5]	40 (27.8) [46.9]	Nasopharyngitis	17 (17.9) [26.4]	25 (19.4) [29.0]
URTI	12 (12.0) [17.2]	13 (9.0) [12.8]	URTI	11 (11.6) [16.1]	13 (10.1) [14.5]
Arthralgia	6 (6.0) [8.2]	2 (1.4) [1.8]	Hypertension	5 (5.3) [7.2]	8 (6.2) [8.6]
Headache	6 (6.0) [8.2]	12 (8.3) [11.7]	Urinary tract infection	5 (5.3) [7.1]	5 (3.9) [5.3]
			Pruritus	2 (2.1) [2.8]	8 (6.2) [8.8]
			Pharyngitis	6 (6.3) [8.5]	3 (2.3) [3.2]
			Bronchitis	2 (2.1) [2.8]	7 (5.4) [7.5]

[a]Incidence of new cases per 100 subject-years
[b]Patients who switched doses could have been counted in both CZP doses
Patients initially randomized to CZP 200 mg Q2W who received CZP 400 mg Q2W in the Escape Arm were counted in both CZP doses
CZP, certolizumab pegol; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection

CONCLUSIONS

- Treatment with CZP 400 mg Q2W or CZP 200 mg Q2W for 16 weeks was associated with statistically significant, clinically meaningful improvements for all endpoints analyzed (PASI 75, PGA 0/1, and PASI 90) compared with placebo
- Response rates were maintained at Week 48 with both CZP doses
- For most measures, improvement at both Week 16 and Week 48 was numerically greatest in patients receiving CZP 400 mg Q2W
- TEAEs were consistent with the known safety profile of anti-TNF therapy and no new safety signals were observed with CZP at any dose over 48 weeks

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