Durable Efficacy of Certolizumab Pegol Dosed at 400 mg Every Two Weeks Over 128 Weeks in Patients with Plaque Psoriasis Enrolled in Three Phase 3 Trials (CIMPASI-1, CIMPASI-2 and CIMPACT)

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SDDS Virtual Experience 2020 | September 11–13, 2020

Objectives

To assess the long-term efficacy of CZP dosed at 400 mg every two weeks, in addition to the durability of response in patients who achieve PASI 75 after an initial 16 weeks of treatment.

Background

Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease that affects around 2–4% of adults.[1]

Certolizumab pegol (CZP) is a unique Fc-free, PEGylated, anti-tumor necrosis factor approved by the FDA and EMA for the treatment of moderate to severe PSO.[2,3]

In phase 3 trials, patients with moderate to severe PSO have demonstrated a durable response to CZP over one year (48 weeks) of double-blinded treatment.[4,5]

Here, we report the long-term clinical responses for patients with PSO who received open-label treatment with CZP dosed at 400 mg every two weeks (Q2W) for up to 128 weeks.

Methods

Study Design

- Data were pooled from three phase 3 trials in adults with PSO: CIMPASI-1 (NCT02326298), CIMPASI-2 (NCT02326272), and CIMPACT (NCT02346240). Full study designs have been reported previously.[4,5]
- At Week 0, patients were randomized to receive CZP 200 mg Q2W (400 mg loading dose at Weeks 0/2/4), CZP 400 mg Q2W, etanercept (CIMPACT only), or placebo.
- Patients included in this analysis:
  - Were randomized to placebo at Week 0
  - Failed to achieve a 50% improvement from baseline in Psoriasis Area and Severity Index (PASI 50) at Week 16
  - Entered the open-label escape arm where they received CZP 400 mg Q2W for up to 128 weeks **(Figure 1)**
- Dosing adjustment was permitted from Week 48 of the study based on PASI response and the investigator's discretion.
- Patients who did not achieve PASI 50 at any visit after receiving unblinded CZP 400 mg Q2W for 16 weeks were withdrawn from the study.

Patients

- Included patients were ≥18 years of age with PSO for ≥6 months (with PASI ≥12, ≥10% body surface area [BSA] affected and Physician's Global Assessment [PGA] ≥3 on a 5-point scale), and were candidates for systemic PSO therapy, phototherapy and/or photochemotherapy.
- Patients were excluded if they had 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; or a history of current, chronic or recurrent viral, bacterial or fungal infections.

Statistical Analysis

- Proportions of patients achieving a 75% or 90% improvement from baseline in PASI (PASI 75 or PASI 90), PGA 0/1, or Dermatology Life Quality Index (DLQI) 0/1 through 128 weeks of treatment with CZP 400 mg Q2W (Weeks 16–144 of the study) are reported.
- Responder rates in the subset of patients who achieved a PASI 75 response following 16 weeks of treatment with CZP 400 mg Q2W in the escape arm are also reported.
- Estimates of responder rate were based on the simple average response. Patients mandatorily withdrawn from the study were treated as non-responders at subsequent timepoints; all other missing data were imputed using Markov Chain Monte Carlo (MCMC) methodology.

Results

Patient Population and Baseline Characteristics

- 116 patients did not achieve PASI 50 after 16 weeks of placebo treatment, and entered the open-label CZP 400 mg Q2W escape arm. Baseline demographics of these patients are shown in **Table 1**.

Response to CZP Treatment

- Patients demonstrated a rapid response during the first 16 weeks of CZP 400 mg Q2W treatment; 74.7% of patients achieved PASI 75 at Week 32, 48.7% achieved PASI 90, and 65.4% achieved PGA 0/1 **(Figure 2A)**.
- Initial responder rates were sustained to Week 144 **(Figure 2A)**.
- Similar trends were observed for DLQI 0/1 **(Figure 2B)**.

Maintenance of Response

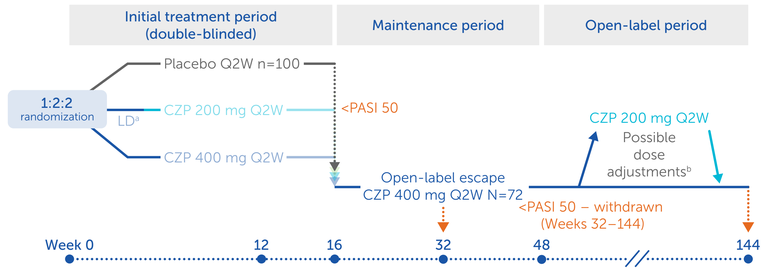
- Of the 82 patients who achieved PASI 75 after 16 weeks of CZP 400 mg Q2W treatment (Week 32):
  - The majority (82.4%) maintained PASI 75 over a further 112 weeks of treatment **(Figure 3A)**
  - 65.9% also achieved PASI 90 at Week 32, and this value was maintained to 64.4% at Week 144 **(Figure 3A)**
  - 61.0% also reported DLQI 0/1 at Week 32 which increased to 68.0% at Week 144 **(Figure 3B)**

Conclusions

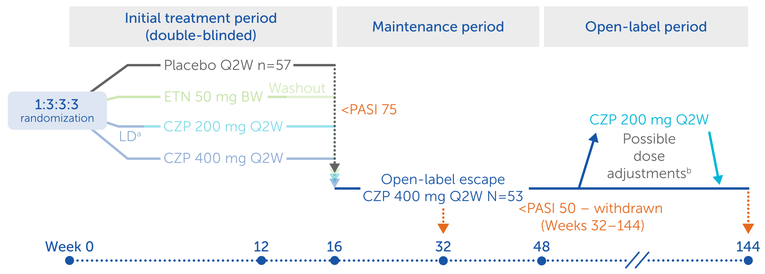
CZP dosed at 400 mg Q2W offers a durable, long-term treatment option for patients with moderate to severe PSO.

Figure 1 Study designs

A) CIMPASI-1 and CIMPASI-2



B) CIMPACT



[a]Loading dose of CZP 400 mg Q2W at Weeks 0, 2, and 4; [b]Depending on PASI response, any dose adjustments were either mandatory or at the investigator's discretion.

Table 1 Demographics and baseline characteristics of included patients

	Placebo → CZP 400 mg Q2W (N=116)
Age (years), mean ± SD	46.4 ± 12.6
Male, n (%)	76 (65.5)
Caucasian, n (%)	108 (93.1)
Weight (kg), mean ± SD	94.0 ± 26.1
Duration of PSO (years), mean ± SD	17.7 ± 12.1
Concomitant PsA,[a] n (%)	19 (16.4)
PASI, mean ± SD	18.8 ± 6.7
BSA (%), mean ± SD	23.2 ± 13.9
PGA score, n (%)	
3: moderate	81 (69.8)
4: severe	35 (30.2)
DLQI total score, mean ± SD	12.9 ± 7.4
Any prior systemic therapy use for PSO, n (%)	87 (75.0)
Prior biologic use, n (%)	33 (28.4)
anti-TNF	19 (16.4)
anti-IL-17	12 (10.3)
anti-IL-12/IL-23	6 (5.2)

[a]Presence of concurrent PsA was self-reported.

Figure 2 Response over 128 weeks of treatment with CZP 400 mg Q2W

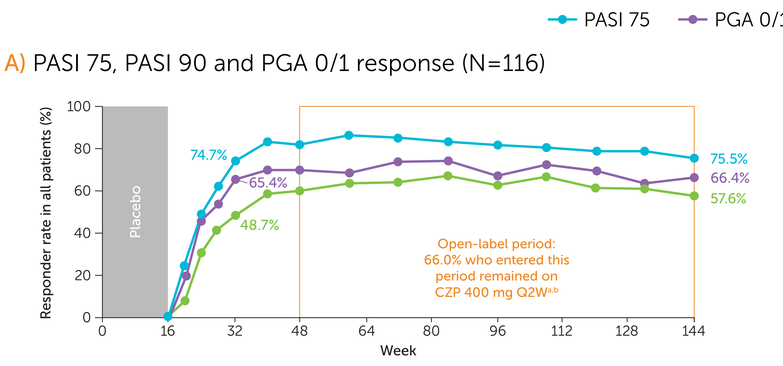
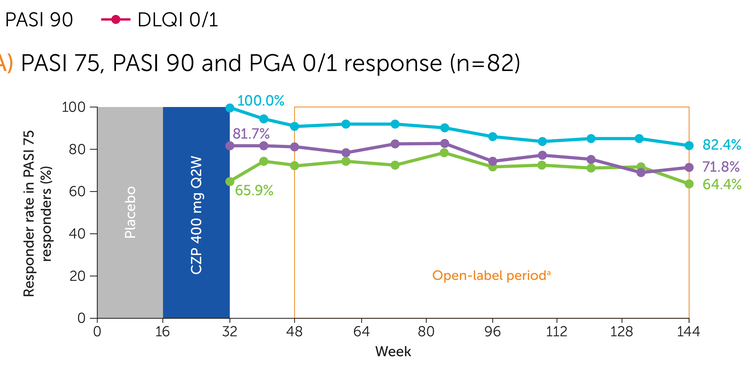


Figure 3 Maintenance of response in patients who achieved PASI 75 following 16 weeks of treatment with CZP 400 mg Q2W



Patients who were mandatorily withdrawn from Week 32 onwards were treated as non-responders at subsequent timepoints. Other missing data were imputed using MCMC methodology and responder rates reflect the simple average response and include patients who did and did not dose adjust during the open-label period. [a]Depending on PASI response, dose reductions to CZP 200 mg Q2W were permitted at the discretion of the investigator; [b]64 of the 97 patients (66.0%) who completed the trial to Week 48 and continued into the open-label period remained on CZP 400 mg Q2W for the remainder of the trial.

BSA: body surface area; BW: bi-weekly CZP: certolizumab pegol; DLQI 0/1: Dermatology Life Quality Index of 0 or 1; no effect of disease on quality of life; ETN: etanercept; IL: interleukin; LD: loading dose; MCMC: Markov Chain Monte Carlo; PASI: Psoriasis Area Severity Index; PASI 50/75/90: 50%/75%/90% improvement from baseline in PASI; PGA 0/1: Physician's Global Assessment score of 0 or 1 ("clear" or "almost clear") with ≥2-point improvement from baseline; PsA: psoriatic arthritis; PSO: plaque psoriasis; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.

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References: [1]Parisi R. *et al.* J Invest Dermatol 2013;133:377–85; [2]Certolizumab Pegol Prescribing Information. Available at http://www.accessdata.fda.gov; [3]Certolizumab Pegol Summary of Product Characteristics. Available at http://www.ema.europa.eu/ema; [4]Gottlieb AB. *et al.* JAAD 2018;79:302–14; [5]Lebwohl M. *et al.* JAAD 2018;79:266–76. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: KG, RBW, ABG, AB, DT, YP, MB, FB, CA, KR; Drafting of the publication, or revising it critically for important intellectual content: KG, RBW, ABG, AB, DT, YP, MB, FB, CA, KR; Final approval of the publication: KG, RBW, ABG, AB, DT, YP, MB, FB, CA, KR. **Author Disclosures: KG:** Honoraria and/or research support from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira Inc., Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; **RBW:** Research grants and/or consulting fees from AbbVie, Almirall, Amgen, Arena, Avillion, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; **ABG:** Current consulting/advisory board agreements with AbbVie, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Incyte, Janssen, LEO Pharma, Novartis, Sun Pharma, UCB Pharma, and XBiotech; Research and educational grants from Boehringer Ingelheim, Incyte, Janssen, Novartis, UCB Pharma, and XBiotech; **AB:** Served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira Inc., Eli Lilly, Forte, Galderma, Janssen, LEO Pharma, Novartis, Ortho, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma, and as a paid speaker for AbbVie; **DT:** Honoraria for participation on ad boards, as a speaker or for consultancy from AbbVie, Almiral, Amgen, Boehringer Ingelheim, Celgene, Dignity, Dr. Reddy's Laboratories, Galapagos, GSK, Janssen, LEO Pharma, Morphosis, MSD, Eli Lilly, Novartis, Pfizer, Sandoz-Hexal, Pfizer, Regeneron, Sanofi, and UCB Pharma; Research grants from Celgene and Novartis; **YP:** Investigator (research grants) from AbbVie, Baxter, Boehringer Ingelheim, Celgene, Centocor/Janssen, Eli Lilly, EMD Serono, GSK, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Takeda, and UCB Pharma; Speaker (honoraria) from AbbVie, Celgene, Janssen, Eli Lilly, LEO Pharma, Novartis, Regeneron, and Sanofi Genzyme; **MB, FB, CA:** Employees of UCB Pharma; **KR:** AbbVie, Affibody, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Covagen, Forward Pharma, GSK, Janssen, Kyowa Kirin, LEO Pharma, Eli Lilly, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Takeda, UCB Pharma, Valeant, and Xenoport. **Acknowledgements:** The studies were funded by Dermira Inc. in collaboration with UCB Pharma. UCB Pharma is the regulatory sponsor of certolizumab pegol in psoriasis. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Susanne Wiegratz, UCB Pharma, Monheim am Rhein, Germany for publication coordination and Joe Dixon, PhD, Costello Medical, Cambridge, UK, for medical writing and editorial assistance. All costs associated with development of this poster were funded by UCB Pharma.

Previously presented at AAD 2020