Reductions in Absolute PASI Over 144 Weeks of Treatment with Certolizumab Pegol in Patients with Plaque Psoriasis: Pooled Analysis from Two Phase 3 Trials (CIMPASI-1 and CIMPASI-2)

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Objectives

To assess the long-term maintenance of absolute PASI <5, <3, and the more stringent <2, over three years in patients enrolled in two identically designed CZP in PSO phase 3 trials, the data from which were pooled.

Background

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

Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-tumor necrosis factor (anti-TNF) that has demonstrated efficacy and safety in the treatment of moderate to severe PSO.[2,3]

An absolute Psoriasis Area and Severity Index (PASI) score ≤5 has been associated with good quality of life in patients with PSO,[4] while a PASI score ≤3 is considered excellent.[5,6]

Methods

Study Design

- Data were pooled from two phase 3 trials in adults with PSO: CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272). Full study designs have been reported previously.[2]
- At Week 0, patients were randomized 2:2:1 to receive CZP 200 mg every 2 weeks (Q2W) (400 mg loading dose at Weeks 0/2/4), CZP 400 mg Q2W, or placebo.
- Patients included in this analysis were either:
  - Randomized to CZP 200 mg Q2W or CZP 400 mg Q2W at Week 0, or;
  - Randomized to placebo at Week 0, did not achieve ≥50% improvement from baseline in PASI (PASI 50) at Week 16, and entered the open-label escape arm where they received CZP 400 mg Q2W for up to 128 weeks **(Figure 1)**
- Patients receiving double-blinded treatment who achieved PASI 50 at Week 48 received CZP 200 mg Q2W upon entry to the open-label extension (OLE).
- Dosing adjustment was permitted from Week 48 onwards based on PASI response and the investigator's discretion.

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; current, or a history of chronic or recurrent viral, bacterial or fungal infections.

Statistical Analysis

- Proportions of patients achieving an absolute PASI score <5, <3, and <2 through Weeks 0–144 (Week 0 CZP-randomized patients) or Weeks 16–144 (placebo-randomized Week 16 PASI 50 non-responders) are reported.
- Patients who were withdrawn at Week 32 or later due to lack of PASI 50 response, and those randomized to CZP who entered the escape arm at Week 16, were treated as non-responders at subsequent timepoints. All other missing data were imputed using Markov Chain Monte Carlo (MCMC) multiple imputation methodology. Responder rates reflect the simple average response; calculations included patients who did and did not dose adjust during the OLE.

Results

Patient Population and Baseline Characteristics

- At Week 0, 186 and 175 patients were randomized to CZP 200 mg Q2W and CZP 400 mg Q2W, respectively.
- 72 placebo-randomized patients did not achieve PASI 50 at Week 16 and entered the open-label CZP 400 mg Q2W escape arm.
- Baseline demographics are shown in **Table 1**.

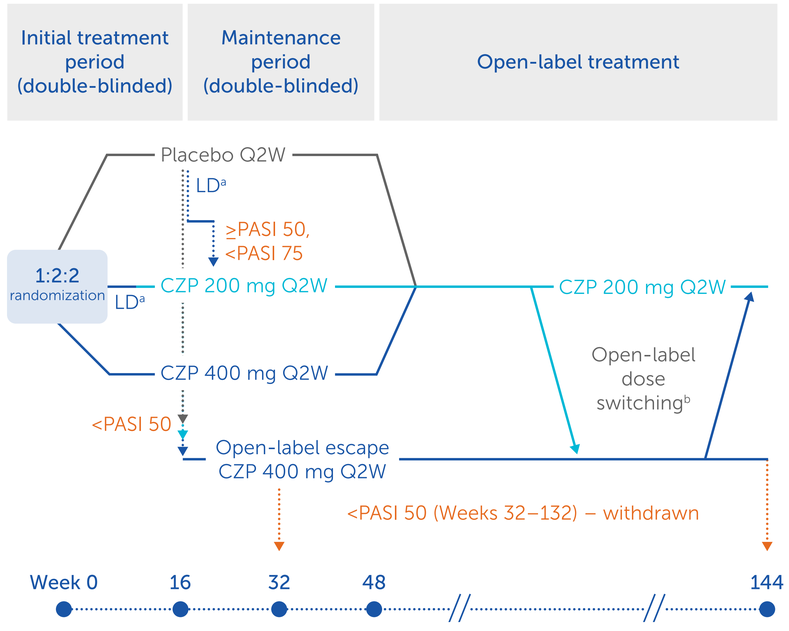
Achievement and Maintenance of Low Absolute PASI Thresholds

- Patients randomized to CZP demonstrated an initial rapid response, maintained to Week 48 **(Figure 2)**.
  - In CZP 400 mg Q2W-randomized patients, responder rates decreased during the OLE following mandatory dose reduction **(Figure 2A)**
  - In CZP 200 mg Q2W-randomized patients, improvements were sustained to Week 144 **(Figure 2B)**
- 32 weeks after switching to open-label CZP 400 mg Q2W treatment (study Week 48), 66.0% of patients initially randomized to placebo achieved PASI <2, and 75.9% achieved PASI <3 **(Figure 2C)**. Responder rates were maintained through 128 weeks' CZP treatment (study Week 144).

Conclusions

High proportions of patients dosed with both CZP 400 mg Q2W and CZP 200 mg Q2W achieved and maintained stringent absolute PASI thresholds.

Figure 1 Study design: CIMPASI-1 and CIMPASI-2



[a]Loading dose of CZP 400 mg Q2W at Weeks 0, 2, and 4 or Weeks 16, 18, and 20; [b]Depending on PASI response, any dose adjustments were either mandatory or at the investigator's discretion. Patients who did not achieve PASI 50 at Week 32, 40, or 48 during double-blinded maintenance treatment, or at any visit after receiving unblinded CZP 400 mg Q2W for 12 weeks, were withdrawn from the study.

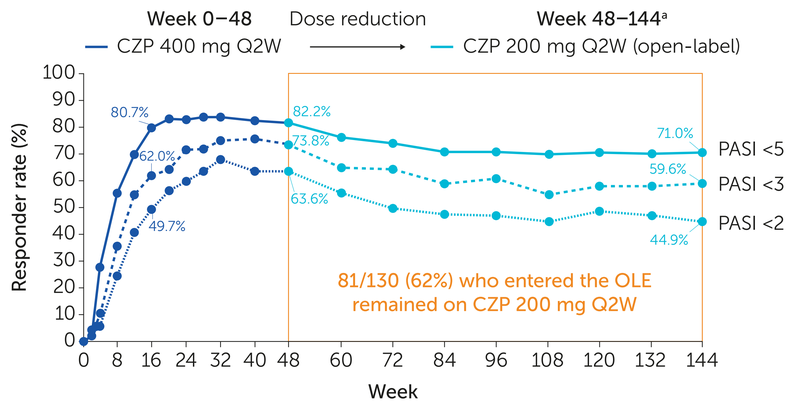
Table 1 Demographics and baseline characteristics of included patients

	CZP 400 mg Q2W (n=175)	CZP 200 mg Q2W[a] (n=186)	Placebo/Escape CZP 400 mg Q2W (n=72)
Age (years), mean ± SD	45.0 ± 12.9	45.6 ± 13.2	46.7 ± 13.1
Male, n (%)	103 (58.9)	125 (67.2)	48 (66.7)
Caucasian, n (%)	160 (91.4)	173 (93.0)	64 (88.9)
Weight (kg), mean ± SD	92.0 ± 24.8	95.1 ± 23.4	91.6 ± 21.6
Duration of PSO (years), mean ± SD	18.5 ± 12.6	17.7 ± 12.9	16.9 ± 11.9
Concomitant PsA,[b] n (%)	41 (23.4)	32 (17.2)	8 (11.1)
PASI, mean ± SD	19.6 ± 7.3	19.2 ± 7.2	18.3 ± 6.3
BSA (%), mean ± SD	23.6 ± 14.3	23.5 ± 14.9	22.4 ± 13.8
PGA score, n (%)			
3: moderate	126 (72.0)	128 (68.8)	53 (73.6)
4: severe	49 (28.0)	58 (31.2)	19 (26.4)
DLQI total score, mean ± SD	13.7 ± 6.9	14.3 ± 7.4	12.9 ± 7.4
Any prior systemic therapy use for PSO, n (%)	124 (70.9)	131 (70.4)	52 (72.2)
Prior biologic use, n (%)	59 (33.7)	62 (33.3)	23 (31.9)
anti-TNF	40 (22.9)	44 (23.7)	14 (19.4)
anti-IL-17	8 (4.6)	16 (8.6)	4 (5.6)
anti-IL-12/IL-23	10 (5.7)	3 (1.6)	6 (8.3)

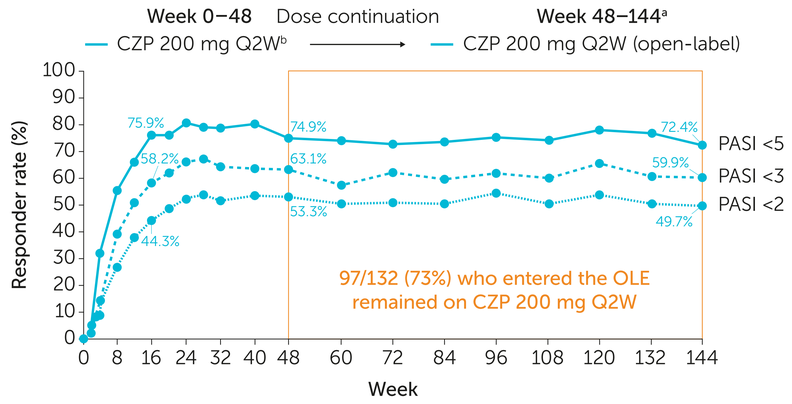
[a]Patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4; [b]Presence of concomitant PsA was self-reported.

Figure 2 Achievement and maintenance of low absolute PASI thresholds through to Week 144

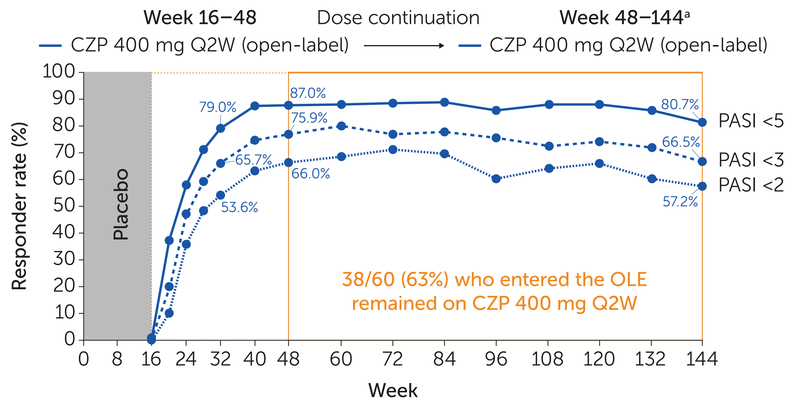
A) CZP 400 mg Q2W-randomized patients (n=175)



B) CZP 200 mg Q2W-randomized patients (n=186)



C) Placebo-randomized patients who entered the open-label CZP 400 mg Q2W escape arm at Week 16 (n=72)



Missing data were imputed using MCMC methodology and responder rates reflect the simple average response; calculations included patients who did and did not dose adjust during the OLE. [a]Dosing adjustment was permitted during the open-label period based on PASI response, and was either mandatory or at the investigator's discretion; [b]Patients received loading dose of CZP 400 mg at Weeks 0, 2, and 4.

BSA: body surface area; CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; IL: interleukin; LD: loading dose; MCMC: Markov Chain Monte Carlo; OLE: open-label extension; PASI: Psoriasis Area and Severity Index; PASI 50/75: 50%/75% or greater improvement from baseline in PASI; PGA: Physician's Global Assessment; 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]Gottlieb AB. *et al.* JAAD 2018;79:302–14; [3]Lebwohl M. JAAD 2018;79:266–76; [4]Zweegers J. *et al.* Br J Dermatol 2017;176:786–93; [5]Carrascosa Carrillo JM. *et al.* J Dermatolog Treat 2017;29:140–4; [6]Puig L. *et al.* Eur J Dermatol 2015;25:410–7. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication, or revising it critically for important intellectual content: ABG, AB, DT, YP, FB, CA, MB, KR; Final approval of the publication: ABG, AB, DT, YP, FB, CA, MB, KR. **Author Disclosures: 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 and for consultancy with AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dignity, Dr. Reddy's Laboratories, Galapagos, GSK, Janssen, LEO Pharma, Morphosis, MSD, Eli Lilly, Novartis, Pfizer, Sandoz-Hexal, Regeneron, Sanofi, and UCB Pharma. Research grants 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; **FB, CA, MB:** 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 Dan Smith, BA (Hons), Costello Medical, Cambridge, UK for medical writing and editorial assistance. All costs associated with development of this poster were funded by UCB Pharma.

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