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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Synopsis

Patients with moderate to severe plaque psoriasis were treated with certolizumab pegol for up to 144 weeks, initially dosed at either 200 mg or 400 mg every two weeks. High proportions of patients achieved and maintained stringent absolute PASI thresholds.

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.

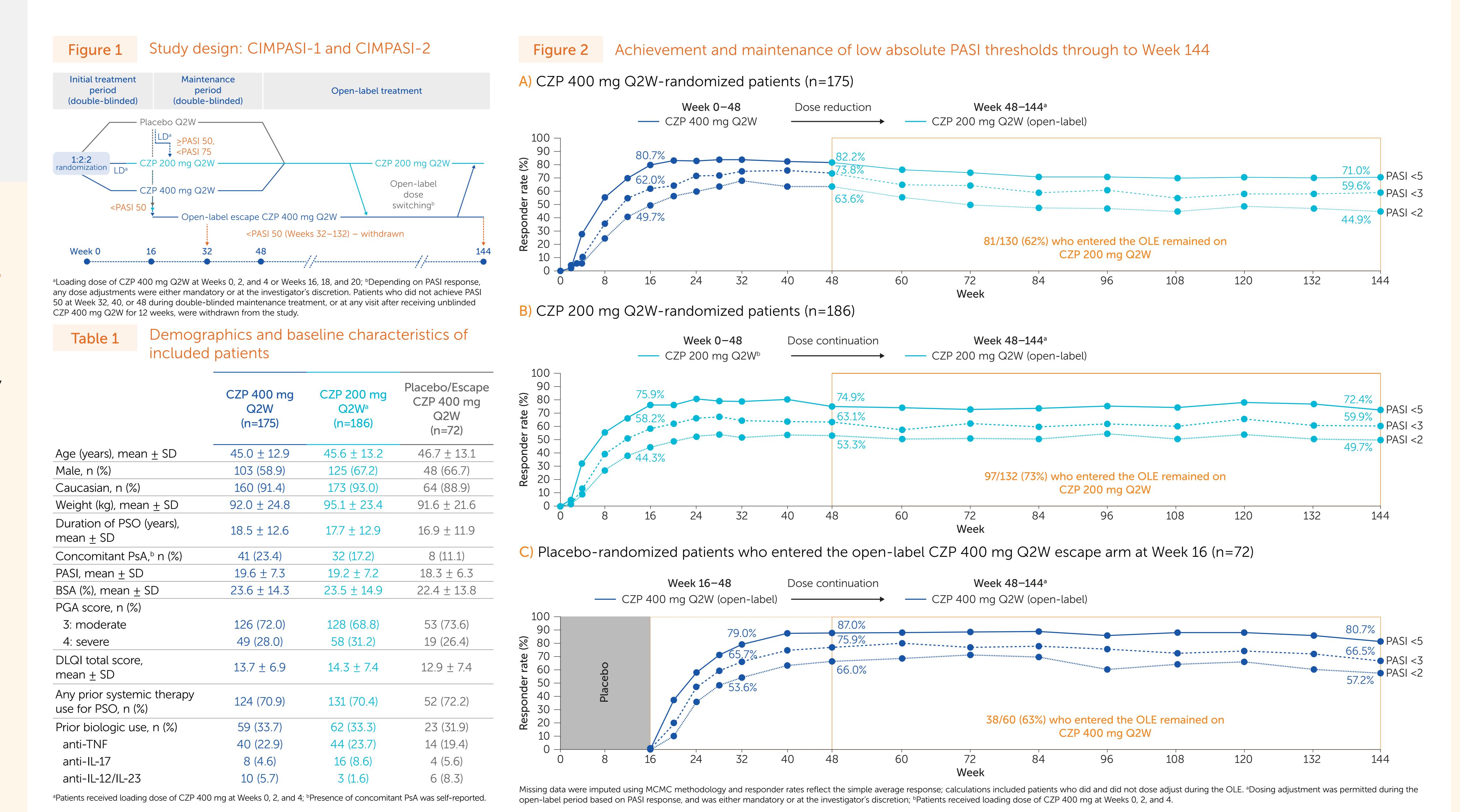
Background

- 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) with 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).
- 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, and 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

 Patient inclusion and exclusion criteria have been reported previously.²

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, 175 and 186 patients were randomized to CZP 400 mg Q2W and CZP 200 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 of 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.

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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;

References: 'Parisi R. J Invest Dermatol 2015;25:410-4; 'Puig L. 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; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; 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; Drafting of the publication; or revising of the publication; or revising of the publication; of the publication; ABG, AB, DT, YP, FB, CA, MB, KR; Drafting of the publication; or revising o

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PSO: plaque psoriasis; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.