Dose Adjustment Patterns in the Open-Label Extension Arms of Three Phase 3 Trials of Certolizumab Pegol in Psoriasis: CIMPASI-1, CIMPASI-2, and CIMPACT

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Objective

To assess Psoriasis Area and Severity Index (PASI) at the time of, and following, dose adjustment in the open-label extension period of three phase 3 clinical trials of certolizumab pegol in psoriasis.

Background

- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease that affects 2–4% of adults.[1]
- Certolizumab pegol (CZP), an Fc-free, PEGylated anti-tumor necrosis factor biologic, has demonstrated efficacy and safety in moderate to severe PSO.[2,3]
- Here, we report patterns of dose adjustment between CZP 400 mg and 200 mg Q2W, and changes from baseline PASI, in phase 3 trials.

Methods

Study Design

- Data were pooled from the CIMPASI-1 (NCT02326298), CIMPASI-2 (NCT02326272), and CIMPACT (NCT02346240) trials (Figure 1). Patient eligibility criteria have been reported previously.[1,2]
- Patients who were randomized to placebo at Week 0 and were PASI 50 non-responders after 16 weeks of placebo treatment entered the open-label escape arm (Weeks 16–48), where they received CZP 400 mg Q2W.
- At Week 48, patients in the escape arm entered the open-label extension period, where dose adjustments were possible from Weeks 48–132, per protocol (Figure 1).

Statistical Analysis

- Proportions of PASI 75 responders and median changes from baseline in PASI at the time of dose adjustments are presented.

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 are shown in Table 1.

PASI 75 Response in Dose Non-Adjusters

- 97 patients entered the open-label extension at Week 48, and the majority (66.0%; 64/97) remained on CZP 400 mg Q2W throughout the entire period (Figure 2).
- 68.8% (44/64) of these patients were PASI 75 responders at Week 144 (Figure 2).

Synopsis

Randomized to **Placebo** at Week 0

↓ <PASI 50

CZP 400 mg Q2W Escape Arm

↓

Open-label extension with possible dose adjustments:

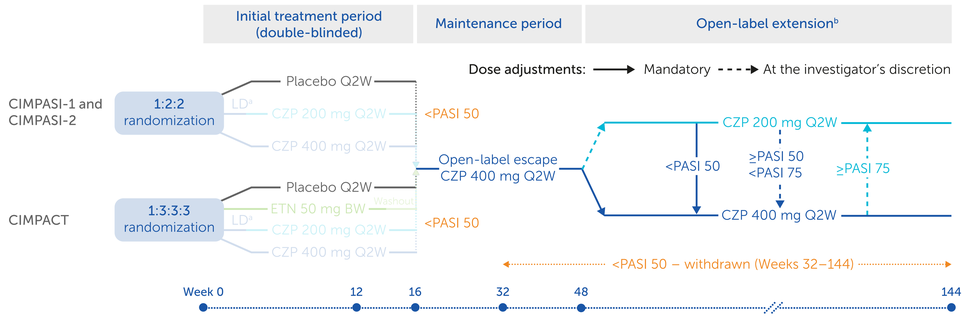
CZP 400 mg Q2W	CZP 200 mg Q2W	
Non-adjusters: 68.8% were PASI 75 responders	**Dose adjustment to 200 mg:** 27.3% of patients lost PASI 75	**Dose re-adjustment to 400 mg:** 77.8% of patients regained PASI 75

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
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)

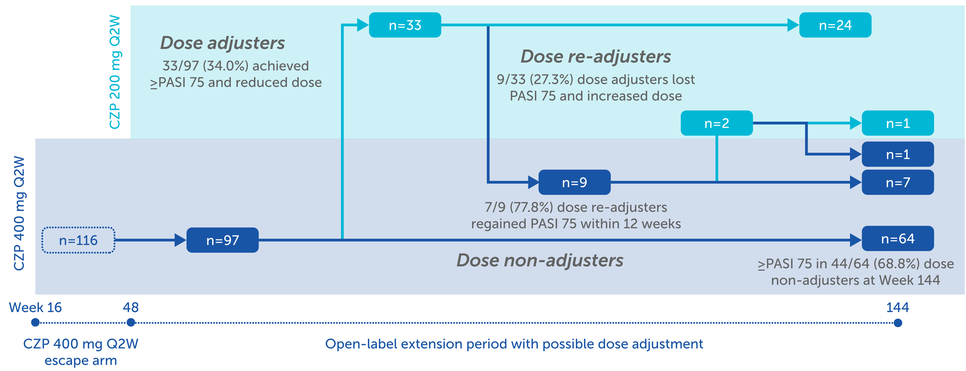
[a]PsA was self-reported.

Figure 1 Study designs



[a]Loading dose of CZP 400 mg Q2W at Weeks 0, 2, and 4; [b]Dose adjustments were mandatory in patients with <PASI 50 and at the investigator's discretion in patients with PASI 50–74; patients who received 12 weeks' CZP 400 mg Q2W could dose reduce at the Investigator's discretion if they achieved PASI 75, and were withdrawn if they did not achieve PASI 50.

Figure 2 Dose adjustment during the open-label extension period



Patients included in this analysis were randomized to placebo at Week 0 and entered the open-label CZP 400 mg Q2W escape arm at Week 16. PASI 75 response is defined as at least 75% improvement from baseline PASI. Missing responder rates were imputed using non-response imputation, except those reported following dose re-adjustment (observed case).

BMI: body mass index; BSA: body surface area; CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area and Severity Index; PGA: Physician's Global Assessment; PsA: psoriatic arthritis; PSO: plaque psoriasis; Q2W: every two weeks.

Table 2 Percent improvement from baseline PASI at time of dose adjustment

	First dose adjustment CZP 400 mg → CZP 200 mg Q2W	Second dose adjustment CZP 200 mg Q2W → CZP 400 mg
Median change from baseline at the time of dose adjustment (%)	100.0	58.1
Min–max (%)	75.9–100.0	44.6–74.7

Median percentage change from baseline was assessed during the open-label extension period at the time of the first dose reduction (CZP 400 mg Q2W down to CZP 200 mg Q2W) and at the time of the second dose adjustment (CZP 200 mg Q2W back up to CZP 400 mg Q2W).

PASI Changes in Dose Adjusters

- Patients who dose reduced to CZP 200 mg Q2W (n=33) achieved at least 75.9% improvement from baseline PASI at the time of first dose adjustment (Table 2).
  - 19/33 (57.6%) of whom showed 100% improvement from baseline PASI at the time of first dose adjustment.
- Following the first dose reduction, 9/33 (27.3%) patients lost PASI 75 response and returned to CZP 400 mg Q2W (Figure 2).
  - 7/9 (77.8%) of these dose re-adjusters regained PASI 75 within 12 weeks of returning to CZP 400 mg Q2W (Figure 2).
  - 2/9 (22.2%) dose re-adjusters reduced their dose again from 400 mg to 200 mg Q2W (Figure 2).

Conclusions

Among patients in the CZP 400 mg Q2W escape arm, the majority of patients did not dose adjust and remained stable on CZP 400 mg Q2W throughout Weeks 48–144.

In most patients who reduced the dose to CZP 200 mg Q2W and lost response, their response was regained with return to the 400 mg Q2W dose.

The small sample size of this population is a limitation of these analyses, and these data should be interpreted with caution.

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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.e6; [3]Lebwohl M. *et al.* JAAD 2018;79:266–76. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AB, ABG, FF, FB, SW, HS**; Drafting of the publication, or revising it critically for important intellectual content: **AB, ABG, FF, FB, SW, HS;** Final approval of the publication: **AB, ABG, FF, FB, SW, HS**. **Author Disclosures: AB:** Served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Forte, Galderma, Incyte, Janssen, LEO Pharma, Novartis, Ortho, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma, and as a paid speaker for AbbVie. **ABG:** Received honoraria as an advisory board member and consultant for Avotres Therapeutics; Beiersdorf; Boehringer Ingelheim; Bristol-Myers Squibb Co.; Incyte; Janssen; LEO Pharma; Eli Lilly; Novartis; Sun Pharmaceutical Industries, Inc.; UCB; and Xbiotech (only stock options which she has not used); and has received research/educational grants from Boehringer Ingelheim, Incyte, Janssen, Novartis, UCB, and Xbiotech. Sun Pharma. **FF, FB, SW:** Employees of UCB Pharma. **HS:** Consulting fees from AbbVie; Amgen; Boehringer Ingelheim; Celgene; Dermira; Janssen; Eli Lilly; Medimmune; Novartis; Pfizer; Sun Pharma; UCB Pharma; Valeant. **Acknowledgements:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Mylene Serna, PharmD, UCB Pharma, Smyrna, GA, USA for publication coordination and Jenna Hebert, PhD, Costello Medical, Boston, MA, USA for medical writing and editorial assistance and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma in accordance with the Good Publication Practice (GPP3) guidelines.