The Efficacy of Certolizumab Pegol Re-Treatment on Plaque Psoriasis Following a Blinded Treatment Break: Results from the CIMPACT Trial

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OBJECTIVE

- To assess the efficacy of certolizumab pegol in patients with moderate to severe plaque psoriasis who responded to initial treatment, relapsed during a treatment break, and were subsequently re-treated.

BACKGROUND

- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease; treatment options include systemic medication, phototherapy and biologic agents.
- Certolizumab pegol (CZP) is a unique, Fc-free, PEGylated, anti-tumor necrosis factor (TNF) biologic, approved by both the FDA and EMA for the treatment of moderate to severe PSO.[1,2]
- Here, we assess efficacy of CZP in patients with PSO who responded to initial treatment, underwent a blinded treatment break, relapsed, and were subsequently re-treated.

METHODS

Study Design

- Patients were enrolled in the ongoing phase 3 trial CIMPACT (NCT02346240); the full study design has been published previously.[3]
- Patients included in this analysis received treatment according to **Figure 1**.
- We focus on CZP-treated patients who achieved a 75% improvement from baseline in Psoriasis Area Severity Index (PASI 75) at the end of the initial period (Week 16), were re-randomized to placebo every two weeks (Q2W) for up to 32 weeks of double-blind maintenance treatment and subsequently relapsed (did not demonstrate a PASI 50 response [50% improvement from baseline]).
- Upon relapse, patients entered the 96-week open-label extension and received open-label CZP 400 mg Q2W.

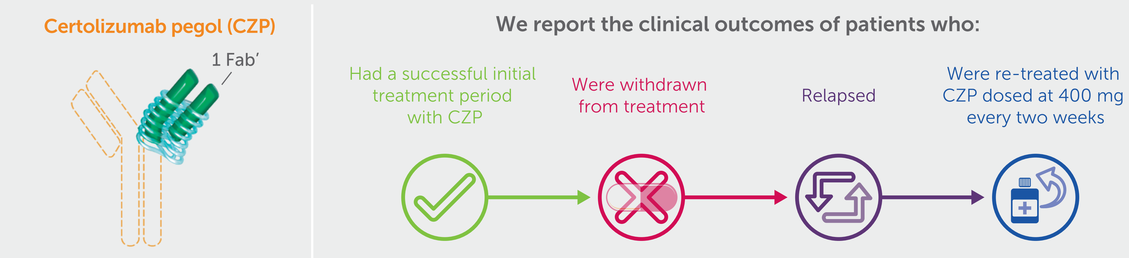
Table 1. Demographics and baseline characteristics

	All CZP (N=18)	CZP 400 mg Q2W (N=10)	CZP 200 mg Q2W[a] (N=8)
Age, years, mean (SD)	42.6 (13.1)	41.4 (8.7)	44.0 (17.7)
Male, n (%)	9 (50.0)	4 (40.0)	5 (62.5)
BMI, kg/m^2, mean (SD)	28.6 (4.1)	26.7 (1.8)	30.9 (5.0)
Prior biologic use, n (%)	6 (33.3)	4 (40.0)	2 (25.0)
Anti-TNF	0	0	0
Anti-IL-17	5 (27.8)	3 (30.0)	2 (25.0)
Anti-IL-12/IL-23	1 (5.6)	0	1 (12.5)
PSO duration, years, mean (SD)	23.0 (16.6)	19.4 (15.9)	27.6 (17.4)
PASI, mean (SD)	23.4 (8.9)	24.0 (7.3)	22.6 (11.2)
BSA affected, %, mean (SD)	33.3 (17.7)	34.3 (17.8)	32.0 (18.6)
PGA score, n (%)			
3 (moderate)	15 (83.3)	8 (80.0)	7 (87.5)
4 (severe)	3 (16.7)	2 (20.0)	1 (12.5)
DLQI, mean (SD)	11.8 (9.2)	13.8 (9.7)	9.3 (8.5)

[a]CZP 400 mg loading dose at Weeks 0, 2 and 4. BMI: body mass index; BSA: body surface area; CZP: certolizumab pegol; DLQI: Dermatology Life Quality Index; IL: interleukin; PASI: Psoriasis Area Severity Index; PGA: physician's global assessment; PSO: plaque psoriasis; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.

SUMMARY

Due to patient circumstances, physicians may recommend that individuals receiving biologic therapy take a treatment break.



Following re-treatment, all patients re-gained the same level of clinical response achieved after 16 weeks of initial treatment.

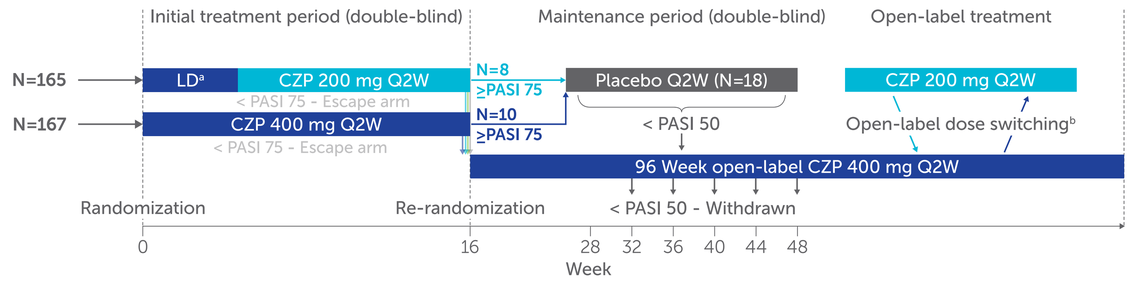
Patients

- ≥18 years of age with PSO for ≥6 months with PASI ≥12, ≥10% body surface area affected, Physician's Global Assessment ≥3 on a 5-point scale.
- Candidates for systemic PSO therapy, phototherapy and/or photochemotherapy.
- Exclusion criteria: previous treatment with CZP, ETN or >2 biologics; history of primary failure to any biologic or secondary failure to >1 biologic; erythrodermic, guttate or generalized PSO types; current or history of chronic or recurrent viral, bacterial or fungal infections.

Study Assessments and Statistical Analyses

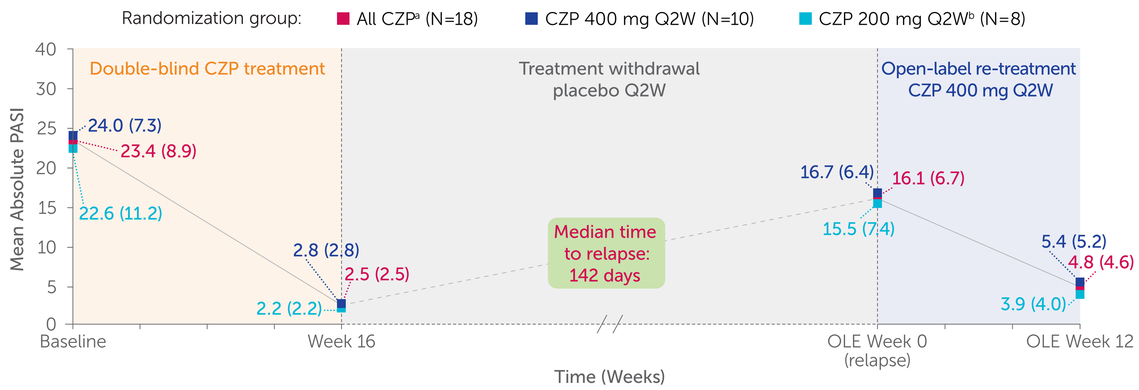
- Patients were assessed throughout the initial, maintenance and open-label periods for:
  - Absolute PASI
  - PASI 75 and PASI 90 (90% improvement from baseline)
- Observed data are reported.
- During re-treatment, time to achieve a 75% or 90% improvement in PASI from Week 16 response was estimated using Kaplan-Meier analysis.

Figure 1. Treatment arms included in this analysis



Patients were enrolled in the phase 3 CIMPACT trial. Only study arms relevant to this analysis are shown. [a]Loading dose of CZP 400 mg Q2W at Weeks 0, 2 and 4; [b]Dosing adjustment was at the Investigator's discretion based on PASI response. CZP: certolizumab pegol; LD: loading dose; PASI: Psoriasis Area Severity Index; Q2W: every two weeks.

Figure 2. Mean absolute PASI through the initial treatment, withdrawal, and open-label re-treatment periods



Observed case (there were no missing data). Standard deviations are shown in parentheses. All patients were re-randomized to placebo at Week 16, and subsequently received open-label CZP 400 mg Q2W at relapse (OLE Week 0). [a]Combined CZP 200 mg Q2W and CZP 400 mg Q2W; [b]CZP 400 mg loading dose at Weeks 0, 2 and 4. CZP: certolizumab pegol; OLE: open-label extension; PASI: Psoriasis Area Severity Index; Q2W: every two weeks.

RESULTS

Patient Population

- Of the patients who were initially randomized to either CZP 400 mg Q2W or CZP 200 mg Q2W, achieved PASI 75 at Week 16, and were re-randomized to placebo Q2W for maintenance treatment, 18 relapsed and received open-label CZP 400 mg Q2W.
- Baseline demographics are shown in **Table 1**.
- Mean PASI reduced rapidly over the initial 16 weeks of CZP treatment **(Figure 2)**.
- At Week 16, in addition to PASI 75, 61% of patients (11/18) also achieved PASI 90.

Clinical Response to Withdrawal and Re-Treatment

- Following re-randomization to placebo, median time to relapse was 142 days **(Figure 2)**.
- After 12 weeks of re-treatment with open-label CZP 400 mg Q2W, mean absolute PASI was comparable to that achieved after the initial 16 weeks **(Figure 2)**.
- Over the course of the re-treatment period and follow-up, all patients who had attained a PASI 75 or PASI 90 response at Week 16 regained the same level of response.
- A high proportion of patients achieved further improvements in PASI during re-treatment, compared to their Week 16 score:
  - 83% of patients (15/18) achieved a further 75% improvement on their Week 16 PASI in a median time of 127 days (95% confidence interval: 76–171) from re-treatment
  - 67% of patients (12/18) achieved a further 90% improvement on their Week 16 PASI, in a median time of 169 days (95% confidence interval: 85–337) from re-treatment.

CONCLUSIONS

- Following re-treatment with open-label CZP 400 mg Q2W, all patients re-achieved or improved upon their initial treatment response.
- The results shown here indicate that CZP may be an appropriate treatment option for patients who require a treatment break.
- Analyses using larger sample sizes would further validate these findings.

References

1. Certolizumab Pegol Prescribing information. Available at http://www.accessdata.fda.gov; **2.** Certolizumab Pegol Summary of Product Characteristics. Available at http://www.ema.europa.eu/ema; **3.** Lebwohl M. *et al.* J Am Acad Dermatol 2018;79:266–76.e5.

Author Contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: ML, VP, HS, AB, CA, SK, MB, MA; Drafting of the publication, or revising it critically for important intellectual content: ML, VP, HS, AB, CA, SK, MB, MA; Final approval of the publication: ML, VP, HS, AB, CA, SK, MB, MA.

Author Disclosures

ML: Allergan, Aqua, LEO Pharma, Promius. Employee of Mount Sinai which receives research funds from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen/Johnson & Johnson, Kadmon, Medimmune/AstraZeneca, Novartis, Pfizer, Valeant, ViDac; **VP**: AbbVie, Almirall, Celgene, Janssen, Novartis, Pfizer, Alliance, Beiersdorf, Biotest, Dermal, Eli Lilly, Galderma, Genus Pharma, GlobeMicro, Janssen, LaRoche-Posay, L'Oreal, LEO Pharma, Meda, MSD, Novartis, Pfizer, Sinclair Pharma, Spirit, GSK, Samumed, Thornton Ross, TyPham, UCB Pharma; **HS**: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira Inc., Janssen, Eli Lilly, MedImmune, Novartis, Pfizer, Sun Pharma, UCB Pharma, Valeant; **AB**: Scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, Arena, Boehringer Ingelheim, Celgene, Dermavant, Dermira Inc., Eli Lilly and Company, Galderma, Genentech/Roche, GSK, Janssen, Leo, Meiji, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac. Paid speaker for Janssen, Regeneron, and Sanofi Genzyme; **CA**, **SK**, **MB**: Employees of UCB Pharma; **MA**: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, GSK, Hexal, Janssen, LEO Pharma, Medac, Merck, MSD, Mundipharma, Novartis, Pfizer, Sandoz, UCB Pharma, Xenoport.

Acknowledgements

The studies were funded by Dermira Inc. in collaboration with UCB Pharma. UCB is the regulatory sponsor of cetolizumab 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 Bartosz Łukowski, MSc, UCB Pharma, Brussels, Belgium 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.