Clinical Response in Plaque Psoriasis Patients Switching from Etanercept to Certolizumab Pegol in a Phase 3, Randomized, Controlled Study

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OBJECTIVE

- To assess the efficacy of certolizumab pegol in patients with moderate to severe plaque psoriasis who initially received 12 weeks of treatment with the anti-TNF etanercept.

BACKGROUND

- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease.
- Treatment options for PSO include topicals, phototherapy or systemic medications (including biologics).
- Certolizumab pegol (CZP) is a unique, Fc-free, PEGylated, anti-tumor necrosis factor (TNF), approved by both the FDA and EMA for the treatment of moderate to severe PSO.[3,4]
- In phase 3 trials, CZP has shown clinical improvements maintained over 48 weeks, and a safety profile consistent with the anti-TNF class, in adults with PSO.[5,6]
- Here, we assessed clinical outcomes in patients with moderate to severe PSO who switched to CZP following 12 weeks of etanercept (ETN) treatment and a 4-week washout period.

METHODS

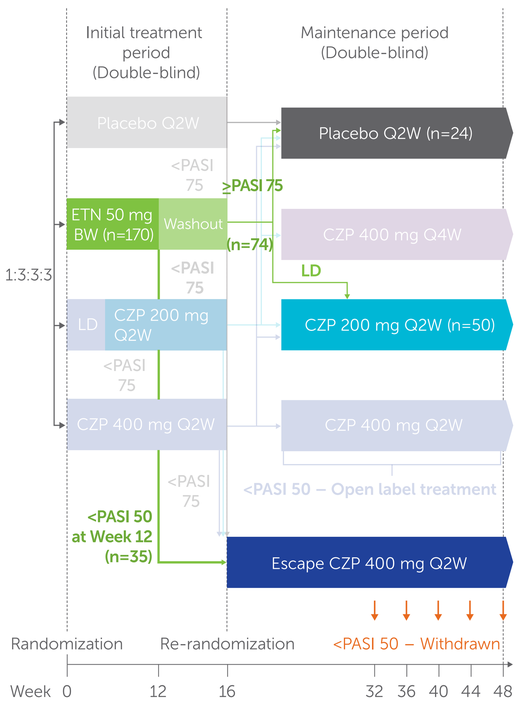
Study Design

- Patients in the ongoing phase 3 trial CIMPACT (NCT02346240) were randomized to placebo, CZP 400 mg every two weeks (Q2W), CZP 200 mg Q2W for 16 weeks, or ETN 50 mg twice weekly for 12 weeks **(Figure 1)**.
- At Week 16, following a 4-week washout, ETN-randomized patients received treatment to Week 48 according to their initial response. This analysis focuses on:
  - Patients who did not achieve a 50% improvement from baseline in Psoriasis Area Severity Index (PASI 50) at Week 12 and entered an escape arm where they received open-label CZP 400 mg Q2W.
  - Patients who achieved a 75% improvement from baseline in PASI (PASI 75) at Week 16 following the washout period and were re-randomized 2:1 to double-blind CZP 200 mg Q2W or placebo (PBO) Q2W.

Patients

- ≥18 years of age with PSO for ≥6 months with PASI ≥12, ≥10% body surface area affected, physician's global assessment (PGA) ≥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; history of current, chronic or recurrent viral, bacterial or fungal infections.
- ETN primary non-response was defined post-hoc as failure to achieve a PASI 50 response at Week 12.

Figure 1. CIMPACT study design



BW: twice weekly (last dose of ETN received at Week 11.5); CZP: certolizumab pegol; ETN: etanercept; LD: 400 mg CZP at Weeks 0,2 and 4 or 16, 18 and 20; PASI: Psoriasis Area Severity Index; Q2W: every two weeks.

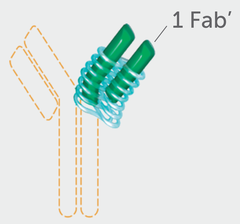
SUMMARY

We report patients with psoriasis who received **etanercept 50 mg twice weekly** for 12 weeks and subsequently switched to **certolizumab pegol** dosed at either **400 mg** or **200 mg** every two weeks.

Psoriasis patients treated with a biologic may require treatment switch to a second agent due to:[1,2]

- Dissatisfaction
- Adverse events
- Change of circumstance
- Primary non-response
- Loss of efficacy

Certolizumab pegol



These data show that CZP may be an effective treatment option in patients who require treatment switch from etanercept.

Table 1. Demographics and baseline characteristics

	All patients (N=559)	ETN 50 mg BW (n=170)	ETN → OL CZP 400 mg Q2W (n=35)	ETN → CZP 200 mg Q2W (n=50)	ETN → Placebo Q2W (n=24)
Age, years, mean (SD)	45.7 (13.3)	44.6 (14.1)	46.4 (15.4)	43.3 (12.9)	47.2 (13.5)
Male, n (%)	381 (68.2)	127 (74.7)	29 (82.9)	37 (74.0)	18 (75.0)
BMI, kg/m², mean (SD)	29.6 (6.4)	29.5 (6.3)	31.4 (6.3)	28.4 (4.7)	29.8 (5.7)
Prior biologic use, n (%)	154 (27.5)	51 (30.0)	12 (34.3)	15 (30.0)	10 (41.7)
Anti-TNF	21 (3.8)	8 (4.7)	0	2 (4.0)	2 (8.3)
Anti-IL-17	122 (21.8)	41 (24.1)	11 (31.4)	13 (26.0)	7 (29.2)
Anti-IL-12/IL-23	32 (5.7)	10 (5.9)	2 (5.7)	2 (4.0)	2 (8.3)
PSO duration, years, mean (SD)	18.3 (12.3)	17.4 (12.0)	14.9 (10.0)	18.6 (12.8)	16.3 (14.2)
PASI, mean (SD)	20.9 (8.1)	21.0 (8.2)	21.6 (8.3)	20.9 (9.0)	22.4 (7.9)
BSA affected, %, mean (SD)	27.4 (15.6)	27.5 (15.5)	30.2 (15.5)	26.6 (15.8)	28.9 (16.1)
PGA score, n (%)					
3 (moderate)	382 (68.3)	115 (67.6)	18 (51.4)	37 (74.0)	17 (70.8)
4 (severe)	177 (31.7)	55 (32.4)	17 (48.6)	13 (26.0)	7 (29.2)

BMI: body mass index; BSA: body surface area; BW: twice weekly; CZP: certolizumab pegol; ETN: etanercept; IL: interleukin; OL: open-label; PASI: Psoriasis Area Severity Index; PGA: physician's global assessment; PSO; plaque psoriasis; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.

Figure 2. Clinical response in ETN PASI 50 non-responders following switch to CZP

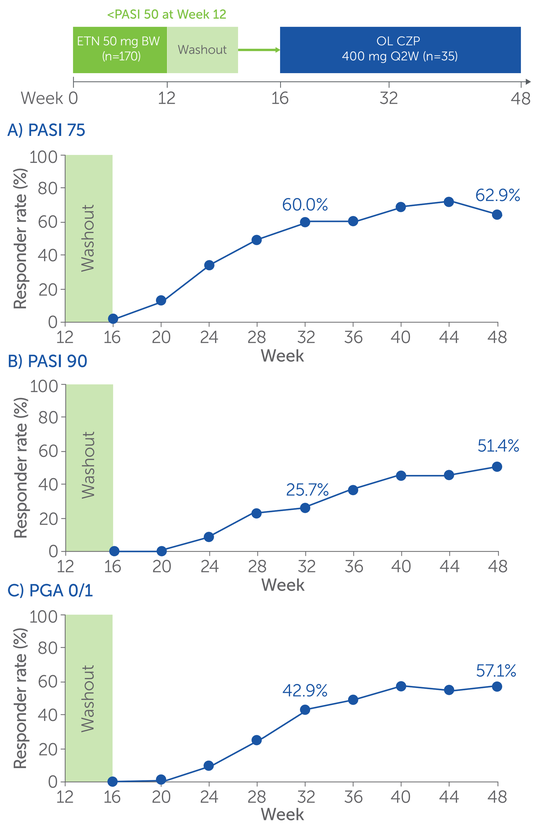
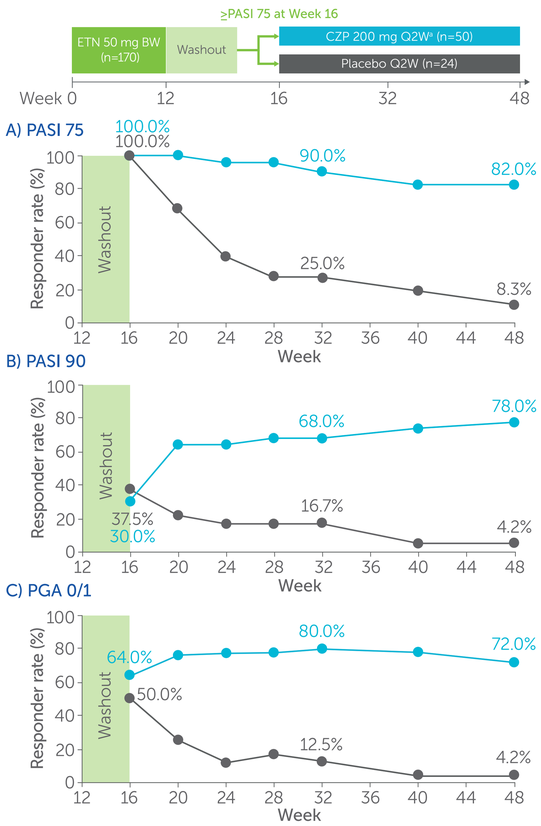


Figure 3. Clinical response in ETN PASI 75 responders re-randomized to CZP and placebo



Non-responder imputation. ETN non-response defined as failure to achieve ≥50% reduction from baseline in PASI at Week 12. [a]CZP 400 mg loading dose at Weeks 16, 18 and 20. BW: twice weekly (last dose of ETN received at Week 11.5); CZP: certolizumab pegol; ETN: etanercept; OL: open-label; PASI: Psoriasis Area Severity Index; PGA: physician's global assessment; Q2W: every two weeks.

Study Assessments

- Patients were assessed through Weeks 16–48 for:
  - PASI 75
  - PASI 90 (≥90% reduction from baseline)
  - PGA 0/1 ("clear" or "almost clear" with ≥2 category improvement from baseline)

Statistical Analyses

- Patients who did not achieve PASI 50 at Week 32 or later were treated as non-responders at subsequent time points.
- Missing data and patients withdrawn during Weeks 16–48 were imputed as non-responders.

RESULTS

Patient Demographics and Baseline Characteristics

- 170 patients were randomized to ETN at Week 0; 159 were still in the study at Week 16.
- 35/159 failed to achieve a PASI 50 response following 12 weeks of ETN treatment and entered the open-label CZP 400 mg Q2W escape arm at Week 16.
- 77/159 patients demonstrated a PASI 75 response at Week 16, 74 of whom entered the double-blind maintenance period; 50 patients were re-randomized to CZP 200 mg Q2W and 24 to placebo Q2W.
- Baseline characteristics are shown in **Table 1**.

Clinical Response to CZP in ETN PASI 50 Non-Responders

- At Week 32 following 16 weeks of CZP 400 mg Q2W:
  - 60.0% of ETN non-responders achieved a PASI 75 response **(Figure 2A)**
  - 25.7% achieved a PASI 90 response **(Figure 2B)**
  - 42.9% achieved a PGA 0/1 response **(Figure 2C)**
- At Week 48 (after 32 weeks of CZP 400 mg Q2W) these proportions were maintained or further increased **(Figure 2)**.

Clinical Response to CZP in ETN PASI 75 Responders

- For ETN responders who switched to CZP 200 mg Q2W at Week 16:
  - 82.0% still achieved a PASI 75 response at Week 48 **(Figure 3A)**
  - The proportion of PASI 90 responders increased to Week 48 **(Figure 3B)**
  - The proportion achieving a PGA 0/1 response remained high **(Figure 3C)**
- The PASI 75, PASI 90 and PGA 0/1 responder rate declined through Weeks 16–48 for ETN patients who switched to placebo **(Figure 3)**.

Safety

- No new safety signals were identified in patients who initially received ETN and switched to CZP treatment at Week 16.

CONCLUSIONS

- Patients with moderate to severe PSO who did not achieve a clinical response after 12 weeks of ETN therapy (<PASI 50) showed improvements following switch to CZP 400 mg Q2W.
- The proportion of patients who did achieve a clinical response with ETN therapy (≥PASI 75) was maintained or further improved following switch to CZP 200 mg Q2W.
- CZP may be an effective treatment option for patients who do not primarily respond to ETN or require treatment switch.

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