Efficacy of Certolizumab Pegol for Psoriasis of the Head and Neck in Two Phase 3 Clinical Trials: CIMPASI-1 and CIMPASI-2

P. van de Kerkhof,[1] A. Pinter,[2] M. Boehnlein,[3] S. Kavanagh,[4] J. J. Crowley[5]

[1]Radboud University Medical Centre, Nijmegen, The Netherlands; [2]University Hospital Frankfurt, Frankfurt, Germany; [3]UCB Pharma, Monheim, Germany; [4]UCB Pharma, Raleigh, NC, USA; [5]Bakersfield Dermatology, Bakersfield, CA, USA

OBJECTIVE

- To report the efficacy of certolizumab pegol for psoriasis of the head and neck region in two phase 3 clinical trials.

BACKGROUND

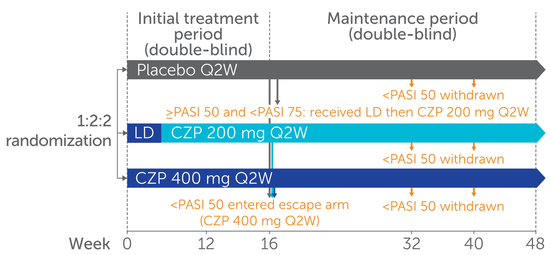
- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease that is associated with significant physical and emotional burden.[1]
- Psoriatic lesions located on visible areas of the body can have a major impact on patients' quality of life (QoL);[2] psoriasis of the head and neck region in particular can cause a high degree of emotional distress, despite only representing 10% of the body surface area (BSA), and the greatest impact on QoL is reported by female patients.[2,3]
- Certolizumab pegol (CZP) is a unique, Fc-free, PEGylated, anti-tumor necrosis factor approved by the FDA and EMA for the treatment of moderate to severe PSO.[4,5]
- In phase 3 trials, CZP has demonstrated significant improvements in the signs and symptoms of PSO.[6]
- The Psoriasis Area and Severity Index (PASI), commonly used by physicians to assess the severity of PSO, accounts for the size and character of psoriatic lesions across four body regions, one of which is the head and neck.
- In this post-hoc analysis, we report CZP efficacy for the head and neck region over 48 weeks.

METHODS

Study Design

- Data were pooled from the CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) phase 3 trials in adults with moderate to severe PSO **(Figure 1)**. Full study designs have been reported previously.[6]
- Patients were randomized 2:2:1 to receive CZP 400 mg every 2 weeks (Q2W), CZP 200 mg Q2W (400 mg loading dose at Weeks 0, 2 and 4), or placebo.
- At Week 16, patients receiving CZP who achieved ≥50% improvement from baseline in PASI (PASI 50) continued to receive the same CZP dose to Week 48.

Figure 1. CIMPASI-1 and -2 study design



CZP: certolizumab pegol; LD: loading dose of CZP 400 mg at Weeks 0, 2 and 4 or Weeks 16, 18 and 20; PASI: Psoriasis Area and Severity Index; Q2W: every two weeks.

Table 1. Patient baseline characteristics

	CZP 400 mg Q2W (N=175)	CZP 200 mg Q2W (N=186)	Placebo (N=100)
Age, years, mean (SD)	45.0 (12.9)	45.6 (13.2)	45.7 (13.8)
Male, n (%)	103 (58.9)	125 (67.2)	61 (61.0)
BMI, kg/m², mean (SD)	31.2 (7.9)	32.0 (7.8)	31.2 (7.4)
Prior biologic use, n (%)	59 (33.7)	62 (33.3)	29 (29.0)
Anti-TNF	39 (22.3)	44 (23.7)	19 (19.0)
Anti-IL-17	8 (4.6)	16 (8.6)	5 (5.0)
Anti-IL-12/IL-23	10 (5.7)	3 (1.6)	6 (6.0)
PSO duration, years, mean (SD)	18.5 (12.6)	17.7 (12.9)	17.0 (12.6)
PASI, mean (SD)	19.6 (7.3)	19.2 (7.2)	18.6 (6.6)
Head and neck score, mean[a]	17.9	16.5	19.1
BSA affected, %, mean (SD)	23.6 (14.3)	23.5 (14.9)	23.1 (13.6)
PGA score, n (%)			
3 (moderate)	126 (72.0)	128 (68.8)	72 (72.0)
4 (severe)	49 (28.0)	58 (31.2)	28 (28.0)

[a]Only patients with head and neck involvement at baseline were included (CZP 400 mg Q2W: N=170; CZP 200 mg Q2W: N=169; Placebo: N=93). BMI: body mass index; BSA: body surface area; CZP: certolizumab pegol; IL: interleukin; PASI: Psoriasis Area and Severity Index; PGA: Physician's Global Assessment; PSO: plaque psoriasis; Q2W: every two weeks SD: standard deviation; TNF: tumor necrosis factor.

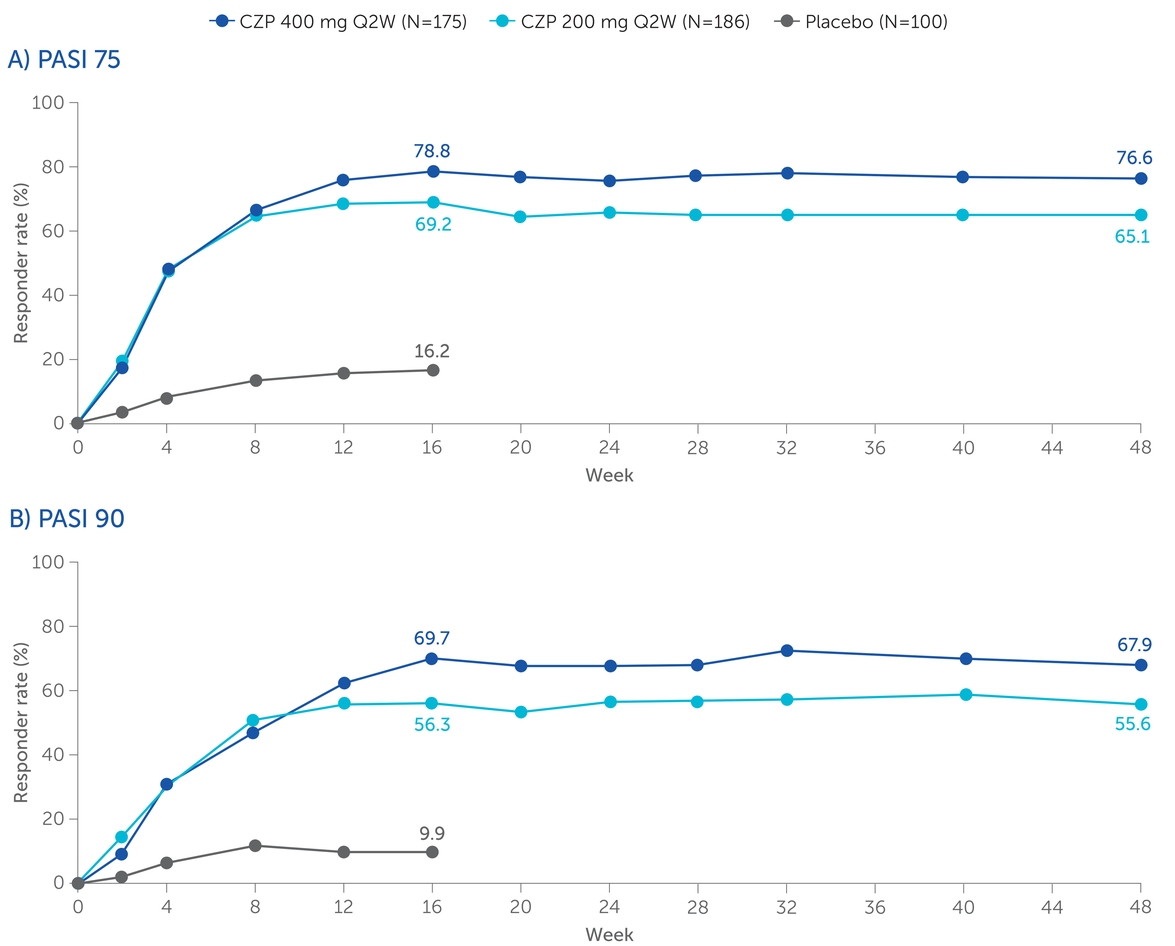
Patients

- ≥18 years of age with moderate to severe PSO for ≥6 months, defined as PASI ≥12, ≥10% BSA affected and 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 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

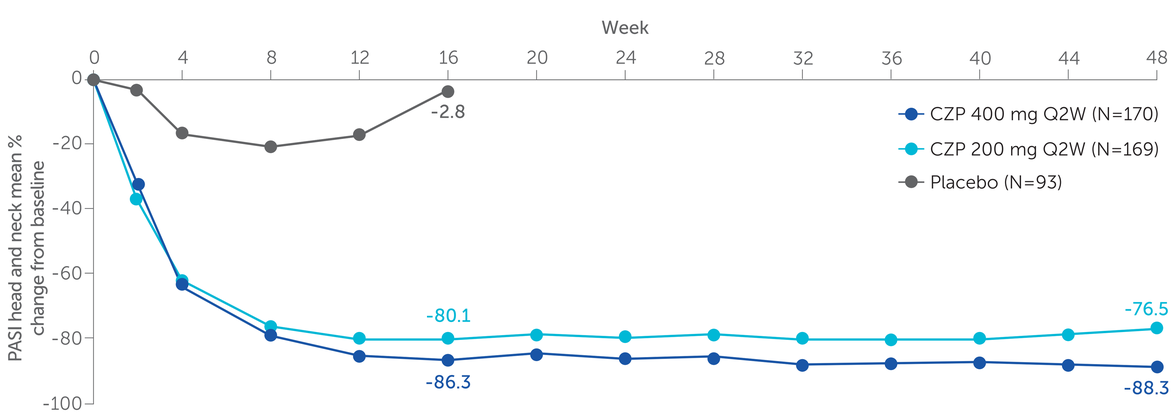
- Patients achieving a 75% and 90% improvement in psoriasis of the head and neck region, and the mean percentage change from baseline in head and neck PASI are reported, through Weeks 0–48.
- Calculation of change from baseline included only patients with head and neck involvement. Calculation of PASI 75 and PASI 90 responder rates included all randomized patients (patients without baseline head and neck involvement were considered non-responders).
- For patients missing one or two severity measures (redness, thickness, or scaling) for the head and neck region at a given study visit, values were substituted with the mean of the measures available for that region at that visit.
- Patients who did not achieve PASI 50 at Week 16 had their Week 16 value carried forwards. Patients who should have been mandatorily withdrawn from study treatment at Week 32 or Week 40 due to not achieving PASI 50 were treated as non-responders for subsequent visits with missing data.
- Estimates of responder rate reflect the simple average response across multiple imputed data sets, with missing data imputed using Markov Chain Monte Carlo (MCMC) methodology. Continuous measures were imputed using Last Observation Carried Forward (LOCF).

Figure 2. Improvements in PASI of the head and neck region through Weeks 0–48



Estimates of responder rate reflect the simple average response across multiple imputed data sets, with missing data imputed using MCMC methodology. Placebo data are shown to Week 16 only; only 9 patients continued with placebo treatment through Weeks 16–48. CZP 200 mg Q2W patients received a loading dose of CZP 400 mg at Weeks 0, 2, and 4. CZP: certolizumab pegol; MCMC: Markov Chain Monte Carlo; PASI 75/90: Psoriasis Area and Severity Index 75% or 90% improvement of the head and neck region; Q2W: every two weeks.

Figure 3. Percentage change from baseline in PASI of the head and neck region through Weeks 0–48



LOCF imputation. Placebo data are shown to Week 16 only; only 9 patients continued with placebo treatment through Weeks 16–48. CZP 200 mg Q2W patients received a loading dose of CZP 400 mg at Weeks 0, 2 and 4. CZP: certolizumab pegol; LOCF: last observation carried forward; PASI: Psoriasis Area and Severity Index; Q2W: every two weeks.

RESULTS

Patient Demographics and Baseline Characteristics

- 175, 186, and 100 patients were randomized to CZP 400 mg Q2W, CZP 200 mg Q2W and placebo, respectively, at Week 0. Patient baseline characteristics are shown in **Table 1**.
- Baseline PASI of the head and neck region was comparable across CZP 400 mg Q2W, CZP 200 mg Q2W and placebo treatment groups **(Table 1)**.

PASI of the Head and Neck Region

- At Week 16, a higher proportion of patients receiving CZP treatment achieved 75% and 90% improvements in PASI of the head and neck region compared with placebo **(Figure 2)**.
- Week 16 responder rates were maintained to Week 48 for patients receiving both CZP doses **(Figure 2)**.
- Mean percentage change from baseline in PASI of the head and neck region was also greater for CZP-treated patients compared with placebo at Week 16, and maintained to Week 48 **(Figure 3)**.
- Although improvements were seen for both CZP doses, responder rates were higher in patients receiving CZP 400 mg Q2W.

CONCLUSIONS

- Rapid improvements in psoriasis of the head and neck region were seen as early as Week 2 of CZP treatment.
- A higher proportion of patients treated with CZP demonstrated a 75% or 90% improvement in PASI of the head and neck region at Week 16 compared with placebo. Improvements in CZP-treated patients were maintained to Week 48, indicating a durable clinical response in this hard-to-treat area.
- The greatest improvements were observed for patients receiving CZP 400 mg Q2W.
- These data suggest that CZP may be a suitable treatment option for patients with moderate to severe PSO affecting the head and neck, a known detractor from patients' QoL.[7]

References

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Author Contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: PvdK, AP, MB, SK, JJC; Drafting of the publication, or revising it critically for important intellectual content: PvdK, AP, MB, SK, JJC; Final approval of the publication: PvdK, AP, MB, SK, JJC.

Author Disclosures

PvdK: Received fees for consultancy service or lectureships from Celgene, Centocor, Almirall, Amgen, Pfizer, Philips, Abbott, Eli Lilly, Galderma, Novartis, Janssen, LEO Pharma, Sandoz, Bristol-Myers Squibb and Dermavant ; **AP:** Worked as an Investigator and/or speaker and/or advisor for AbbVie, Almirall Hermal, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Schering-Plough and UCB Pharma; **MB:** Employee of UCB Pharma; **SK:** Received fees for consultancy service from AveXis, Colorado Prevention Center, DiaMedica, PureTech, UCB Pharma, and Zosano; **JJC:** Received research/grant support from AbbVie, Amgen, Boehringer Ingelheim, Janssen, Lilly, MC2 Therapeutics, Merck & Co., Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Sun Pharmaceuticals, UCB Pharma and Verrica Pharmaceuticals; has served as consultant for AbbVie, Amgen, Celgene, Dermira Inc., Lilly, Novartis, Sun Pharmaceuticals and UCB Pharma; has worked on speakers bureau for AbbVie, Janssen, Lilly, Novartis, Regeneron, Sanofi, and UCB Pharma.

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