Durability of Response in Patients with Psoriatic Arthritis Treated with Certolizumab Pegol over 216 Weeks: Post-Hoc Analyses from the RAPID-PsA Study

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OBJECTIVE

- To assess the durability of response in patients with psoriatic arthritis who were treated with certolizumab pegol over 216 weeks.

BACKGROUND

- Certolizumab pegol (CZP) is a unique, Fc-free, PEGylated anti-tumour necrosis factor (TNF) that is approved by the FDA and EMA for the treatment of psoriatic arthritis (PsA).[1,2]
- In the 4-year, phase 3 RAPID-PsA trial (NCT01087788), substantial proportions of CZP-treated patients achieved targets such as minimal disease activity (MDA) and very low disease activity (VLDA), consistent with other biologics, including anti-TNFs.[3,4]
- In phase 3 trials in plaque psoriasis (PSO), CZP-treated patients showed clinical improvements, which were sustained over three years of treatment.[5]
- Responder rates observed at Weeks 16 and 48 were durable over time.[6,7]
- Here, we assess the durability of the initial clinical response to CZP in patients with PsA.

METHODS

Study Design

- RAPID-PsA was a 4-year, phase 3 trial, double-blind and placebo-controlled to Week 24, dose-blind to Week 48 and open-label to Week 216.
- Patients with PsA were randomised 1:1:1 to CZP 200 mg every two weeks (Q2W), CZP 400 mg every four weeks (Q4W) or placebo;
  - All patients randomised to CZP received CZP 400 mg loading dose at Weeks 0, 2 and 4, and continued their assigned dose during the open-label period to Week 216 **(Figure 1)**.

Patients

- Included patients were aged ≥18 years with a diagnosis of active PsA of ≥6 months' duration, and had failed treatment with ≥1 disease-modifying anti-rheumatic drug (DMARD).

Table 1. Patient baseline characteristics

n (%) unless otherwise stated	All CZP (N=273)
Age, years, mean (SD)	47.7 (11.6)
Male	126 (46.2)
BMI, kg/m^2, mean (SD)	30.0 (6.4)
CRP, mean (SD)	14.3 (22.3)
HLA-B27 positivity	41 (15.0)
Psoriasis BSA ≥3%	166 (60.8)
Nail psoriasis	197 (72.2)
Enthesitis	172 (63.0)
Dactylitis	94 (34.4)
Suspected axial involvement	213 (78.0)
Prior use of synthetic DMARDs	
1	165 (60.4)
≥2	103 (37.7)
Prior anti-TNF exposure	54 (19.8)

BMI: body mass index; BSA: body surface area; CRP: C-reactive protein; CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug; HLA-B27: human leukocyte antigen B27; SD: standard deviation; TNF: tumour necrosis factor.

SUMMARY

We assessed durability of the initial clinical response to certolizumab pegol (CZP) in patients with psoriatic arthritis (PsA)

PsA activity and severity were measured using seven criteria:

- Tender joint count ≤1
- Swollen joint count ≤1
- Psoriasis Area and Severity Index ≤1 or ≤3% body surface area affected
- Patient pain visual analogue score ≤15
- Patient global disease activity visual analogue score ≤20
- Health Assessment Questionnaire Disability Index ≤0.5
- Tender entheseal points ≤1

Proportions of patients at Week 216 who maintained their clinical response from Week 24:

Minimal disease activity (MDA) ≥5/7 MDA criteria[8]: **MDA: 87%**

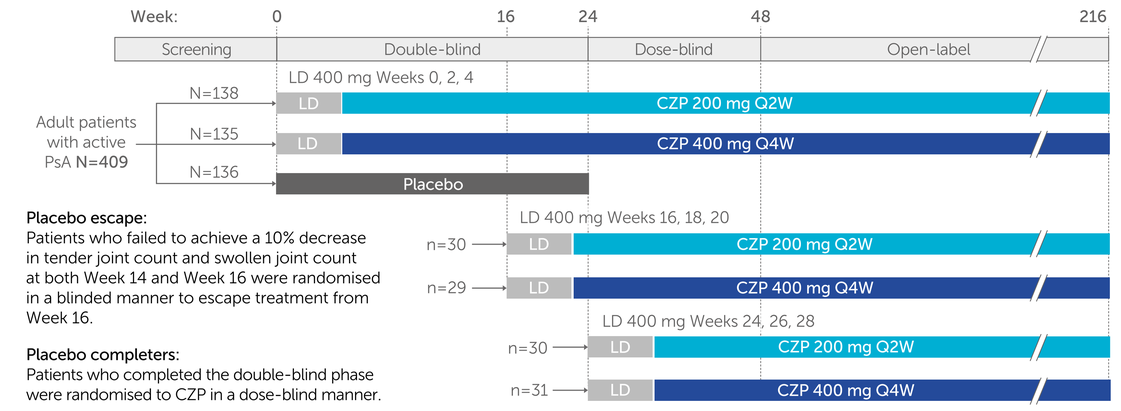
Very low disease activity (VLDA) =7/7 MDA criteria[8]: **VLDA: 82%**

- Patients with prior exposure to >2 biologic agents (>1 anti-TNF) for the treatment of PsA or PSO were excluded.
- In this analysis, data were pooled for patients randomised to CZP 200 mg Q2W and CZP 400 mg Q4W.

Study Assessments and Statistical Analyses

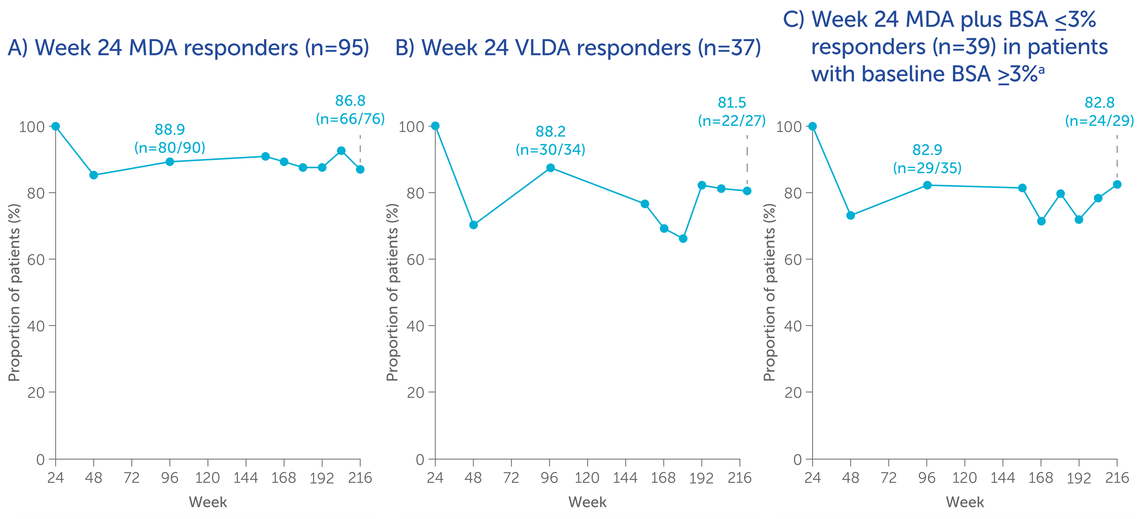
- PsA severity was assessed using seven MDA criteria **(see Summary box)**.
- Week 24–216 data are reported for patients who were randomised to CZP at Week 0 and who achieved:
  - Week 24 MDA (≥5/7 MDA criteria)
  - Week 24 VLDA (7/7 MDA criteria)
  - Baseline psoriatic BSA ≥3% and Week 24 BSA ≤3% plus ≥4/6 of the remaining MDA criteria (MDA plus BSA ≤3%)
- Data are shown for patients randomised to CZP at Week 0 as observed case.

Figure 1. RAPID-PsA study design



CZP: certolizumab pegol; LD: loading dose; PsA: psoriatic arthritis; Q2W: every two weeks; Q4W: every four weeks.

Figure 2. Durability of response through Weeks 24–216



Week	48	96	156	168	180	192	204	216
MDA, % (n/N)	85.1 (80/94)	88.9 (80/90)	90.7 (78/86)	89.4 (76/85)	87.8 (72/82)	87.7 (71/81)	92.3 (72/78)	86.8 (66/76)
VLDA, % (n/N)	71.4 (25/35)	88.2 (30/34)	77.4 (24/31)	70.0 (21/30)	66.7 (20/30)	82.8 (24/29)	82.1 (23/28)	81.5 (22/27)
MDA plus BSA ≤3% (n/N)	73.7 (28/38)	82.9 (29/35)	81.8 (27/33)	71.9 (23/32)	80.0 (24/30)	72.4 (21/29)	78.6 (22/28)	82.8 (24/29)

Data are observed case. Data are pooled for patients treated with CZP 200 mg Q2W and CZP 400 mg Q4W. [a]MDA plus BSA ≤3% responses are reported in patients who had BSA ≥3% at baseline. BSA: body surface area; CZP: certolizumab pegol; MDA: minimal disease activity; Q2W: every two weeks; Q4W: every four weeks; VLDA: very low disease activity.

RESULTS

Patient Disposition

- 273 patients were randomised to CZP 200 mg Q2W (N=138) or CZP 400 mg Q4W (N=135) at Week 0 **(Figure 1)**.
- Patient baseline characteristics are shown in **Table 1**.

Week 24 Response

- Of the patients randomised to CZP, at Week 24:
  - 95/273 (34.8%) patients achieved MDA
  - 37/273 (13.6%) achieved VLDA
- At baseline 166/273 patients had BSA ≥3%, 39 (23.5%) of whom achieved MDA plus BSA ≤3% at Week 24.
- There was no clear trend observed in the components that contributed to failure to achieve VLDA response.

Durability of Response

- Responder rates for all three composite outcome measures remained high to Week 216 in patients who demonstrated a Week 24 response and completed Week 216 **(Figure 2)**.
- Numerically, the greatest durability to Week 216 was seen for MDA **(Figure 2)**.

CONCLUSIONS

- Of patients with PsA who initially responded to CZP treatment and achieved an MDA response at Week 24 and completed treatment to Week 216, >85% maintained this clinical response after four years of treatment.
- Even at the more stringent VLDA threshold, >80% of Week 24 responders who completed to Week 216 maintained their response to four years.
- These findings highlight the long-term durability of the clinical response to CZP in patients with moderate to severe PsA, with substantial proportions of patients reaching and maintaining stringent treatment targets.

References

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Author Contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: ABG, PG, JE, LP, AK; Drafting of the publication, or revising it critically for important intellectual content: ABG, PG, JE, LP, AK; Final approval of the publication: ABG, PG, JE, LP, AK.

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