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ORIGINAL RESEARCH

Long-Term Health-Related Quality of Life in Patients with Plaque Psoriasis Treated with Certolizumab Pegol: Three-Year Results from Two Randomised Phase 3 Studies (CIMPASI-1 and CIMPASI-2)

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ABSTRACT

Introduction: Certolizumab pegol (CZP) is an Fc-free, PEGylated, anti-tumour necrosis factor biologic. Safety and efficacy data for CZP over 3 years have been previously reported. We report 3-year quality of life (QoL) outcomes for patients treated with CZP, pooled from two phase 3 trials.

Methods: Adults with moderate-to-severe plaque psoriasis for ≥ 6 months were initially randomised 1:2:2 to double-blinded placebo every 2 weeks (Q2W), CZP 200 mg Q2W (loading dose of CZP 400 mg at weeks 0/2/4) or CZP 400 mg Q2W. All patients received open-label CZP (200 mg or 400 mg Q2W) from week 48. Dermatology Life Quality Index (DLQI), 36-Item Short Form Survey (SF-36), EuroQol 5-Dimen-

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sions 3-Level (EQ-5D-3L) and Work Productivity and Activity Impairment (WPAI) scores are reported as observed.
Results: At week 0, 100 patients were randomised to placebo, 186 to CZP 200 mg Q2W and 175 to CZP 400 mg Q2W. For CZP-randomised patients, 60.9% had a DLQI score of 0 or 1 by week 48. Both the physical and mental component scores of SF-36 also improved from baseline to week 48 (mean change from baseline: 4.4 and 5.4, respectively). The proportion of patients with a score of 1 in the EQ-5D-3L Pain/Discomfort dimension increased (week 0, 21.1%; week 48, 66.2%), and WPAI Presenteeism, Work Impairment, and Activity Impairment improved from baseline to week 48, with the strongest gains observed for Activity Impairment (week 0, 33.3% of time impaired; week 48, 6.7%). Across patient-reported outcomes, gains were sustained through week 144, with durable improvements observed regardless of sex, psoriatic arthritis status or prior exposure to biologics.
Conclusion: CZP treatment was associated with sustained and tangible improvements in health-related QoL (DLQI and SF-36), health status (EQ-5D-3L) and functional impairment at work and in other daily activities (WPAI).
Trial Registration: ClinicalTrials.gov NCT02326298 (CIMPASI-1) and NCT02326272 (CIMPASI-2).

Keywords: Biologic; Certolizumab pegol; Clinical trial; Patient-reported outcomes; Plaque psoriasis; Quality of life

Key Summary Points

Why carry out this analysis?

Plaque psoriasis is associated with significant physical and psychological impairment. Although effective treatment of psoriasis has been shown to improve quality of life (QoL), loss of clinical response over time has been observed for some biologics.

Treatment with certolizumab pegol has been shown to result in sustained and durable improvements in the signs and symptoms of moderate-to-severe plaque psoriasis.

It is important to understand whether improvements in patients' health-related QoL were sustained throughout long-term treatment.

What was learned from this analysis?

Treatment with certolizumab pegol was associated with sustained and tangible improvements in patients' health-related quality of life over 3 years, with increased work productivity, decreased pain and improved ability to engage in daily activities, as observed across multiple patient-reported outcomes.

These improvements were consistent across patient subgroups regardless of sex, psoriatic arthritis status and prior exposure to biologics.

INTRODUCTION

Plaque psoriasis is associated with significant physical and psychological impairment, and is linked to alterations in daily activities and social stigmatisation, as well as an increased risk of depression [1–3]. Effectively treating psoriasis improves quality of life (QoL) [2, 3], and biologic therapies, including agents that target

tumour necrosis factor (TNF), interleukin (IL)-12, IL-17 and IL-23 cytokines [4], are central to the treatment of moderate-to-severe psoriasis [4, 5]. Greater treatment satisfaction is generally seen among patients treated with biologics versus non-biologic therapies [6]: this class of therapy offers unparalleled treatment potential for skin clearance and improved QoL [2, 3]. However, loss of response over time has been observed for some biologics [7]; it is therefore important to understand whether improvements in patients' health-related QoL (HRQoL), in addition to skin clearance [8], are sustained throughout long-term treatment.

Certolizumab pegol (CZP) is an Fc-free, PEGylated, anti-TNF biologic approved for the treatment of adults with moderate-to-severe plaque psoriasis, alongside axial spondyloarthritis, psoriatic arthritis (PsA), Crohn's disease and rheumatoid arthritis [9, 10]. Unlike other anti-TNF agents, CZP does not bind to the neonatal Fc receptor for IgG, resulting in minimal or no placental transfer of CZP from mothers to infants [11]. Outcomes for CZP in moderate-to-severe plaque psoriasis over 144 weeks have previously been reported from three phase 3 trials conducted in North America and Europe: CIMPASI-1 (NCT02326298), CIMPASI-2 (NCT02326272) and CIMPACT (NCT02346240) [8, 12–15]. After 16 weeks of CZP treatment in these trials, significant improvements in the signs and symptoms of plaque psoriasis were observed versus placebo, and improvements from baseline were sustained to week 144 [8, 15]. A pooled analysis of the safety data from these trials over 3 years of treatment identified no new safety signals compared to previous CZP studies [13, 14, 16].

Sustained improvements in HRQoL have been previously reported by dosing regimen over 144 weeks of CZP treatment using Dermatology Life Quality Index (DLQI). The proportion of CZP-treated patients with a score of 0 or 1 (DLQI 0/1) was sustained from weeks 48–144. A numerically higher proportion of patients receiving CZP 400 mg every 2 weeks (Q2W) than CZP 200 mg Q2W achieved DLQI 0/1 at week 48 [8]. Here, we investigate the durability of response across several patient-reported outcome (PRO) measures in patients with moderate-to-severe plaque psoriasis treated with CZP over 3 years. We present data pooled from the CIMPASI-1 and CIMPASI-2 trials, using the following PRO measures: DLQI, 36-Item Short Form Survey (SF-36), EuroQol 5-Dimensions 3-Level (EQ-5D-3L) and Work Productivity and Activity Impairment (WPAI).

METHODS

Patients and Study Designs

CIMPASI-1 and CIMPASI-2 were 3-year (144-week) phase 3, randomised, multicentre trials with identical study designs conducted in North America and Europe. The trials were double-blinded and placebo-controlled to week 16, double-blinded to week 48, and open-label to week 144 (Supplementary Material Fig. S1).

Each trial enrolled adults (≥ 18 years of age) with moderate-to-severe plaque psoriasis of disease duration ≥ 6 months, with Psoriasis Area and Severity Index (PASI) ≥ 12, ≥ 10% body surface area affected and Physician's Global Assessment (PGA) ≥ 3 on a 5-point scale [8]. Patients were excluded if they had previously been treated with CZP and/or more than two biologics, had a history of primary failure to any biologic or secondary failure to more than one biologic. Full inclusion/exclusion criteria have been published previously [8, 13].

Patients were randomised 1:2:2 to placebo Q2W, CZP 200 mg Q2W (loading dose of CZP 400 mg at weeks 0/2/4) or CZP 400 mg Q2W. Patients without a ≥ 50% improvement from baseline in PASI (PASI 50) at week 16 entered the escape arm and received open-label CZP 400 mg Q2W. Those with PASI 50 at week 48 entered the open-label period. All patients entering the open-label period from blinded treatment at week 48 initially received CZP 200 mg Q2W. Adjustments between the two doses of CZP were permitted at study visits (every 12 weeks) through weeks 60–132 of the study and were either mandatory or at the investigator's discretion. Full study designs, including conditions for dose adjustment, have been reported previously.[8, 13].

As previously reported, CIMPASI-1 and CIMPASI-2 were carried out according to good clinical practice requirements and the Declaration of Helsinki, and were approved by local institutional review boards/independent ethics committees [13]. Informed consent was obtained from all participants.

Outcomes

We report outcomes through weeks 0–144 for patients by initial randomisation group and for the following subgroups of patients who were randomised to CZP at baseline: female or male, concomitant PsA or no concomitant PsA (self-reported at baseline) and biologic-exposed or biologic-naïve. PRO measures, including DLQI, SF-36, EQ-5D-3L and WPAI, were completed every 2–8 weeks until week 32 and every 12–-24 weeks thereafter. License or user agreements were obtained for the use of the DLQI, SF-36 and EQ-5D-3L questionnaires; permission is not required to use the WPAI questionnaire.

DLQI measures QoL specifically in relation to skin diseases. The total DLQI score ranges from 0 to 30 (DLQI 0/1 denotes no effect of disease on patient's life). The scale consists of ten questions asking how much patients' skin has affected aspects of their life over the previous week, with each question scored 0–3 (0, not at all; 1, a little; 2, a lot; 3, very much). These ten questions are grouped into six domains: Symptoms and Feelings, Leisure, Personal Relationships, Daily Activities, Work and School, and Treatment [17]. We report the proportion of patients achieving an overall DLQI 0/1 score, the proportion achieving a score of 0 for each of the six domains and absolute scores for total DLQI and each of the domains.

SF-36 is a generic HRQoL measure that covers eight health domains (Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health). Domain scores are combined to generate the physical and mental component summary scores (PCS/MCS). The scores are standardised against a normative sample from the US general population in 2009, for whom the mean score was 50 (standard deviation, 10); higher scores indicate better health [18]. We report change from baseline (CfB) at week 48 and week 144 for each of these domains individually and for the two component summary scores.

EQ-5D-3L is a five-dimension health status measure, assessing Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression. For these components, patients choose 1 of 3 levels of severity (1, none; 2, moderate; 3, severe/extreme) [19]. We report the proportion of patients with a score of 1 for each of these five dimensions. Additionally, we report the EQ Visual Analogue Scale (VAS), for which patients rate their perception of their overall health from 0 (worst imaginable health status) to 100 (best imaginable health status) [19].

The WPAI Specific Health Problem questionnaire assesses the impact of a health problem (for these trials, psoriasis) on work productivity and daily life activities. WPAI is split into four domains: Absenteeism, Presenteeism, Work Impairment and Activity Impairment. Patients report the number of hours of work they have missed owing to their psoriasis and the number of hours they have worked, how much their psoriasis affected their productivity while working (0–10 scale) and how much it affected their ability to do their regular activities outside work (0–10 scale). Scores are expressed as percentage of time impacted (0–100); lower scores indicate better outcomes [20].

Statistical Analyses

Data are reported as observed for all patients randomised to CZP 200 mg or 400 mg Q2W through week 144 and placebo through week 16 and are additionally reported using last observation carried forward imputation for missing data (Supplementary Material Table S1). CZP-randomised patients who failed to achieve PASI 50 at week 16 and entered the open-label escape arm continued to be included in these analyses. Post hoc subgroup analyses are also reported as observed, pooled for all patients initially randomised to either CZP dose and split by sex,

Table 1 Demographics and baseline characteristics

	CZP 200 mg Q2W (*N* = 186)	CZP 400 mg Q2W (*N* = 175)	All CZP (*N* = 361)	Placebo (*N* = 100)
Age (years), mean ± SD	45.6 ± 13.2	45.0 ± 12.9	45.3 ± 13.0	45.7 ± 13.8
Caucasian, *n* (%)	173 (93.0)	160 (91.4)	333 (92.2)	89 (89.0)
Male, *n* (%)	125 (67.2)	103 (58.9)	228 (63.2)	61 (61.0)
Concurrent PsA (self-reported), *n* (%)	32 (17.2)	41 (23.4)	73 (20.2)	13 (13.0)
Prior biologic therapy, *n* (%)	62 (33.3)	59 (33.7)	121 (33.5)	29 (29.0)
Disease duration (years), mean ± SD	17.7 ± 12.9	18.5 ± 12.6	18.1 ± 12.7	16.9 ± 12.6
Weight (kg), mean ± SD	95.1 ± 23.4	92.0 ± 24.8	93.6 ± 24.1	91.3 ± 23.4
PASI, mean ± SD	19.2 ± 7.2	19.6 ± 7.3	19.4 ± 7.3	18.6 ± 6.6
BSA affected (%), mean ± SD	23.5 ± 14.9	23.6 ± 14.3	23.5 ± 14.6	23.1 ± 13.6
PGA, *n* (%)				
3, moderate	128 (68.8)	126 (72.0)	254 (70.4)	72 (72.0)
4, severe	58 (31.2)	49 (28.0)	107 (29.6)	28 (28.0)
DLQI, mean ± SD[a]	14.3 ± 7.4	13.7 ± 6.9	14.0 ± 7.1	13.4 ± 7.8
DLQI 0/1, *n* (%)[a]	6 (3.3)	1 (0.6)	7 (2.0)	2 (2.1)
DLQI domain score of 0, *n* (%)[b]				
Symptoms and feelings	2 (1.1)	0	2 (0.6)	2 (2.0)
Daily Activities	19 (10.3)	12 (6.9)	31 (8.7)	11 (11.2)
Leisure	32 (17.4)	36 (20.7)	68 (19.0)	26 (26.5)
Work and School	80 (43.5)	70 (40.2)	150 (41.9)	48 (49.0)
Personal Relationships	54 (29.3)	57 (32.8)	111 (31.0)	38 (38.8)
Treatment	61 (33.2)	57 (32.8)	118 (33.0)	33 (33.7)
EQ-5D-3L score of 1, *n* (%)[a]				
Mobility	123 (67.2)	125 (72.3)	248 (69.7)	73 (75.3)
Self-Care	165 (90.2)	153 (88.4)	318 (89.3)	91 (93.8)
Usual Activities	125 (68.3)	115 (66.5)	240 (67.4)	65 (67.0)
Pain/Discomfort	33 (18.0)	42 (24.3)	75 (21.1)	16 (16.5)
Anxiety/Depression	93 (50.8)	87 (50.3)	180 (50.6)	50 (51.5)
EQ VAS, mean ± SD[a]	65.9 ± 22.7	66.1 ± 22.2	66.0 ± 22.4	66.2 ± 21.2
SF-36 PCS, mean ± SD[a]	46.9 ± 9.3	48.5 ± 9.2	47.7 ± 9.3	47.7 ± 8.9
SF-36 MCS, mean ± SD[a]	46.9 ± 11.0	45.5 ± 10.6	46.2 ± 10.8	45.3 ± 12.6

Table 1 continued

	CZP 200 mg Q2W (*N* = 186)	CZP 400 mg Q2W (*N* = 175)	All CZP (*N* = 361)	Placebo (*N* = 100)
WPAI, mean ± SD				
Absenteeism[c]	4.5 ± 16.4	3.4 ± 13.9	4.0 ± 15.2	3.9 ± 10.1
Presenteeism[c]	19.6 ± 25.6	19.6 ± 22.7	19.6 ± 24.2	18.8 ± 22.2
Work Impairment[c]	23.1 ± 29.2	22.1 ± 25.5	22.6 ± 27.4	20.8 ± 24.4
Activity Impairment[a]	33.0 ± 30.6	33.6 ± 28.8	33.3 ± 29.7	29.9 ± 25.8

All CZP arm includes all patients randomised to certolizumab pegol (CZP) at baseline
[a]CZP 200 mg Q2W *N* = 183; CZP 400 mg Q2W *N* = 173; all CZP *N* = 356; placebo *N* = 97
[b]CZP 200 mg Q2W *N* = 184; CZP 400 mg Q2W *N* = 174; all CZP *N* = 358; placebo *N* = 98
[c]Assessed in employed patients only; patient numbers: CZP 200 mg Q2W *N* = 130; CZP 400 mg Q2W *N* = 127; all CZP *N* = 257; placebo *N* = 68
BSA body surface area, *CZP* certolizumab pegol, *DLQI* Dermatology Life Quality Index, *EQ-5D-3L* EuroQol 5-Dimensions 3-Level, *EQ VAS* EuroQol Visual Analogue Scale, *MCS* mental component summary, *PASI* Psoriasis Area and Severity Index, *PCS* physical component summary, *PGA* Physician's Global Assessment, *PsA* psoriatic arthritis, *Q2W* every 2 weeks, *SD* standard deviation, *SF-36* 36-Item Short Form Survey, *WPAI* Work Productivity and Activity Impairment

concomitant PsA status and prior exposure to biologics.

RESULTS

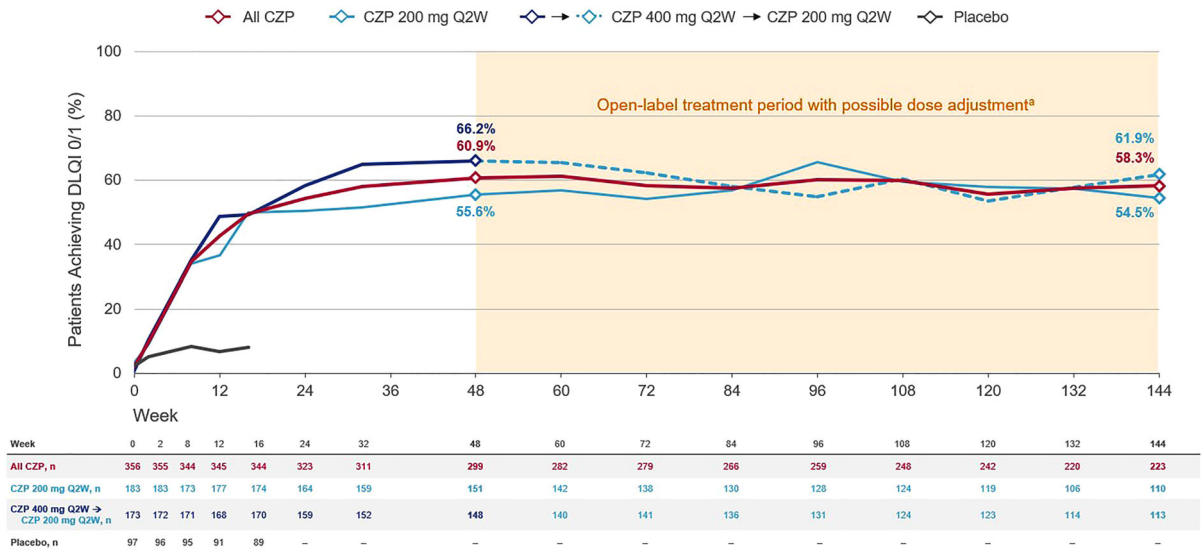
Patient Disposition and Baseline Characteristics

At week 0, 100 patients were randomised to placebo, 186 to CZP 200 mg Q2W and 175 to CZP 400 mg Q2W. At week 16, 118 patients (26 randomised to CZP 200 mg Q2W, 20 to CZP 400 mg Q2W and 72 to placebo) did not achieve PASI 50, so entered the escape arm, receiving open-label CZP 400 mg Q2W [8]. Additionally, from weeks 32–48, 16 patients (5 receiving double-blinded CZP 200 mg Q2W, 4 receiving double-blinded CZP 400 mg Q2W and 7 receiving open-label CZP 400 mg Q2W) did not achieve PASI 50 and were withdrawn from the study. Of the 361 patients initially randomised to CZP 200 mg Q2W and CZP 400 mg Q2W arms, 55% (103/186) and 63% (110/175) completed week 144, respectively [8]. Demographics and baseline characteristics were balanced across treatment groups and were representative of a population with moderate-to-severe plaque psoriasis eligible for biologic therapy (Table 1).

Overall Response

When considering HRQoL using DLQI across CZP-randomised patients, 58.2% had DLQI 0/1 by week 32 (data reported as observed; at time-points after week 0, 'CZP-randomised patients' refers to those remaining in the study), and this responder rate was sustained through week 48 (60.9%) and week 144 (58.3%) (Fig. 1).

This sustained response was reflected across all DLQI domains. The highest burden was seen in the Symptoms and Feelings domain: at week 0, CZP-randomised patients had a mean score of 4.2 on a scale of 0–6, with only 0.6% reporting a score of 0. At weeks 48 and 144, this score had decreased to 1.0 and 1.1 for CZP-randomised patients, with 46.5% and 44.4% reporting a score of 0, respectively (Supplementary Material Fig. S2a–b). The greatest improvement was seen for Daily Activities, where 8.7% of CZP-randomised patients had a score of 0 at week 0, increasing to 71.7% at week 144 (Supplementary Material Fig. S2a). The Daily Activities mean absolute score for CZP-randomised patients improved from 3.2 at week 0 to 0.5 at week 144 (Supplementary Material Fig. S2b). Across the remaining DLQI domains, 19.0–41.9% and 78.9–87.9% of CZP-



Week	0	2	8	12	16	24	32	48	60	72	84	96	108	120	132	144
All CZP, n	356	355	344	345	344	323	311	299	282	279	266	259	248	242	220	223
CZP 200 mg Q2W, n	183	183	173	177	174	164	159	151	142	138	130	128	124	119	106	110
CZP 400 mg Q2W → CZP 200 mg Q2W, n	173	172	171	168	170	159	152	148	140	141	136	131	124	123	114	113
Placebo, n	97	96	95	91	89	–	–	–	–	–	–	–	–	–	–	–

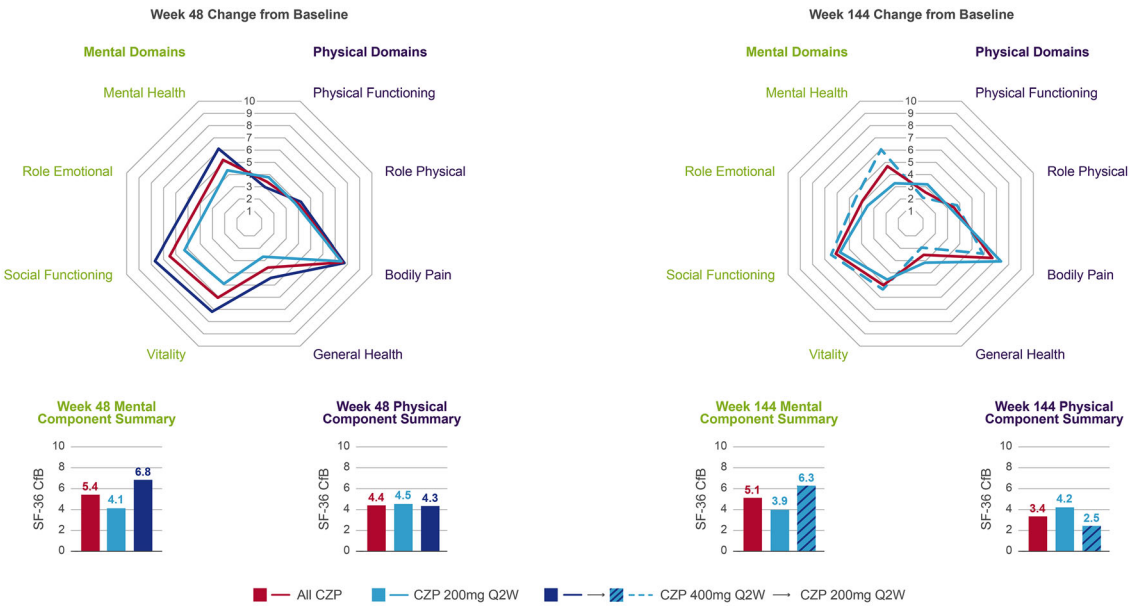
Fig. 1 The proportion of patients with a DLQI (Dermatology Life Quality Index) score of 0 or 1 over time (%). Data are presented as observed for all patients according to initial randomisation group; CZP-randomised patients who did not achieve a ≥ 50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50) at week 16 and entered the open-label escape arm continued to be included in these analyses. Data by dose for CZP-randomised patients at weeks 16, 32, 48, 96 and 144 have been reported previously [8]. [a]Dose adjustments were mandatory or at the investigator's discretion, based on PASI response. *DLQI* Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index, *Q2W* every 2 weeks

randomised patients had a score of 0 at week 0 and 144, respectively. Improvements were also reflected in decreases in absolute mean scores across all domains.

For CZP-randomised patients, mean SF-36 PCS change from baseline (week 0 score, 47.7) was 4.4 at week 48 and 3.4 at week 144. The mean MCS change from baseline (week 0 score, 46.2) was 5.4 at week 48 and 5.1 at week 144 (Fig. 2). Across domains, both the highest baseline burden and the greatest mean improvement for CZP-randomised patients were seen in the Bodily Pain (week 0, 45.9; gain of 6.7 at week 144) and Social Functioning (week 0, 45.2; gain of 6.1 at week 144) domains.

Of the five EQ-5D-3L dimensions, the greatest baseline burden and the largest improvements from week 0 through week 144 were observed for Pain/Discomfort. For this dimension, 21.1% of CZP-randomised and 16.5% of placebo-randomised patients reported a rating of 1, indicating no pain or discomfort, at week 0. This improved to 61.0% of CZP-randomised patients at week 16, which was sustained through week 48 (66.2%) and week 144 (62.3%); by contrast, only 30.3% of patients in the placebo group had a score of 1 at week 16. Across the remaining four EQ-5D-3L dimensions, a majority of patients had a score of 1 at week 0 (CZP-randomised patients, 50.6–89.3%) and this proportion remained high through week 144 (CZP-randomised patients, 74.4–95.5%). For the EQ VAS, CZP-randomised patients reported a mean score of 66.0 at week 0, which improved to 82.6 at week 48 and was sustained to 81.7 at week 144 (Fig. 3).

Among the WPAI domains, mean Presenteeism, Work Impairment and Activity Impairment improved from week 0 (percentage of time impaired across domains, 19.6–33.3%) to week 48 (5.6–8.7%) for CZP-randomised patients, and these improvements were sustained at week 144 (8.0–11.8%). The largest gains were observed for Activity Impairment (33.3% of time impaired at week 0 versus 8.9% at week 144). Low levels of Absenteeism were reported at baseline and the percentage of work



Week 0 SF-36 Scores, mean ± SD							
Mental Domains	All CZP	CZP 200 mg Q2W	CZP 400 mg Q2W	Physical Domains	All CZP	CZP 200 mg Q2W	CZP 400 mg Q2W
Mental Health	46.5 ± 10.4	46.8 ± 10.7	46.3 ± 10.1	Physical Functioning	48.4 ± 9.5	47.7 ± 9.6	49.1 ± 9.4
Role Emotional	46.4 ± 10.6	46.8 ± 10.4	46.1 ± 10.8	Role Physical	47.0 ± 9.7	46.7 ± 9.5	47.3 ± 10.0
Social Functioning	45.2 ± 11.0	45.4 ± 11.1	45.1 ± 11.0	Bodily Pain	45.9 ± 10.7	45.3 ± 10.4	46.6 ± 11.1
Vitality	48.1 ± 9.9	48.5 ± 9.8	47.6 ± 10.0	General Health	47.3 ± 9.7	47.1 ± 10.1	47.5 ± 9.3
Mental Component Summary	46.2 ± 10.8	46.9 ± 11.0	45.5 ± 10.6	Physical Component Summary	47.7 ± 9.3	46.9 ± 9.3	48.5 ± 9.2

Fig. 2 Mean change from baseline (CfB) in 36-Item Short Form Survey (SF-36) at weeks 48 and 144. Data are presented as observed for all patients according to initial randomisation group; CZP-randomised patients who did not achieve a ≥ 50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50) at week 16 and entered the open-label escape arm continued to be included in these analyses. From week 48, dose adjustments were mandatory or at the investigator's discretion, based on PASI response. Patient numbers: CZP 200 mg Q2W, week 0 n = 183; week 48 n = 151; week 144 n = 110; CZP 400 mg Q2W, week 0 n = 173; week 48 n = 148; week 144 n = 113; all CZP, week 0 n = 356; week 48 n = 299; week 144 n = 223. *CfB* change from baseline, *CZP* certolizumab pegol, *PASI* Psoriasis Area and Severity Index, *SF-36* 36-Item Short Form Survey, *Q2W* every 2 weeks

time missed remained low following CZP treatment (Fig. 4).

Outcomes were also assessed for subgroups of patients grouped by sex, self-reported PsA status at baseline and prior exposure to biologics. Across all above-mentioned outcomes, no differences were observed between biologic-exposed (n = 121) and biologic-naïve (n = 240) CZP-randomised patients (Supplementary Material Table S2).

Outcomes by Sex

Of the 361 patients randomised to CZP at week 0, 133 were female and 228 were male. CZP-treated female patients had similar relative improvements through week 144 compared with male patients, despite a numerically higher baseline burden in several outcomes.

At week 144, a similar proportion of female and male patients had DLQI 0/1 (Supplementary Material Fig. S3a). However, differences were observed in the proportion of female and male patients with a score of 0 in the DLQI Daily Activities domain. At week 0, 6.0% of female patients versus 10.2% of male patients had a score of 0; this difference was observed through week 144, with a Daily Activities score of 0 observed for 63.3% of female patients

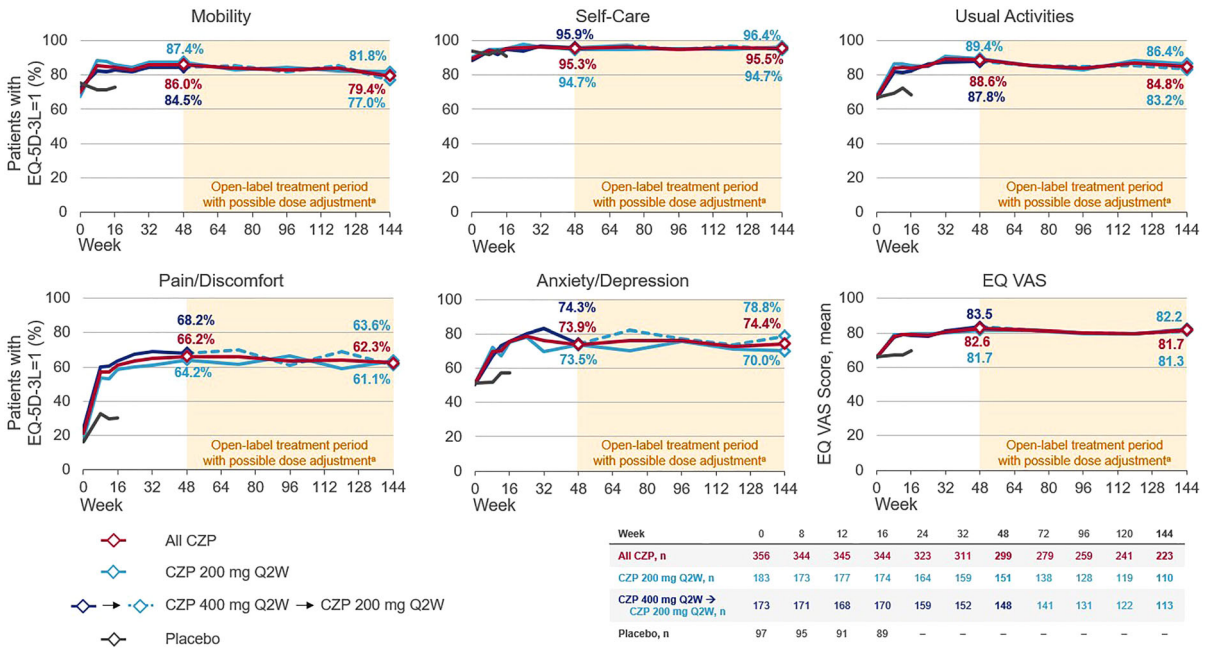


Fig. 3 The proportion of patients with a EuroQoL 5-Dimensions 3-Level (EQ-5D-3L) dimension score of 1 and mean EQ Visual Analogue Scale (EQ VAS) score over time. Data are presented as observed for all patients according to initial randomisation group; CZP-randomised patients who did not achieve a ≥ 50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50) at week 16 and entered the open-label escape arm continued to be included in these analyses. [a]Dose adjustments were mandatory or at the investigator's discretion, based on PASI response. *CZP* certolizumab pegol, *EQ-5D-3L* EuroQol 5-Dimensions 3-Level, *EQ VAS* EuroQol Visual Analogue Scale, *PASI* Psoriasis Area and Severity Index, *Q2W* every 2 weeks

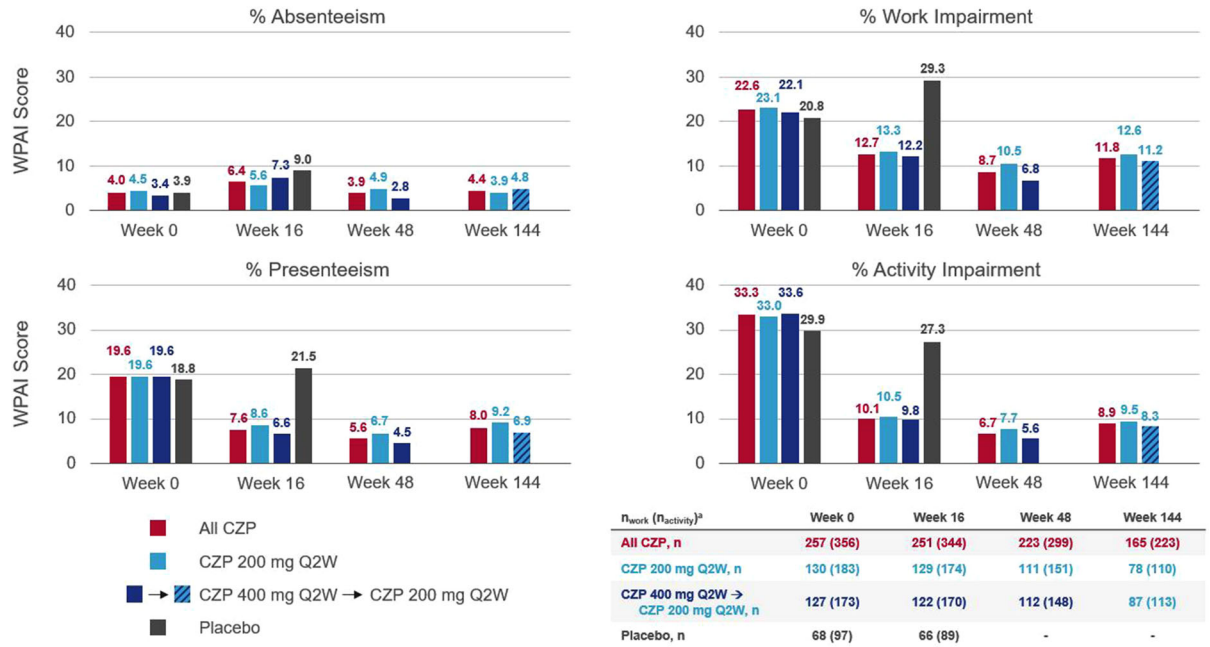
versus 76.4% of male patients (Supplementary Material Fig. S3b).

This pattern, whereby a numerically higher burden for female patients was observed at baseline, but CZP treatment was associated with improvements of similar magnitude for female and male patients, was also observed for the EQ-5D-3L Anxiety/Depression dimension and across the WPAI domains, except for Absenteeism (Supplementary Material Fig. S3c–d).

Outcomes by Concomitant PsA Status at Baseline

Of the 361 patients randomised to CZP at week 0, 73 reported having concomitant PsA and 288 reported not having concomitant PsA. A higher baseline pain and Mobility burden was seen for patients with concomitant PsA compared with those without across all physical domains of SF-36 at week 0, particularly in the Bodily Pain (mean score, PsA 39.7; no PsA 47.5) and Physical Functioning (PsA 42.1; no PsA 50.0) domains (Fig. 5). While all CZP-randomised patients experienced improvements across the physical domains of SF-36, numerically greater improvements were observed in those with concomitant PsA as compared with those without, at both week 48 (PCS change from baseline, PsA 6.3; no PsA 4.0) and week 144 (PsA 6.1; no PsA 2.8).

Patients with concomitant PsA also had a higher week 0 burden in the EQ-5D-3L Pain/Discomfort (proportion of patients with a score of 1, PsA 9.7%; no PsA 23.9%) and Mobility (PsA 38.9%; no PsA 77.5%) dimensions (Supplementary Material Fig. S4c). A similar improvement for CZP-randomised patients was seen through week 144 regardless of PsA status across these dimensions (Pain/Discomfort, PsA



n_{work} ($n_{activity}$)[a]	Week 0	Week 16	Week 48	Week 144
All CZP, n	257 (356)	251 (344)	223 (299)	165 (223)
CZP 200 mg Q2W, n	130 (183)	129 (174)	111 (151)	78 (110)
CZP 400 mg Q2W → CZP 200 mg Q2W, n	127 (173)	122 (170)	112 (148)	87 (113)
Placebo, n	68 (97)	66 (89)	-	-

Fig. 4 Mean Work Productivity and Activity Impairment (WPAI) at weeks 0, 16, 48 and 144. Data are presented as observed for all patients according to initial randomisation group; CZP-randomised patients who did not achieve a ≥ 50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50) at week 16 and entered the open-label escape arm continued to be included in these analyses. From week 48, dose adjustments were mandatory or at the investigator's discretion, based on PASI response. [a]The n_{work} category includes Absenteeism, presenteeism and overall Work Impairment; $n_{activity}$ includes overall Activity Impairment. *CZP* certolizumab pegol, *PASI* Psoriasis Area and Severity Index, *PsA* psoriatic arthritis, *Q2W* every 2 weeks

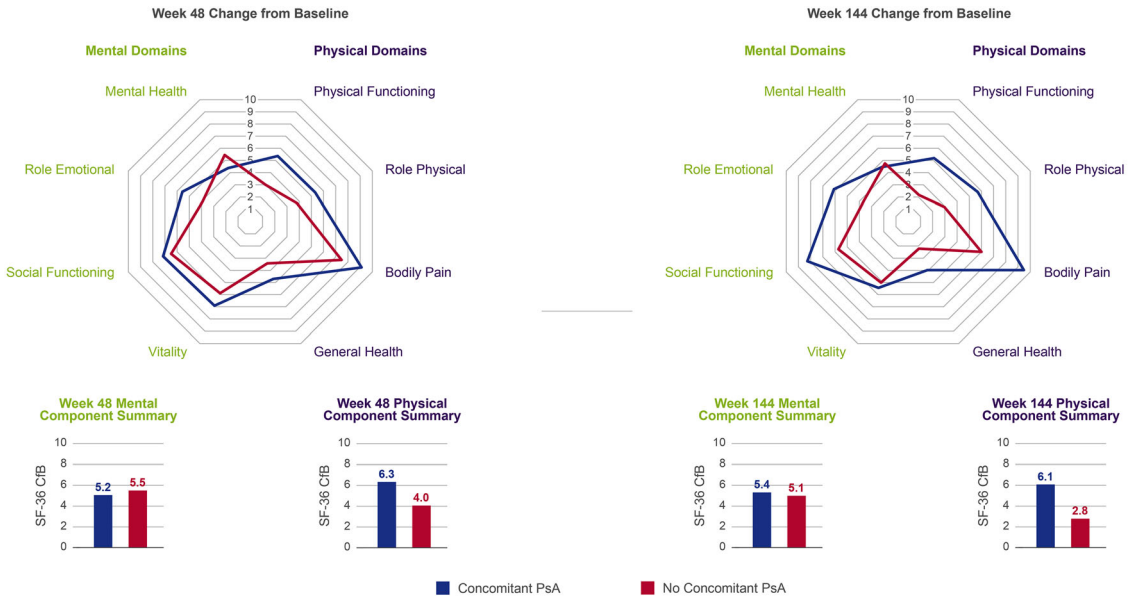
39.5%; no PsA 67.0% and Mobility, PsA 55.3%; no PsA 84.3%).

Through week 144, a numerically higher proportion of patients without PsA had DLQI 0/1 than did those with PsA (Supplementary Material Fig. S4a). Of the DLQI domains, a particularly large difference was seen for Symptoms and Feelings. Although < 1% of patients had a score of 0 at week 0 regardless of PsA status, at week 144, 31.6% of patients with PsA had a score of 0 in this domain versus 47.0% of patients without PsA (Supplementary Material Fig. S4b).

Across the WPAI domains, week 0 scores were higher for patients with PsA as compared with those without (Supplementary Material Fig. S4d). Considering these higher week 0 scores, CZP treatment resulted in improvements of similar magnitude across domains for patients with PsA when compared with those without.

DISCUSSION

Patients with plaque psoriasis in the CIMPASI-1 and CIMPASI-2 trials had sustained HRQoL, health status and functional impairment improvements over 144 weeks of CZP treatment. Since plaque psoriasis is a chronic disease, patients are likely to require treatment over many years [21], and long-term trial data can help guide clinical decision-making [4]. These results demonstrate that CZP treatment is associated with meaningful improvements in patients' lives, including greater work productivity (indicated by Work and School [DLQI] and Work Impairment [WPAI] and increased physical and social activity (Daily Activities [DLQI], Leisure [DLQI] and Activity Impairment [WPAI]). Patients also reported experiencing lessened discomfort and pain ([Bodily Pain [SF-36] and Pain/Discomfort [EQ-5D-3L]), whilst improved scores in the domains of Personal



Week 0 SF-36 Scores, mean ± SD					
Mental Domains	Concomitant PsA	No Concomitant PsA	Physical Domains	Concomitant PsA	No Concomitant PsA
Mental Health	44.8 ± 11.7	47.0 ± 10.0	Physical Functioning	42.1 ± 11.6	50.0 ± 8.2
Role Emotional	43.4 ± 12.8	47.2 ± 9.8	Role Physical	41.5 ± 11.2	48.4 ± 8.8
Social Functioning	43.5 ± 12.4	45.7 ± 10.6	Bodily Pain	39.7 ± 10.4	47.5 ± 10.3
Vitality	44.3 ± 11.7	49.0 ± 9.2	General Health	44.1 ± 10.1	48.1 ± 9.4
Mental Component Summary	45.5 ± 12.5	46.4 ± 10.4	Physical Component Summary	41.2 ± 10.3	49.4 ± 8.3

Fig. 5 Mean change from baseline (CfB) in 36-Item Short Form Survey (SF-36) at weeks 48 and 144 for CZP-randomised patients by psoriatic arthritis (PsA) status. Data are presented as observed for all patients randomised to CZP at baseline according to PsA status; patients who did not achieve a ≥ 50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50) at week 16 and entered the open-label escape arm continued to be included in these analyses. From week 48, dose adjustments were mandatory or at the investigator's discretion, based on PASI response. Patient numbers: concomitant PsA, week 0 n = 72, week 48 n = 50, week 144 n = 38; no concomitant PsA, week 0 n = 284, week 48 n = 249, week 144 n = 185. *CZP* certolizumab pegol, *PASI* Psoriasis Area and Severity Index, *SF-36* 36-Item Short Form Survey, *Q2W* every 2 weeks

Relations (DLQI), greater Social Functioning (SF-36) and an increased proportion of patients reporting no Anxiety/Depression (EQ-5D-3L) suggest that patients' overall wellbeing increased. These improvements were sustained through week 144, demonstrating the potential of CZP treatment to positively impact patient QoL in the long term.

At week 48, numerically higher responder rates and improved scores were observed in the CZP 400 mg Q2W-randomised group across outcomes as compared with the CZP 200 mg Q2W-randomised group. However, after mandatory dose reduction to CZP 200 mg Q2W at week 48 for all patients not in the escape arm, responder rates among the patients initially randomised to the higher dose gradually reduced, with similar week 144 responses between the two populations. These findings are reflected in the previously reported clinical efficacy data and suggest that some patients may require ongoing treatment with CZP 400 mg Q2W to maintain optimal response [8].

When considering patient subgroups, a difference in outcomes was seen when comparing patients with concomitant PsA to those without, at baseline and throughout the treatment period. Female patients also reported a slightly higher QoL burden than male patients at baseline and through week 144 across multiple metrics. However, the amplitude and durability of improvement with CZP treatment was

generally similar regardless of PsA status or sex except for the SF-36 physical domains, for which greater numerical improvements were observed in patients with concomitant PsA. No difference in outcomes was observed between biologic-exposed and biologic-naïve patients.

When considering skin clearance, of the patients initially randomised to CZP 200/400 mg Q2W, 70.6%/72.9% and 48.7%/42.7% had PASI 75 and PASI 90, respectively, at week 144 [8]. This sustained skin improvement underscores the connection between the stable clinical efficacy and durable PRO responses associated with CZP treatment.

As with all clinical trials, CIMPASI-1 and CIMPASI-2 had strict inclusion/exclusion criteria that may affect generalisability of these results to clinical practice. Moreover, patients were asked to self-report their PsA status, which could introduce bias as patients do not always accurately self-report diagnoses [22]. Real-world data can be used alongside clinical trial data to better understand the impact of treatment on patients' QoL. Although the PROs used in this study are not specific to patients with plaque psoriasis, they have been frequently used in psoriasis studies and have demonstrated their capacity to provide a valid and reliable assessment of HRQoL, health status and functional impairment, and reflect meaningful clinical change.

CONCLUSION

A considerable baseline QoL burden was observed for patients with moderate-to-severe plaque psoriasis in the CIMPASI-1 and CIMPASI-2 trials. CZP treatment was associated with long-term improvement in health status (EQ-5D-3L), HRQoL (DLQI and SF-36) and functional impairment at work and in other Daily Activities (WPAI). Rapid improvement during the initial phase of the trials and sustained response for CZP-treated patients, including female patients and those with concomitant PsA at baseline, highlight the benefits of CZP treatment for a broad spectrum of patients.

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Compliance with Ethics Guidelines. As previously reported, CIMPASI-1 and CIMPASI-2 were carried out according to good clinical practice requirements and the Declaration of Helsinki, and were approved by local institutional review boards/independent ethics committees [13]. Informed consent was obtained from all participants.

Data Availability. Underlying data from this manuscript may be requested by qualified researchers 6 months after product approval in the USA and/or Europe, or global development is discontinued, and 18 months after trial completion. Investigators may request access to anonymised individual patient-level data and redacted trial documents, which may include analysis-ready datasets, study protocol, annotated case report form, statistical analysis plan, dataset specifications and clinical study report. Prior to the use of this data, proposals will need to be approved by an independent review panel at www.Vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a prespecified time, typically 12 months, on a password-protected portal. The authors would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study.

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