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ORIGINAL RESEARCH

# Certolizumab Pegol for the Treatment of Plaque Psoriasis in Routine Clinical Practice: One-Year Results from the CIMREAL Study

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## ABSTRACT

***Introduction***: Certolizumab pegol (CZP) is an anti-tumor necrosis factor alpha (TNFα) approved for the treatment of moderate to severe plaque psoriasis (PSO). However, data on its real-world use is currently limited. The objective of this study was to describe the 1-year real-world effectiveness of CZP, its impact on health-related quality of life (HRQoL), and safety outcomes in patients with moderate to severe PSO in multi-country settings.

***Methods***: CIMREAL, a prospective, noninterventional study, was conducted across Europe and Canada from August 2019 to December 2022. Patients were followed for 1-year, receiving CZP 400 mg initial doses at weeks 0, 2, and 4, followed by CZP 200 mg every 2 weeks (Q2W) or CZP 400 mg Q2W maintenance dosing. Effectiveness was assessed using the Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI). Safety was also evaluated.

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***Results***: Overall, 399 patients with moderate to severe PSO were included. Of these, 93.7% (374/399) and 77.9% (311/399) completed months 3 and 12, respectively. Mean age (± standard deviation) was 42.9 ± 13.5 years and body mass index was 28.5 ± 6.8 kg/m$^2$, with the majority of patients being female (68.2%). At 12 months, CZP showed substantial effectiveness, achieving PASI 75 and PASI 90 response rates (≥ 75% and ≥ 90% improvement from baseline, respectively) of 77% and 56.5%, respectively. Patients with PASI score of ≤ 3 and ≤ 2 experienced improvement from 3 months (49.8% and 41.1%, respectively) to 12 months (82.0% and 75.3%, respectively). HRQoL considerably improved, with mean DLQI scores decreasing from 12.4 to 2.3 after 12 months of treatment, and the proportion of patients with DLQI 0/1 increased from 28.6% at 3 months to 59.4% at 12 months. The 1-year probability of persistence was approximately 85%. Overall, 30.6% of the patients experienced any adverse events and 9.3% had serious adverse events.
***Conclusion***: In routine clinical practice, CZP exhibited consistent effectiveness, positively impacting both skin psoriasis activity and HRQoL. The 1-year persistence of CZP was high, and no new safety signals were identified.
***Trial Registration Number***: ClinicalTrials.gov Identifier: NCT04053881 https://www.clinicaltrials.gov/study/NCT04053881.

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## Key Summary Points

*Why carry out this study?*

Real-world assessment of certolizumab pegol (CZP) effectiveness and safety in moderate to severe psoriasis is lacking but essential for comprehensive evaluation due to diverse patient populations and characteristics.

CIMREAL, a multinational noninterventional study, aimed to assess the effectiveness, health-related quality of life (HRQoL), and safety of certolizumab pegol over a 1-year treatment period.

*What was learned from the study?*

In this study (68.2% women), CZP demonstrated considerable effectiveness with PASI 75 and PASI 90 response rates (≥ 75% and ≥ 90% improvement from baseline, respectively, on Psoriasis Area and Severity Index) of 77% and 56.5%, respectively, at 12 months.

Among all patients, 82.0%, 75.3%, and 59.4% reached PASI score ≤ 3, PASI score ≤ 2 and Dermatology Life Quality Index 0/1 after 1-year of treatment.

The 1-year probability of persistence was approximately 85%. The overall incidence rate of adverse events (AEs) and severe AEs was 30.6% and 9.3%, respectively.

Improvements in PSO skin symptoms and HRQoL were noted across all participating countries and all patient demographics, regardless of sex, comorbidities, or prior biologic treatment.

In clinical settings, CZP may improve plaque psoriasis outcomes by accommodating patient preferences and clinical characteristics, supporting personalized management.

## INTRODUCTION

Plaque psoriasis (PSO) is an immune-mediated chronic and disabling noncommunicable disease diagnosed in 2–3% of the global population [1, 2]. Immune cells and inflammatory cytokines play a crucial role in the pathogenesis of PSO. Interleukin (IL)-17 and IL-23, along with tumor necrosis factor alpha (TNF-α), induce inflammation, abnormal skin cell growth, and further immune cell activation, thereby contributing to the persistence of psoriatic plaques [1]. PSO has systemic implications beyond skin involvement that could affect the psychosocial well-being of patients. This effect causes cumulative life course impairment (CLCI), a phenomenon exacerbated by persistent disease burden over time [3]. The introduction of biologics that decrease the inflammatory cascade has revolutionized PSO treatment, significantly enhancing symptom control and patients' health-related quality of life (HRQoL) in clinical trials and practice. Multiple biologics, including anti-TNFs, are approved for treating moderate to severe PSO, providing flexibility for physicians and patients to select the most appropriate treatment based on the individual patient's clinical condition and preferences, to provide a more personalized treatment [4, 5].

Certolizumab pegol (CZP) is a humanized Fc-free, PEGylated, anti-TNF biologic approved for the treatment of moderate to severe PSO and other chronic inflammatory diseases. Following US Food and Drug Administration and the European Medicines Agency approval of CZP for adults with PSO in 2018, this indication gained approval in various countries worldwide, including Australia, Canada, Japan, and Switzerland. Unlike other anti-TNFs, CZP lacks the immunoglobulin G (IgG) Fc region that binds to the neonatal Fc receptor, which is responsible for the active placental transfer of IgG, minimizing such transfer during the second and third trimesters of pregnancy [6].

The current understanding of the efficacy and safety of CZP in moderate to severe PSO is largely based on clinical trial data [7–10], and real-world CZP treatment outcomes remain relatively unexplored in a multi-country setting. Real-world evidence studies, which draw insights from diverse patient populations, complement clinical trial data, thereby providing a comprehensive understanding of efficacy and safety of biologic therapy. In routine practice settings, patients frequently have several comorbidities and a higher disease burden [11, 12], even with milder skin symptoms, which warrant a more comprehensive evaluation.

Here, we present results from the CIMREAL study, which aimed to assess the effectiveness of CZP treatment in patients with moderate to severe PSO as part of routine clinical practice in eight European countries and Canada. We describe the key effectiveness, HRQoL, and safety outcomes through 1-year of treatment.

## METHODS

### Study Design

CIMREAL (ClinicalTrials.gov Identifier: NCT04053881) was a prospective, noninterventional, multinational, multicenter study conducted at 79 sites across Europe and Canada, recruiting patients from August 2019 to December 2022. Patients received an initial dose of CZP 400 mg at weeks 0, 2, and 4, followed by a maintenance dose of CZP 200 mg every 2 weeks (Q2W) or CZP 400 mg Q2W, and were followed for 1 year (Fig. 1). Four observational points (OPs) aligned with routine practice visits: CZP treatment start (OP1, baseline); month 3 (OP2, approx. week 12 [weeks 10–18]); month 6 (OP3, approx. week 24 [weeks 19–37]); month 12 (OP4, approx. week 48 [weeks 38–56]).

CIMREAL was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and with the Helsinki Declaration of 1975, as revised in 1983. Approval to conduct this study was obtained from the respective ethics committees of all participating centers. The patients in this manuscript have given written informed consent to the publication of their case details.

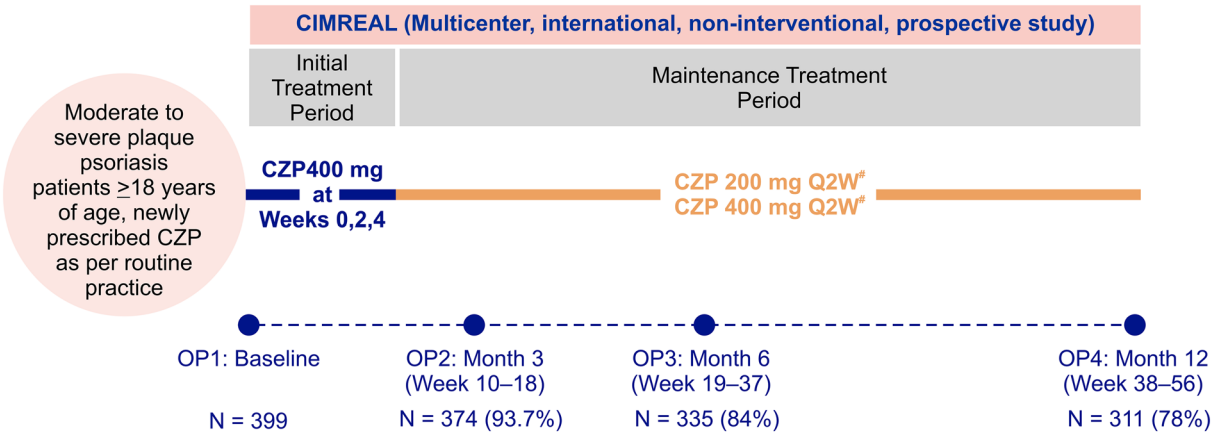



**Fig. 1** Study design and patient disposition (SAS). Hashtag (#) indicates that as per routine practice and label, patients could be prescribed CZP 200 mg Q2W or 400 mg Q2W as maintenance dosing or switch between the doses. *CZP* Certolizumab pegol, *OP* observational point, *Q2W* every 2 weeks, *SAS* safety analysis set

## Study Participants

Data for this study were collected from patients aged ≥ 18 years and who had a clinical diagnosis of moderate to severe PSO and were eligible for CZP treatment according to the physician's routine clinical practice criteria. Specific inclusion or exclusion criteria were not imposed upon enrollment regarding disease activity level as per Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) scores. Patients were newly prescribed with CZP with no previous CZP exposure, including clinical trials. The decision to prescribe CZP and the specific drug delivery presentation were based on the investigators' judgment and were independent of patients' participation in this noninterventional study. The protocol did not exclude patients who were pregnant or breastfeeding. Patients had the right to withdraw from this study and discontinue using CZP at any time without affecting their medical care.

## Outcome Measures and Assessments

The primary endpoint was the proportion of patients achieving 75% improvement from baseline in PASI (PASI 75) at month 3. Secondary endpoints were change from baseline in DLQI score at month 3 and month 12, the proportion of patients achieving PASI 75 at month 12, and the percentage of patients achieving PASI 90 (90% improvement from baseline in PASI) at month 3 and month 12. Other endpoints were absolute and included percent change from baseline in PASI at each visit, absolute and percent change from baseline in DLQI at month 3 and month 12, the proportion of patients achieving minimal clinically important difference (MCID: ≥ 4-point reduction from baseline) [13] in DLQI at each visit, the percentage of patients achieving DLQI 0/1 at each visit, the percentage of patients continuing on CZP up to month 12, self-injection assessment questionnaire (SIAQ) scores at month 3, and all reported adverse events (AEs). AEs were classified according to system organ class, high level term, and preferred terms following the Medical Dictionary for Regulatory Activities/MedDRA/ver. 25.1. SIAQ, which is a validated questionnaire, assessed patient-perceived experiences of self-injection (see the Electronic Supplementary Material (ESM) files for more details). The ESM also shows the assessment details of PASI, DLQI, and safety.

## Statistical Analyses

This study conducted the analyses on two sets: the safety analysis set (SAS), consisting of

all patients who received at least one dose of CZP and provided valid data consent, and the full analysis set (FAS), which included patients from the SAS with a valid baseline and at least one valid post-baseline PASI measurement. FAS was used to evaluate variables describing effectiveness.

Effective analysis reported here uses methods of observed data. A sensitivity analysis using multiple imputation (MI) was performed on PASI data. A subgroup analysis was performed for category sex, biologic pretreatment, comorbidity, PASI and DLQI at baseline, and maintenance dose at baseline. All data are presented as mean ± standard deviation (SD) for continuous variables and frequency (*n*) and percentage for categorical variables. GraphPad Prism 9.1 (GraphPad Software, San Diego, CA, USA) was used to generate descriptive and unadjusted drug survival Kaplan–Meier plots. SAS software Version 9.3 or higher (SAS Institute, Cary, NC, USA) was used for other statistical analyses.

## RESULTS

### Baseline Characteristics

Overall, the analysis included 399 patients (SAS). Of them, 374 completed the Month 3 visit, 335 completed the Month 6 visit, and 311 completed the study (Fig. 1). At baseline, the mean age of the patients was 42.9 ± 13.5 years, mean body mass index (BMI) was 28.5 ± 6.8, and 272 (68.2%) of the patients were female. Of the 272 female patients, 193 (70.9%) were of childbearing potential, as described by the investigators. In total, 14 women were reported at baseline to breastfeed and 24 pregnancies were reported during the study, with 8 of them reported at baseline. Comorbidities were reported in 149 (43.6%) patients (Table 1).

Analysis of demographic and clinical data across countries revealed variations in the proportion of women, ranging from 60% in the Czech Republic and 62.8% in Germany to 86% in Italy and 94.7% in the UK (ESM Table S1). Three-quarters of patients received CZP 200 mg Q2W maintenance dosing after the initial dose, with higher rates of CZP 400 mg prescription in Greece (56.5%) and Canada (41.7%) than in other countries (24.5%).

CZP was administered using different delivery methods. Overall, the proportion of patients using prefilled syringe (PFS) and auto-injector (AI, known as a prefilled pen in the EU), was generally similar, with variations observed among countries. AI was more prevalently used in Canada and Germany, followed by France. Conversely, PFS was the primary choice in the Czech Republic, Greece, Italy, and Belgium. The use of devices was proportionally similar in the UK and Spain.

### Effectiveness Outcomes

PASI 75 response rates were achieved by 45% of patients at month 3, with this response rate improving further to 77.0% at month 12 (observed cases [OC]; Fig. 2a). Likewise, PASI 90 response rates increased from 23.4% after 3 months to 56.5% after 12 months (Fig. 2a). Additionally, the proportion of patients with PASI score ≤ 3 and ≤ 2 improved from month 3 (49.8% and 41.1%, respectively) to month 12 (82.0% and 75.3%, respectively) (Fig. 2b).

PASI 75 and PASI 90 response rates using MI were 45.0% and 23.7% at month 3, respectively, and 70.2% and 50.0% at month 12.

Mean (± SD) PASI decreased from 13.1 ± 8.6 at baseline to 1.8 ± 2.7 at 12 months (Fig. 3). Similarly, the mean DLQI values decreased from 12.4 ± 7.5 at baseline to 2.3 ± 3.6 at 12 months (Fig. 4). Furthermore, the proportion of patients with a DLQI 0/1 (no impact on QoL) increased from 28.6% at 3 months to 59.4% at 12 months. The proportion of patients with an MCID in DLQI (baseline score reduction of ≥ 4 points) increased from 73.2% to 93.3%.

Mean PASI and DLQI scores improved among pregnant and breastfeeding women over the course of study. After 1 year of treatment, 66.7% of pregnant and 75.4% of breastfeeding women achieved a PASI ≤ 2. Mean DLQI decreased from 11.9 at baseline to 4.3 at 12 months in pregnant

**Table 1** Demographics, baseline, and clinical characteristics (SAS)

| Characteristics | Total $N = 399$ |
|---|---|
| Age, years, mean ± SD | 42.9 ± 13.5 |
| Female, *n* (%) | 272 (68.2) |
| BMI, kg/m$^2$, mean ± SD | 28.4 ± 6.8 [$N = 373$] |
| Country, *n* (%) | |
| Belgium | 33 (8.3) |
| Canada | 36 (9.0) |
| Czech Republic | 25 (6.3) |
| France | 20 (5.0) |
| Germany | 86 (21.6) |
| Greece | 106 (26.6) |
| Italy | 57 (14.3) |
| Spain | 17 (4.3) |
| United Kingdom | 19 (4.8) |
| Duration since diagnosis of PSO, years, mean ± SD | 16 ± 11.8 [$N = 397$] |
| Duration since first symptoms of PSO, years, mean ± SD | 17.2 ± 12.2 |
| PASI score, mean ± SD | 13.2 ± 8.7 [$N = 389$] |
| PASI ≤ 10, *n* (%) | 139 (35.7) [$N = 389$] |
| DLQI score, mean ± SD | 12.3 ± 7.5 [$N = 376$] |
| DLQI ≤ 10, *n* (%) | 164 ± 41.1 [$N = 376$] |
| Comorbidities[a], *n* (%) | 175 (43.8) |
| Vascular disorders | 53 (13.3) |
| Musculoskeletal and connective tissue disorders | 58 (14.5) |
| Metabolism and nutritional disorders | 59 (14.8) |
| Psychiatric disorders | 35 (8.8) |
| Any PSO medication history, *n* (%) | 369 (92.5) |
| Prior systemic treatment with a nonbiologic, *n* (%) | 272 (68.2) |
| Methotrexate | 148 (37.1) |
| Cyclosporine | 107 (26.8) |
| Apremilast | 69 (17.3) |
| Any prior biologic therapy, *n* (%) | 144 (36.1) |
| 1 | 85 (21.3) |
| ≥ 2 | 59 (14.8) |

**Table 1** continued

| Characteristics | Total $N = 399$ |
|---|---|
| anti-TNF[b] | 110 (27.5) |
| anti-IL-17[b] | 84 (21.1) |
| anti-IL-23[b] | 13 (3.2) |
| anti-IL-12/23[b] | 20 (5.0) |
| Others | 6 (1.5) |
| CZP drug delivery[c], *n* (%) | |
| Prefilled syringe | 211 (53.0) [$N = 398$] |
| Auto-injector | 185 (46.4) [$N = 398$] |
| Dose-dispenser cartridge and ava® electronic device[d] | 2 (0.5) [$N = 398$] |
| Maintenance dose prescribed at baseline[e], *n* (%) | |
| CZP 200 mg Q2W | 301 (75.4) |
| CZP 400 mg Q2W | 98 (24.5) |

*BMI* Body mass index, *CZP* certolizumab pegol, *DLQI* Dermatology Life Quality Index, *IL* interleukin, *PASI* Psoriasis Area and Severity Index, *PSO* plaque psoriasis, *Q2W* once every 2 weeks, *SAS* safety analysis set, *SD* standard deviation, *TNF* tumor necrosis factor alpha

[a]Any previous and ongoing medical history conditions classified by preferred term and system organ class according to the Medical Dictionary for Regulatory Activities (MedDRA) version 18.1

[b]Anti-TNF includes etanercept, infliximab, adalimumab, and golimumab; anti-IL-17 includes bimekizumab, brodalumab, ixekizumab, and secukinumab; anti-IL-23 includes guselkumab, risankizumab, and tildrakizumab; and anti-IL-12.23 includes ustekinumab. Some patients may have received more than one biologic

[c]There were patients switching delivery system during the study

[d]Dose-dispenser cartridges and ava® electronic devices are no longer available in the market

[e]Both the doses are as per CZP Summary of Product Characteristic (SmPC) approved in participating countries. There were patients switching between both maintenance doses during the study. Some patients at baseline are already on initial dose

women, and from 18.4 to 4.9 in breastfeeding women.

In line with the overall trends observed in the entire study population, a consistent reduction in both PASI and DLQI absolute mean values was observed across all participating countries (ESM Table S2). Some variability intrinsic to the different routine practice settings cannot be excluded.

The proportion of patients achieving an absolute PASI score ≤ 3 or ≤ 2 was mainly consistent across patients who were biologic naïve and biologic experienced, and irrespective of the type of prior systemic treatment, including apremilast, anti-TNF, and anti-IL-17 (Fig. 5).

ESM Table S3 shows detailed descriptive outcomes for PASI and DLQI in the various subgroups, including biological sex, baseline disease severity, comorbidities, previous biologic treatment, and maintenance dose of CZP.

Overall, PASI 75 and 90 responses achieved at month 3 were sustained in 89.3% (108/121) and 75.9% (44/58) of patients at month 12, respectively, indicating a good maintenance of the response.

## Drug Retention

The mean (± SD) duration of CZP treatment was 293.7 ± 96.1 days. A total of 311/399

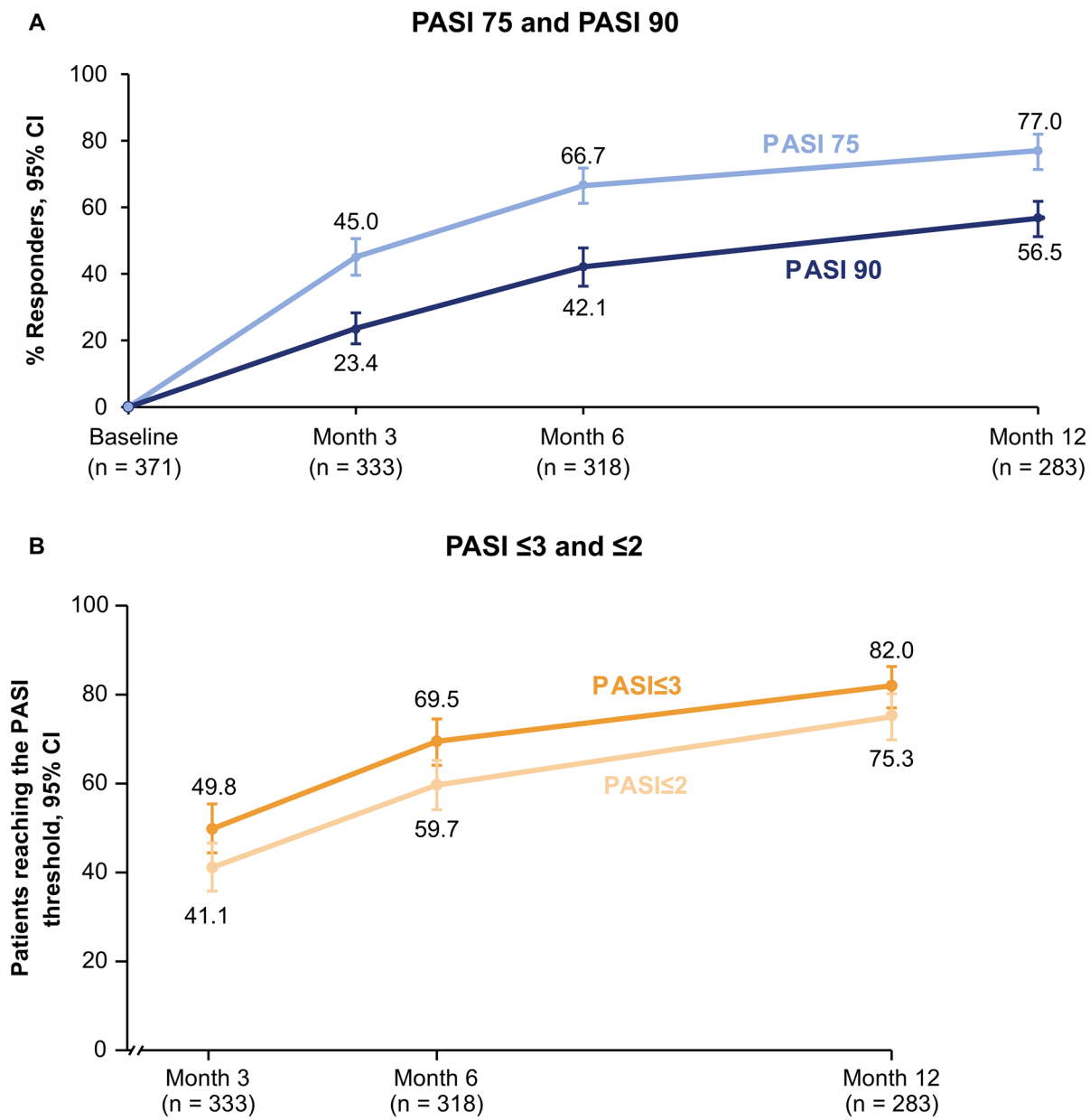



**Fig. 2** PASI response rates at months 3, 6, and 12 (observed cases). *CI* Confidence interval, *PASI 75, PASI 90* ≥ 75% or ≥ 90% reduction in a patient's Psoriasis Area and Severity Index score from baseline

(77.9%) subjects completed the study. Primary reasons for discontinuation were lack of effectiveness (11.8%), lost to follow-up (3.3%), and AEs (2.8%). The overall 1-year on-treatment survival rate was 84.6% (Kaplan–Meier analysis; Fig. 6).

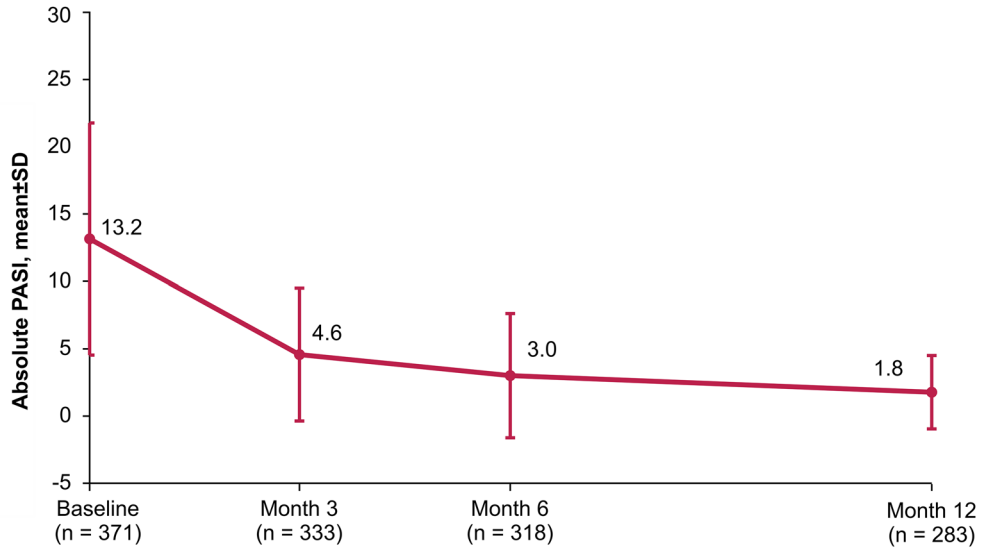



**Fig. 3** Mean PASI score over time (observed cases). The *y*-axis starts from − 5 for presentation clarity purposes *PASI*, Psoriasis Area and Severity Index, *SD* standard deviation

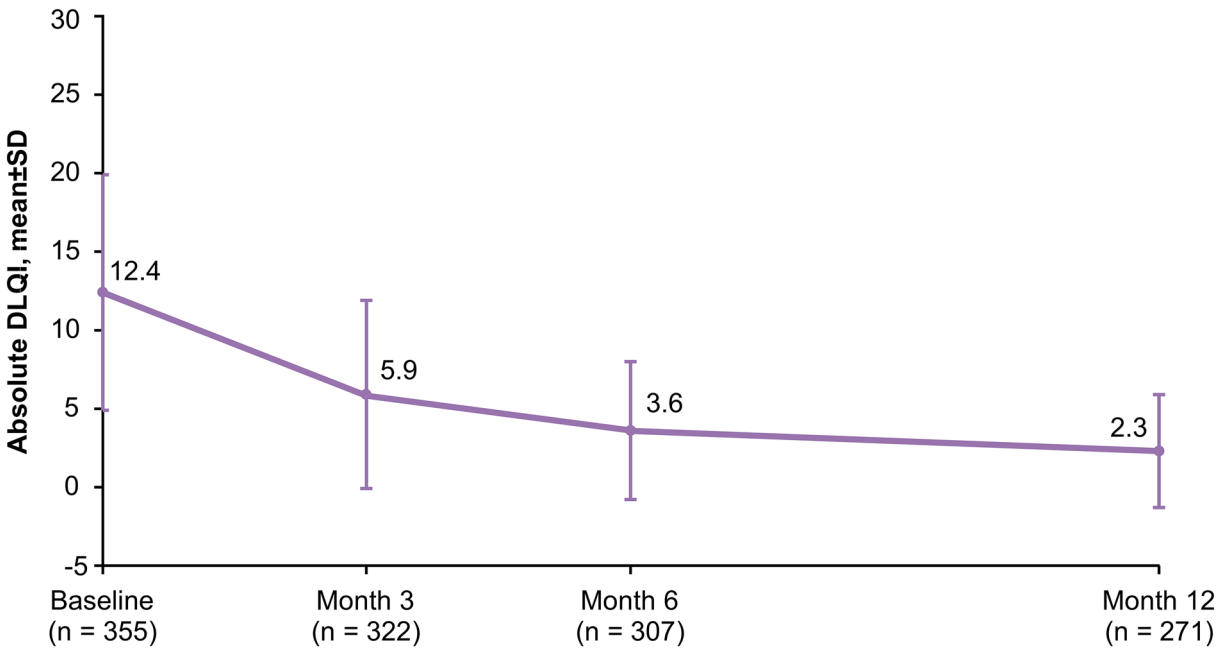
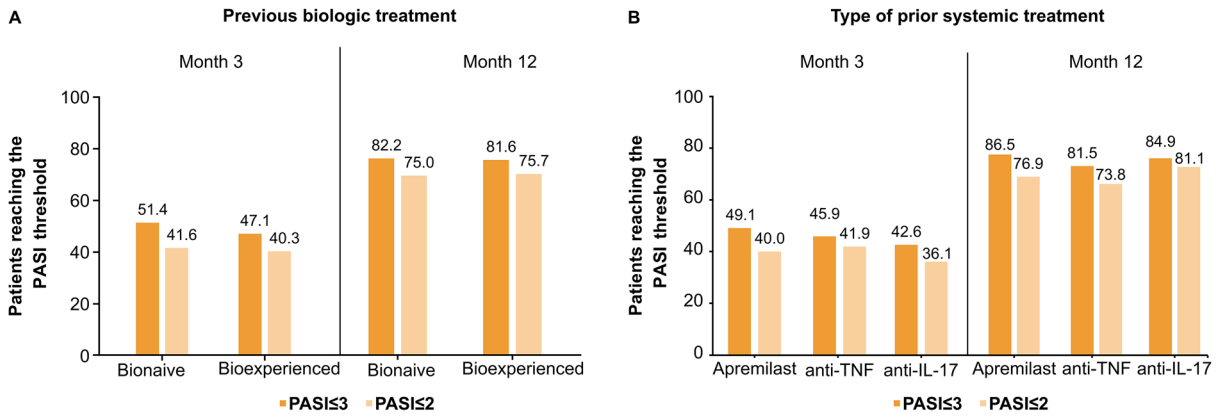



**Fig. 4** Mean DLQI score over time (observed cases). The *y*-axis starts from − 5 for presentation clarity purposes. *DLQI* Dermatology Life Quality Index, *SD* standard deviation

## CZP Adherence and Device Satisfaction

Overall, approximately 95% of patients adhered to the planned medication intake during the study, regardless of the used device.

Patient satisfaction was comparable between the use of PFS and AI, with 76.2% and 77.1% of patients, respectively, reporting moderate to




| | Month 3 | | Month 12 | |
|---|---|---|---|---|
| PASI ≤3, n/N | 110/214 | 56/119 | 148/180 | 84/103 |
| PASI ≤2, n/N | 89/214 | 48/119 | 135/180 | 78/103 |

| | Month 3 | | | Month 12 | | |
|---|---|---|---|---|---|---|
| PASI ≤3, n/N | 27/55 | 34/74 | 26/62 | 45/52 | 53/65 | 45/53 |
| PASI ≤2, n/N | 22/55 | 31/74 | 31/74 | 40/52 | 48/65 | 43/53 |

**Fig. 5** Absolute PASI mean score by previous biologic treatment and type of prior systemic treatment (observed cases). *Anti-IL-17* Interleukin-17 inhibitors (bimekizumab, brodalumab, ixekizumab, secukinumab), *anti-TNF* tumor necrosis factor inhibitors (adalimumab, etanercept, infliximab and golimumab) *PASI* Psoriasis Area and Severity Index

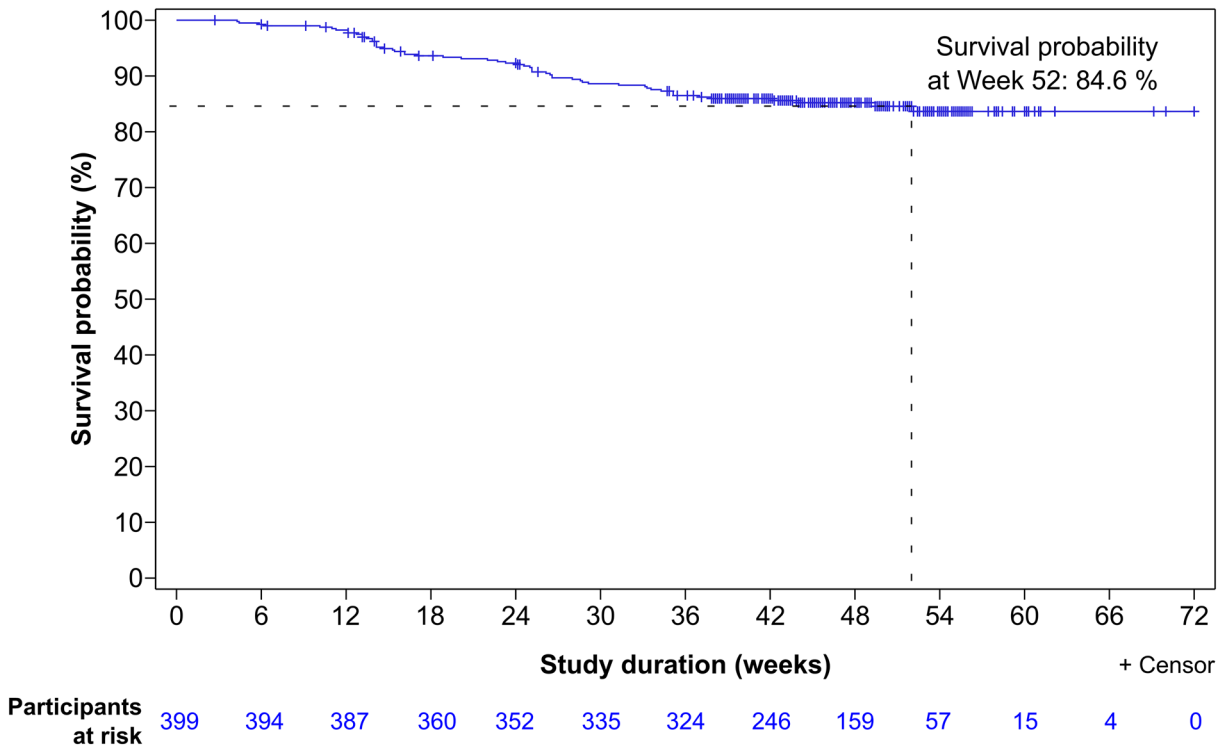



**Fig. 6** Kaplan–Meier curve of survival over the treatment period (SAS). Note: Kaplan–Meier plots were constructed accounting for discontinuations due to lack of treatment effectiveness and adverse events. SAS, Safety analysis set

very high satisfaction (defined as > 7 on the SIAQ scale; see ESM) at month 3.

### Safety Outcomes

Overall, 30.6% of patients experienced any AEs (Table 2); 9.3% of AEs were serious and 2.3% were specifically reported as being related to CZP treatment. The most frequently reported serious AEs were in the categories of infections and infestations ($n = 9$ [2.3%]), skin and subcutaneous tissue disorders ($n = 8$ [2.0%]), and pregnancy, puerperium, and perinatal conditions ($n = 7$ [1.8%]). The most frequently reported serious AEs related to CZP in ≥ 2 patients was drug ineffectiveness ($n = 2$ [0.5%]). A total of 22.1% (88/399) of patients discontinued CZP treatment, of whom 2.8% (11/399) discontinued due to AEs. AEs of interest, such as serious cardiovascular events, serious hematopoietic cytopenia, serious bleeding events, serious hypersensitivity (including anaphylactic reactions), or demyelinating-like disorders were not reported during the study. One patient with diabetes mellitus experienced a serious AE of hypoglycemic shock, which resulted in death. The investigators assessed it as unrelated to CZP treatment.

## DISCUSSION

CIMREAL is the largest multinational observational study that offers insights into the real-world effectiveness and safety of CZP in treating moderate to severe PSO across eight European countries and Canada. In CIMREAL, CZP demonstrated effectiveness and improved HRQoL over 1 year, even for patients who might not qualify for randomized clinical trials. Our study stands out for its high proportion of women (68.2%), which is notably higher than in other clinical [7, 8] and real-world studies with other biologic agents [14, 15]. Women with PSO experience lower disease activity but higher impairment of QoL, lower biologic treatment satisfaction, and increased side effects compared to men, potentially contributing to higher discontinuation rates [16, 17]. In the current study, despite similar baseline mean (± SD) PASI scores (13.0 ± 8.9 for women, 13.6 ± 8.3 for men), women had a higher mean DLQI score (13.1 ± 7.3) than men

**Table 2** Overview of adverse events (SAS)

| Adverse events | Total $N = 399$ (314.71 patient years) | | |
|---|---|---|---|
| | *n* (%) | Individual occurrences | Rate (in per 100 patient-years) |
| Any AEs | 122 (30.6) | 247 | 48.3 |
| Serious AEs | 37 (9.3) | 45 | 12.3 |
| Drug-related AEs | 36 (9) | 59 | 11.9 |
| Drug-related serious AEs | 9 (2.3) | 9 | 2.9 |
| Deaths (AEs leading to death) | 1 (0.3) | 1 | 0.3 |
| *AE of interest* | | | |
| Opportunistic infections | 1 (0.3) | 1 | 0.3 |
| Hepatic events | 1 (0.3) | 1 | 0.3 |
| Malignant or unspecified tumors | 2 (0.5) | 2 | 0.6 |
| Malignant tumors | 2 (0.5) | 2 | 0.6 |

*AE* Adverse events, *SAS* safety analysis set

(10.8 ± 7.6). However, after 1 year of CZP treatment, both sexes demonstrated similar rates of PASI 75 and PASI 90 responses. These sex-based differences in participant distribution observed in CIMREAL have also been noted in real-world settings among PSO patients treated with CZP [18]. However, this contrasts with similarly designed psoriasis studies involving other biologics, which could impact the comparability of these results with other published cohorts. The high on-drug retention rate observed in this study indicates sustained therapeutic benefits achieved under CZP treatment within the nuanced and dynamic context of real-world clinical settings.

A substantial decline in PASI scores was observed after 3 months of CZP therapy, and the effectiveness was sustained for 1 year. Additionally, 77.0% and 56.5% of the study participants achieved PASI 75 and 90, respectively, after CZP treatment for 1 year, meeting the targets for treatment success and disease activity control [19]. In patients who achieved these responses at month 3, they remained well-maintained through 1 year (PASI 75, 89.3%; PASI 90, 75.9%), indicating the durability of treatment effects over time. These findings align with those of a phase 3 randomized trial on CZP for PSO, where at 48 weeks, individuals on CZP 200 mg achieved PASI 75 and 90 at rates of 70.7% and 50.3%, respectively, while those on CZP 400 mg showed rates of 83.6% and 61.6%, respectively. Additionally, real-world data reported from Turkey and Canada also showed a substantial decrease in mean PASI scores from baseline, although with a smaller sample size than CIMREAL [20, 21].

Patient-reported outcomes, particularly those focusing on HRQoL, are essential in making informed treatment decisions [10]. Studies have reported meaningful and tangible improvements in HRQoL after CZP treatment [22]. CIMREAL demonstrated improvements in HRQoL, with DLQI reduction from baseline to 12 months of CZP treatment, consistent with real-world data from other biologic treatments [23, 24]. Interestingly, our findings indicate a considerable proportion of patients achieving a DLQI score of 0/1 with no impact on QoL, following CZP treatment, with this proportion appearing to be numerically higher among men (ESM Table S2). This difference may be attributed to lower mean (± SD) DLQI scores observed at baseline in males compared to females (10.8 ± 7.6; 50.0% with DLQI ≤ 10 and 13.1 ± 7.3; 36.8% with DLQI ≤ 10), consistent with trends reported in other cohorts [16, 25, 26]. Also, a higher proportion of patients achieving DLQI 0/1 was observed among those with PASI and DLQI scores ≤ 10 at baseline (ESM Table S2). This tendency may reflect the potential for higher CLCI experienced by women with PSO due to factors such as depression, stigmatization, stress, and loneliness, which are reported to be more prominent in women with PSO [17, 27, 28].

In recent years, there has been significant progress in the landscape of PSO treatment, leading to a broader array of options and advancements. This has resulted in a shift toward higher treatment goals, including achieving PASI 90 or PASI 100. Moreover, the focus has evolved from percentage reduction to targeting specific final outcomes, such as PASI ≤ 2, DLQI < 2, or Physician Global Assessment clear or almost clear [19]. Considering these changes, achieving a low level of disease activity and minimizing the impact on patients' lives may hold greater significance than solely focusing on a specific percentage reduction. In this study, after 1 year of CZP treatment, a notable proportion of patients achieved PASI ≤ 2 (75.3%) and DLQI 0/1 (59.4%), indicating adequate control of PSO symptoms.

In the present study, we observed patients receiving both approved CZP maintenance doses, with 75% receiving the 200 mg dose Q2W and 25% receiving the 400 mg dose Q2W. Country-wise variations exist due to regional access and/or restrictions. Relative responses showed no distinct differences between patients on 200 mg or 400 mg, although there was a higher inclination to prescribe the 400 mg dose among patients with high baseline BMI and prior exposure to biologics, both characteristics associated with a population historically described as more challenging to treat [29, 30]. CZP was administered using either PFS or AIs, with no discernible differences noted in patient satisfaction. These findings

from CIMREAL underscore the nuanced approach employed by physicians in routine clinical practice, highlighting the flexibility in tailoring CZP maintenance doses based on baseline demographic characteristics, such as BMI, or history of previous biologic treatment. Additionally, physicians adjust device usage according to patient needs, preferences, and availability, thereby facilitating a more personalized approach to management and treatment.

Our observations indicate that CZP effectively treats PSO across various patient demographics, irrespective of sex, comorbidities, or prior biologic treatment exposure. Furthermore, the effectiveness of CZP remained consistent across countries, even when differences in baseline characteristics were observed due to local conditions, guidelines, and treatment algorithms.

The high cumulative probability of on-drug survival observed with CZP (84.6%) is consistent with the expected first-year rates for a biologic, including anti-TNFs, as reported by the BioCAPTURE [30] (approx. 75%) and BADBIR [31] (71–80%) studies. High effectiveness and persistence suggest the benefits of CZP on a long-term basis.

This study identified no new safety concerns. A proportion of 22.1% discontinued the study at various time points, with 2.8% due to AEs. AEs related to pregnancy in this study are likely due to the patient population, while those related to COVID-19 are likely due to the recruitment period, which coincided with the pandemic. The prevalence of AEs aligns with the findings reported in clinical trials [8, 32–34] and other real-world data of CZP in patients with PSO [35].

Our study has some inherent limitations, including a lack of a control group, as this was a real-world study focused on patients treated with CZP. We employed descriptive analyses for subgroups; thus, observed differences were not adjusted for potential confounders. Patients included were CZP-naïve with moderate to severe PSO, self-selected based on their willingness to participate, potentially leading to baseline characteristic disparities compared to those receiving other biologic treatments or CZP outside this study. Although providing insights into the durability of effect, the study's follow-up period was limited to 1 year. COVID-19 and guideline recommendations limited the use of CZP, posing challenges in recruitment. A higher proportion of female patients was included possibly due to recommendations for CZP use during pregnancy [19]. Outcomes for women of childbearing potential, pregnant women, and breastfeeding women will be addressed in a separate manuscript. The external validity and representativeness of the recruited population cannot be established.

## CONCLUSION

CIMREAL is the largest observation of CZP effectiveness in patients with moderate to severe PSO in routine clinical practice. Notable improvements in disease symptoms and QoL were observed in both the overall cohort and various subgroups after 1 year of CZP treatment. No new safety concerns were identified for CZP. These results indicate that CZP contributes to enhanced PSO outcomes in clinical settings considering clinical characteristics and patients' preferences toward personalized management and treatment.

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## *Declarations*

***Conflict of Interest.*** Bernhard Korge was an advisor to, and/or received speakers' honoraria from, and/or received grants from, and/or participated in clinical trials from Abbvie, Almirall Hermal, Amgen, Beiersdorf Dermo Medical, Biogen, Bristol Myers Sqibb, Celgene, Dr. Pfleger, Galderma, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pierre Fabre, UCB Pharma. Charles W Lynde received speaker fees and/or research grants from and/or participated in advisory boards of Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Novartis, Sanofi Genzyme UCB Pharma. Alena Machovcova participated in clinical trials and/or received honoraria as an investigator from, and/or participated in advisory boards, and/or received speaker fees from AbbVie, Almirall, Amgen, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sanofi Genzyme and UCB Pharma. Elisavet Lazaridou received speaker fees and research grants from and/or participated in advisory boards from UCB Pharma. David Vidal Sarro participated in clinical trials and/or received honoraria as a consultant and/or investigator, and/or received speaker fees from AbbVie, Almirall, Janssen, Lilly, Novartis and UCB Pharma. Ines D Pousa, Frederik Fierens, Paulette Williams, Saori Shimizu, and Tanja Heidbred are employees of UCB Pharma. Richard B Warren received consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; and honoraria from Astellas, DiCE, GSK, and Union. Richard B Warren is an Editor-in-Chief of *Dermatology and Therapy*. Richard Warren was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Olivier Vanhooteghem, Marc Perrussel, and Claudio Marasca report no conflicts of interest in this work.

***Ethical Approval.*** CIMREAL was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and with the Helsinki Declaration of 1975, as revised in 1983. Approval to conduct this study was obtained from the respective ethics committees of all participating centers. The patients in this manuscript have given written informed consent to the publication of their case details.

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