Certolizumab Pegol for the Treatment of Moderate to Severe Plaque Psoriasis: 16-Week Results from a Phase 2/3 Japanese Study

Yoshinori Umezawa · Shinya Sakurai · Naoki Hoshii · Hidemi Nakagawa · for the PS0017 Study Group

Received: December 21, 2020 / Accepted: January 23, 2021 / Published online: February 19, 2021 © The Author(s) 2021, corrected publication 2022

ABSTRACT

Introduction: Certolizumab pegol (CZP), the Fc-free, PEGylated anti-tumor necrosis factor, is approved for the treatment of moderate to severe plaque psoriasis (PSO) in Western countries and in Japan, among other indications.

Methods: We report results from the first 16 weeks of a 52-week phase 2/3 trial of CZP in Japanese patients with PSO. Patients ≥ 20 years with PSO ≥ 6 months (Psoriasis Area and Severity Index [PASI] ≥ 12, body surface area affected ≥ 10%, and Physician’s Global Assessment [PGA] ≥ 3 on a 5-point scale) were randomized 2:2:1 to CZP 400 mg every 2 weeks (Q2W), CZP 200 mg Q2W (400 mg weeks 0/2/4), or placebo Q2W. Outcomes assessed to week 16: PASI 75, PASI 90, PGA 0/1 (Markov chain Monte Carlo), Dermatology Life Quality Index (DLQI 0/1) and Itch Numeric Rating Scale (INRS 0) (non-responder imputation), and DLQI and INRS change from baseline (last observation carried forward). Safety data were reported for patients receiving ≥ 1 dose of study medication through weeks 0–16; adverse events were evaluated using Medical Dictionary for Regulatory Activities version 18.1.

Results: A total of 127 patients were randomized to CZP 400 mg Q2W (N = 53), CZP 200 mg Q2W (N = 48), placebo (N = 26). Week 16 responder rates for CZP 400 mg/200 mg Q2W versus placebo were 87.1%/73.0% versus 7.9% for PASI 75; 75.7%/53.8% versus 0.2% for PASI 90; 66.7%/52.7% versus 0.0% for PGA 0/1 (all p < 0.0001 for both CZP doses versus placebo). Significant improvements in DLQI and INRS were reported at week 16 by patients receiving both CZP doses compared with placebo (p < 0.0001). Incidence of treatment-emergent adverse events within the CZP 400 mg Q2W, CZP 200 mg Q2W, and placebo groups were 326.1, 404.9, and 682.4 per 100 patient-years. No new safety signals were identified compared to previously reported data.

Conclusion: CZP dosed at 400 mg or 200 mg Q2W was associated with improved PSO signs and symptoms.

Trial Registration: ClinicalTrials.gov identifier, NCT03051217.

Keywords: Certolizumab pegol; Japan; Plaque psoriasis; Tumor necrosis factor-alpha
**Key Summary Points**

Why carry out this study?  
Plaque psoriasis (PSO) is an immune-mediated inflammatory disease, associated with multiple comorbidities and reduced health-related quality of life.

Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-tumor necrosis factor (TNF) which has demonstrated favorable efficacy and safety in moderate to severe PSO over three global phase 3 trials.

As the epidemiology of PSO may be different in the Japanese population as compared with the Western population, this study was conducted to evaluate the effectiveness of CZP in a Japanese population of patients with moderate to severe PSO.

What was learned from the study?  
CZP dosed at 400 mg or 200 mg every 2 weeks (Q2W) was associated with improved PSO signs and symptoms over 16 weeks, with numerically higher responses in the CZP 400 mg Q2W group.

These interim data provide evidence that CZP may be a suitable treatment option for moderate to severe PSO in Japanese patients.

Results over the full 52-week trial period are needed to further define the efficacy and safety of CZP for the treatment of PSO in this population.

**INTRODUCTION**

Plaque psoriasis (PSO) is an immune-mediated inflammatory disease that affects around 0.3% of the population in Japan [1]. PSO manifests as red, raised, sharply demarcated, dry plaques which are usually covered by white or silvery scales [2, 3]. These plaques most often affect the scalp, elbows, knees and lower back, and cause itching and stinging [2, 3]. In addition to skin involvement, PSO can also affect the nails, and some patients develop psoriatic arthritis (PsA), affecting the joints [2]. The pathogenic effects of PSO have a systemic impact, and patients have an increased risk of metabolic syndrome and cardiovascular disease, with the latter reported to reduce the life expectancy of patients with moderate to severe PSO by approximately 5 years [4–8]. In addition, conditions associated with chronic systemic inflammation, such as obesity, are known aggravating factors for PSO [9–12].

Alongside the physical manifestations, PSO is associated with reduced health-related quality of life (QoL), with some patients experiencing a psychological burden that affects their relationships, social activities, and emotional well-being [13, 14]. Factors that contribute towards decreased QoL include the negative effect on body image caused by skin lesions, and the itching and interference with sleep that can accompany PSO flares [14].

Therapies for PSO vary according to disease severity. Treatment options for patients with a mild form of the disease include topical therapies such as corticosteroids or vitamin D analogues, whilst more severe disease can be treated with phototherapy, methotrexate, retinoids, cyclosporine A, apremilast, or biologics, including agents that interfere with the function of tumor necrosis factor (TNF)-α, interleukin (IL)-17, IL-23, or IL-12/23 [15–19].

Certolizumab pegol (CZP) is an Fc-free, PEGylated, anti-TNF biologic. CZP lacks the immunoglobulin G (IgG) Fc region that binds the neonatal Fc receptor for IgG (FcRn), retained on other anti-TNFs [20], and the conjugation to polyethylene glycol (PEG) increases the half-life of the agent [21]. CZP was first approved in the
USA and European Union in 2008 and 2009, respectively, for the treatment of rheumatoid arthritis (RA). Currently, it is additionally approved for the treatment of moderate to severe plaque psoriasis (PSO), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) (comprising both ankylosing spondylitis [AS] and non-radiographic axial spondyloarthritis [nr axSpA]) [22, 23]. In the USA and Switzerland, it is also approved for the treatment of Crohn’s disease [22, 24]. In Japan, CZP is currently approved for the treatment of RA, PSO, PsA, generalized pustular psoriasis (GPP), and erythrodermic psoriasis (EP) [25]. Three phase 3 trials, conducted in North America and Europe, have evaluated CZP in moderate to severe PSO over the long-term (CIMPASI-1 [NCT02326298], CIMPASI-2 [NCT02326272], and CIMPACT [NCT02346240]). In these 3-year trials, with a combined total of 1020 randomized patients, CZP has demonstrated favorable efficacy, and a safety profile consistent with the anti-TNF class, with data currently reported through 48 weeks [26–28]. Here, we report efficacy and safety results from the initial 16 weeks of a 52-week phase 2/3 trial of CZP in Japanese patients with moderate to severe PSO (NCT03051217); this study is the first to evaluate CZP for the treatment of psoriasis in this patient population.

METHODS

Study Design

This was a phase 2/3, randomized, double-blind, placebo-controlled trial conducted at 33 sites in Japan, beginning February 21, 2017 (NCT03051217). Following a 2–5 week screening period to confirm eligibility, an interactive response technology (IRT) was used to randomize patients 2:2:1 to CZP 400 mg every 2 weeks (Q2W), CZP 200 mg Q2W (with a loading dose of CZP 400 mg Q2W at weeks 0, 2, and 4), and placebo, according to the randomization schedule produced by the IRT vendor (stratified by prior biologic exposure [yes/no] and concurrent PsA [yes/no]). All CZP and placebo treatments were administered subcutaneously at the study site by unblinded, trained site personnel not involved in any other study procedures. At week 16, patients either continued for a further 36 weeks of double-blind maintenance treatment or entered an open-label escape arm (Fig. 1). Here, outcomes from the first 16 weeks of the study are presented.

The study was carried out in accordance with the applicable regulatory and International Council for Harmonization-Good Clinical Practice requirements, and the Helsinki Declaration of 1964, and its later amendments. The study protocol was reviewed and approved by an institutional review board prior to implementation. Written informed consent was obtained from all patients.

Study Participants

Eligible patients were at least 20 years of age with moderate to severe PSO for at least 6 months with baseline Psoriasis Area and Severity Index (PASI) ≥ 12, body surface area (BSA) affected ≥ 10% and Physician’s Global Assessment (PGA) ≥ 3 on a 5-point scale, and were candidates for systemic PSO therapy, phototherapy, or chemophototherapy. All patients were of Japanese ethnicity.

Patients were excluded if they had a history of treatment with CZP or more than two biologic agents; had a history of primary failure to any biologic (no response within the first 12 weeks of treatment) or secondary failure to more than two biologics (patients who initially responded then discontinued treatment due to loss of response after 12 weeks of treatment); had a diagnosis of any inflammatory arthritis other than psoriatic arthritis; had guttate, drug-induced, erythrodermic or pustular psoriasis; had a history of chronic or recurrent infection, including active or untreated latent tuberculosis (assessed using an interferon-γ release assay), or were at high risk of infection; had a history of a lymphoproliferative disorder; had class III or IV congestive heart failure (New York Heart Association 1964 criteria) [29]; had a history of, or suspected to have, demyelinating disease of the central nervous system; were breastfeeding, pregnant, planned to become pregnant/had a partner who planned to become pregnant.
during the study or within 5 months of the last dose of study drug.

**Efficacy Evaluations and Patient-Reported Outcomes**

The primary endpoint was the proportion of patients achieving at least 75% improvement from baseline in PASI (PASI 75) for each CZP dose versus placebo at week 16. Secondary endpoints at week 16 were at least 90% improvement from baseline in PASI (PASI 90), “clear” or “almost clear” PGA with at least a 2-point improvement from baseline (PGA 0/1), change from baseline in Dermatology Life Quality Index (DLQI), and change from baseline in Itch Numeric Rating Scale (INRS). The INRS is a simple questionnaire that asks the patient to describe the worst level of itching due to PSO in the 24 h prior to the clinic visit on a scale from 0 (no itching) to 10 (worst itch imaginable) [30].

The rate of DLQI 0/1 (remission), defined as the achievement of a DLQI score of 1 or less, and the rate of INRS 0 (remission), defined as the achievement of an INRS score of 0, were also evaluated.

**Safety Evaluations**

Week 16 safety data are presented for all patients who received at least one dose of study medication through weeks 0–16 (the safety set). Adverse events (AEs) were classified according to the Medical Dictionary for Regulatory Activities (MedDRA) version 18.1.

Serious AEs were defined as AEs that met one or more of the following criteria: death; life-threatening; significant or persistent disability or incapacity; congenital anomaly or birth defect (including that occurring in a fetus); an important medical event that may jeopardize the patient and may require surgical intervention; initial inpatient hospitalization or prolongation of hospitalization. In this analysis, an AE was defined as treatment-emergent (a TEAE) if it occurred within the first 16 weeks of treatment. For patients who discontinued during this period, AEs were also considered treatment-emergent if they occurred within 70 days of the last dose of study medication. Incidence rates (IR) were calculated as incidence of new cases per 100 patient-years (PY).

The pre-defined AEs of interest were serious infections, including opportunistic infections; malignancies, including lymphoma; congestive heart failure; demyelinating-like disorders;
aplastic anemia, pancytopenia, thrombocytopenia, neutropenia, and leukopenia; serious bleeding events; lupus and lupus-like illness; serous skin reactions such as Stevens–Johnson syndrome, toxic epidermal necrosis, and erythema multiforme; potential Hy’s law case, defined as at least three times the upper limit of normal (ULN) in alanine transaminase (ALT) or aspartate transaminase (AST) with coexisting at least two times the ULN total bilirubin, in the absence of at least two times the ULN in alkaline phosphatase (ALP), with no alternative explanation for the biochemical abnormality.

Calculation of Sample Size

Week 16 PASI 75 responses were assumed to be 75%, 70%, and 15% for CZP 400 mg Q2W, CZP 200 mg Q2W, and placebo, respectively. Under these assumptions, a sample size of 125 (allocated 2:2:1 to CZP 400 mg Q2W, CZP 200 mg Q2W, and placebo) was calculated to provide more than 99% power to detect a difference between either dose of CZP and placebo, with a two-sided test significance level of 0.025.

Statistical Analyses

For PASI and PGA outcomes, missing data were imputed using Markov chain Monte Carlo (MCMC) multiple imputation methodology. Responder rates and treatment group comparisons were based on a logistic regression model with factors for treatment group and prior biologic exposure. If there were no responders in one or more treatment groups, the logistic regression model may have been unable to converge. In such instances, prior biologic exposure was removed from the model. If the model was still unable to converge, exact logistic regression was applied and odds ratios, associated exact confidence intervals, and exact p values were determined. For PASI and PGA outcomes, sensitivity analyses were performed wherein missing data was imputed using non-responder imputation (NRI).

For DLQI and INRS change from baseline values, missing data were imputed using the last observation carried forward (LOCF) approach, and treatment group comparisons were performed using an analysis of covariance (ANCOVA) model with treatment group and prior biologic exposure as factors and baseline

Fig. 2 Patient disposition. CZP certolizumab pegol, Q2W every 2 weeks. Screen failure are reported for patients with PSO, erythrodermic psoriasis, and generalized pustular psoriasis, the reasons being ineligibility (n = 39/43; 20.3%), adverse event (n = 3/43; 1.6%) and consent withdrawn (n = 1/43; 0.5%)
scores as covariates. For DLQI 0/1 and INRS 0 responder rates, missing data were imputed using NRI. Treatment group comparisons were made using logistic regression models based on these imputed data.

Multiplicity was controlled via a fixed sequence testing procedure split by dose (the overall alphas of 0.05 were allocated as 0.025 to each dose).

#### RESULTS

**Patient Disposition and Baseline Characteristics**

Of the 168 patients screened, 127 were randomized to CZP 400 mg Q2W (N = 53), CZP 200 mg Q2W (N = 48), or placebo (N = 26) (Fig. 2). Demographics and baseline characteristics were balanced across treatment groups.
Table 2  Efficacy outcomes at week 16

|                          | CZP 400 mg Q2W (N = 53) | CZP 200 mg Q2W (N = 48) | Placebo (N = 26) |
|--------------------------|-------------------------|-------------------------|-----------------|
| **Primary endpoint**     |                         |                         |                 |
| PASI 75 responder rate, % | 87.1                    | 73.0                    | 7.9             |
| OR vs placebo (97.5% CI) | 79.1 (11.7 to 533.2)    | 31.7 (5.1 to 195.9)    | –               |
| p value                  | < 0.0001                | < 0.0001                | –               |
| **Secondary endpoints**  |                         |                         |                 |
| PASI 90 responder rate,a % | 75.7                    | 53.8                    | 0.2             |
| OR vs placebo (97.5% CI) | 100.5 (15.5 to 649.4)   | 38.7 (6.0 to 247.6)    | –               |
| p value                  | < 0.0001                | < 0.0001                | –               |
| PGA 0/1 responder rate, % | 66.7                    | 52.7                    | 0.0             |
| OR vs placebo (97.5% CI) | 69.6 (11.1 to 434.7)    | 38.2 (6.1 to 238.6)    | –               |
| p value                  | < 0.0001                | < 0.0001                | –               |
| DLQI change from baseline, mean ± SD | – 6.4 ± 7.1 | – 7.2 ± 5.8 | – 0.7 ± 4.9 |
| AMD vs placebo (97.5% CI) | – 6.5 (– 9.1 to – 3.9) | – 6.5 (– 9.1 to – 3.8) | – |
| p value                  | < 0.0001                | < 0.0001                | –               |
| INRS change from baseline, mean ± SD | – 4.0 ± 2.9 | – 2.9 ± 3.1 | 0.0 ± 1.4 |
| AMD vs placebo (95% CI)  | – 4.2 (– 5.3 to – 3.1)  | – 3.1 (– 4.3 to – 2.0) | –               |
| p value                  | < 0.0001                | < 0.0001                | –               |
| **Other outcomes**       |                         |                         |                 |
| DLQI 0/1, %              | 62.3                    | 56.3                    | 7.7             |
| OR vs placebo (97.5% CI) | 19.7 (4.2 to 92.5)      | 15.5 (3.3 to 73.1)     | –               |
| p value                  | 0.0002                  | 0.0005                  | –               |
| INRS 0, %                | 37.7                    | 22.9                    | 0.0             |
| OR vs placebo (97.5% CI) | 20.8 (4.2 to 101.5)     | 10.4 (2.0 to 53.1)     | –               |
| p value                  | 0.0002                  | 0.0104                  | –               |

AMD adjusted mean treatment difference, CI confidence interval, CZP certolizumab pegol, DLQI Dermatology Life Quality Index, DLQI 0/1 achievement of a DLQI score of ≤ 1 (remission), INRS Itch Numeric Rating Scale, INRS 0 achievement of an INRS score of 0 (remission), OR odds ratio, PASI 75/90 ≥ 75%/90% improvement from baseline in Psoriasis Area and Severity Index, PGA 0/1 Physician’s Global Assessment clear/almost clear with ≥ 2-category improvement from baseline, Q2W every 2 weeks
a Exact regression was used to estimate odds ratios, associated exact confidence intervals and exact p values, and simple proportions were calculated for PASI 90 responder rate
a PASI 75 responder rate

b PASI 90 responder rate

c PGA 0/1
Fig. 3 Efficacy outcomes to week 16 (MCMC). *p < 0.05; **p ≤ 0.0001 versus placebo; At weeks 4, 8, 12, and 16 exact regression was used to estimate odds ratios and simple proportions were calculated for PASI 90 responder rate. CZP certolizumab pegol, MCMC Markov chain Monte Carlo, PASI 75/90 ≥ 75%/90% improvement from baseline in Psoriasis Area and Severity Index, PGA 0/1 Physician’s Global Assessment clear/almost clear with ≥ 2-category improvement from baseline, Q2W every 2 weeks.

Of the randomized patients, 120 completed the initial 16-week treatment period; completion rates were slightly higher in the two CZP groups (greater than 95%) compared with the placebo group (89%) (Fig. 2).

Primary Efficacy Outcome

PASI 75 responder rates at week 16 were 87.1% for the CZP 400 mg Q2W group, 73.0% for the CZP 200 mg Q2W group, and 7.9% for the placebo group (Table 2). The PASI 75 responder rate was significantly higher for both CZP dose groups compared with placebo from week 8 onwards (Fig. 3a). Similar results were observed at week 16 with NRI analysis (Table S1 in Supplementary Material).

Secondary Efficacy Outcomes

The PASI 90 and PGA 0/1 responder rates were also significantly greater for both groups of CZP-treated patients than for placebo-treated patients through weeks 8–16 (Fig. 3b, c). PASI 90 responder rates at week 16 were 75.7% for the CZP 400 mg Q2W group, 53.8% for the CZP 200 mg Q2W group, and 0.2% for the placebo group (Table 2). At weeks 4, 8, 12, and 16, the logistic regression model was unable to converge and PASI 90 responder rates were calculated as simple proportions, as per the statistical analysis plan, with exact regression used to calculate odds ratios and associated confidence intervals, and exact p values determined (Table 2). PGA 0/1 responder rates at week 16 were 66.7% for the CZP 400 mg Q2W group, 52.7% for the CZP 200 mg Q2W group, and 0.0% for the placebo group (Table 2). Similar results were observed at week 16 with NRI analysis (Table S1 in Supplementary Material).

Quality of Life: Patient-Reported Outcomes

CZP-treated patients reported significantly greater changes from baseline in DLQI at week 16 than patients treated with placebo, and more patients achieved DLQI 0/1 (Table 2; Fig. 4). Similarly, significantly greater changes from baseline in INRS were reported by patients treated with CZP than patients treated with placebo, with more patients achieving INRS 0 (Table 2; Fig. 5).

Safety Assessments

After 16 weeks, the total treatment exposure was 16.2 PY in the CZP 400 mg Q2W group, 14.8 PY in the CZP 200 mg Q2W group, and 7.6 PY in the placebo group. The greatest incidence of TEAEs was reported in the placebo group, and the IR of TEAEs was similar between the CZP 400 mg Q2W and CZP 200 mg Q2W treatment groups (Table 3).

Regarding AEs of interest, there was one serious infection, a case of herpes zoster reported by a patient receiving CZP 400 mg Q2W. No other AEs of interest were reported in this period. There were no malignancies (including lymphoma), TEAEs related to congestive heart failure, serious cardiovascular events, serious skin disorders (such as Stevens–Johnson or lupus), or deaths.

DISCUSSION

In this phase 2/3 trial, 16 weeks of treatment with CZP dosed at either 400 mg or 200 mg Q2W resulted in significant improvements in the symptoms of PSO in Japanese patients, compared with placebo. The response to treatment was rapid and significantly greater proportions of CZP-treated patients achieved PASI 75, PASI 90, and PGA 0/1 as early as week 8, compared with the placebo group, with
further improvements to week 16. At week 16, PASI and PGA responses were numerically higher for patients receiving CZP 400 mg Q2W compared with those receiving CZP 200 mg Q2W, particularly for the more stringent outcome of PASI 90. No new safety signals were identified with 16 weeks of CZP treatment, compared to previously reported data in North America and Europe [26–28], and the overall incidence of TEAEs, serious TEAEs, and discontinuations due to TEAEs were low for all CZP-treated patients.

The results from this study in Japanese patients were comparable with the larger

Fig. 4 DLQI outcomes to week 16. A reduced DLQI score represents an improvement. DLQI is measured on a scale of 0–30. a p < 0.05; b p < 0.0001 versus placebo. CZP certolizumab pegol, DLQI Dermatology Life Quality Index, DLQI 0/1 achievement of a DLQI score of ≤1 (remission), LOCF last observation carried forward, NRI non-responder imputation, Q2W every 2 weeks

△ Adis
phase 3 trials conducted in North America and Europe [28]. For example, PASI 75 responder rates at week 16 in this trial were 87.1% and 73.0% for CZP 400 mg Q2W and CZP 200 mg Q2W, respectively, compared to 80.1% and 74.5% in the pooled analysis of the CIMPASI-1, CIMPASI-2, and CIMPACT trials; PASI 90 and PGA 0/1 responder rates also follow similar trends [28].

The PASI response after 16 weeks reported here was comparable with that of other biologic agents in Japanese patients in the initial periods.
of their respective trials [31–35]. For example, the PASI 75 responder rate for adalimumab, another anti-TNF agent, dosed at 80 mg every other week is reported as 81.0% after 16 weeks [31]. PASI 75 responder rates in Japanese patients for guselkumab (anti-IL-23) after 16 weeks, and secukinumab (anti-IL-17A), ustekinumab (anti-IL12/23), brodalumab (anti-IL-17 receptor), and ixekizumab (anti-IL-17A) after 12 weeks were also comparable to the CZP 400 mg Q2W results after the first 16 weeks of this trial [32–36].

A meaningful impact on QoL from CZP treatment was demonstrated in this study, with over half of CZP-treated patients achieving DLQI 0/1 at week 16. Patients receiving CZP also reported significant reductions in INRS score. In a survey on patient perspectives in the management of PSO, 43% of patients indicated itching to be among the most bothersome signs or symptoms of PSO [37]. Therefore, the results reported here are likely to represent an important improvement in QoL.

Limitations of this trial include the lack of active comparator and the exclusion of patients with a history of primary failure to biologic therapy. While this trial included a smaller sample size to those conducted in North America and Europe, the results from the 127 patients in this analysis were comparable with those from the 850 CZP- or placebo-treated patients included in a pooled week 16 analysis of the CIMPASI-1, CIMPASI-2, and CIMPACT trials. [28] Although the patient background was different, the effectiveness and safety of CZP was demonstrated in a real-world study conducted in Italy [38]. These results indicate that the results of this study may be generalizable to the wider patient population, including in the real-life setting in Japan.

Table 3 Summary of TEAEs and serious TEAEs from baseline to week 16

|                      | CZP 400 mg Q2W (N = 53) | CZP 200 mg Q2W (N = 48) | Placebo (N = 26) |
|----------------------|-------------------------|-------------------------|-----------------|
| Exposure, PY         | 16.2                    | 14.8                    | 7.6             |
| All TEAEs, n (%), IR (95% CI) | 33 (62.3), 326.1 (224.5, 458.0) | 33 (68.8), 404.9 (278.7, 568.6) | 21 (80.8), 682.4 (422.4, 1043.1) |
| Serious              | 2 (3.8), 12.6 (1.5, 45.5) | 0                       | 1 (3.8), 13.4 (0.3, 74.4) |
| Gastrointestinal disorders | 1 (1.9), 6.2 (0.2, 34.6) | 0                       | 1 (3.8), 13.4 (0.3, 74.4) |
| Large intestine poly | 1 (1.9), 6.2 (0.2, 34.6) | 0                       | 1 (3.8), 13.4 (0.3, 74.3) |
| Dental disorders NEC | 0                       | 0                       | 1 (3.8), 13.4 (0.3, 74.4) |
| Dental cyst          | 0                       | 0                       | 0               |
| Infections and infestations | 1 (1.9), 6.3 (0.2, 34.9) | 0                       | 0               |
| Herpes zoster        | 1 (1.9), 6.3 (0.2, 34.9) | 0                       | 0               |
| Drug-related TEAEs, n (%) | 11 (20.8)               | 6 (12.5)                | 6 (23.1)        |
| Discontinuations due to TEAE, n (%) | 2 (3.8)               | 2 (4.2)                | 2 (7.7)         |
| Deaths, n (%)        | 0                       | 0                       | 0               |

CI confidence interval; CZP certolizumab pegol, IR incidence rate of new cases per 100 patient-years, NEC not elsewhere classified, PY patient-years, Q2W every 2 weeks, TEAE treatment-emergent adverse event

△ Adis
CONCLUSIONS

These data show that CZP is an effective treatment in Japanese patients with moderate to severe PSO over 16 weeks of treatment and CZP may provide a suitable treatment option for patients with PSO in Japan. Data over the full 52 weeks of this trial will further define the efficacy and safety profiles of CZP for the treatment of PSO in this population.

ACKNOWLEDGEMENTS

The authors thank the patients, the investigators and their teams who took part in this study.

Funding. This study was sponsored by UCB Pharma. This article was based on the original study PS0017 (NCT03051217) sponsored by UCB Pharma. The journal’s Rapid Service Fee was funded by UCB Pharma.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Medical Writing Editorial and Other Assistance. The authors acknowledge Bartosz Łukowski, MSc, UCB Pharma, Brussels, Belgium for publication coordination and Joe Dixon, PhD, from Costello Medical, UK, for medical writing and editorial assistance based on the authors’ input and direction. Support for third-party writing assistance for this article was funded by UCB Pharma in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3). The authors would like to thank the PS0017 Study Group: Masatoshi Abe of Kojinkai Sapporo Skin Clinic, Satoru Arai of St Luka’s International Hospital, Akihiko Asahina of The Jikei University Hospital, Yoshihide Asano of The University of Tokyo Hospital, Koki Endo of Iwate Medical University Hospital, Takafumi Etoh of Tokyo Teishin Hospital, Susumu Fujiwara of Kobe University Hospital, Mari Higashiyama of Nippon Life Saiseikai Public Interest Foundation and Nippon Life Hospital, Masaru Homma of Asahikawa Medical University Hospital, Atsuyuki Igarashi of NTT Medical Center Tokyo, Shinichi Imafuku of Fukuoka University Hospital, Norito Katoh of University Hospital Kyoto Prefectural University, Akira Kawada of Kindai University Hospital, Mayumi Komine of Jichi Medical University Hospital, Atsuko Matsuo of Kumamoto Shinto General Hospital, Hiroshi Mitsui of The Fraternity Memorial Hospital, Akimichi Morita of Nagoya City University Hospital, Osamu Nemoto of Kojinkai Sapporo Skin Clinic, Eisaku Ogawa of Shinshu University Hospital, Chika Ohata of Kurume University Hospital, Yukari Okubo of Tokyo Medical University Hospital, Shigetoshi Sano of Kochi Medical School Hospital, Mariko Seishima of Gifu University Hospital, Fumiaki Shirasaki of Shirasaki Dermatology Clinic, Yayoi Tada of Teikyo University Hospital, Shunsuke Takahagi of Hiroshima University Hospital, Hidetoshi Takahashi of Takagi Dermatological Clinic, Chiharu Tateishi of Osaka City University Hospital, Tadahis Terui of Nihon University Itabashi Hospital, Yoshiki Tokura of Hamamatsu University Hospital, Hideshi Torii of Tokyo Yamate Medical Center, Noriko Umegaki of Keio University Hospital, Toshiyuki Yamamoto of Fukushima Medical University Hospital, Keiichi Yamanaka of Mie University Hospital, Kenshi Yamasaki of Tohoku University Hospital, and Masahiro Amano of University of Miyazaki Hospital.

Prior Presentation. Results from this manuscript have been previously presented at the 34th Annual Meeting of the Japanese Society for Psoriasis Research (JSPR), which took place in Kyoto, Japan, 30–31 August 2019. Abstract number: 103.

Disclosures. Yoshinori Umezawa has received consulting agreements and/or speaker fees from Maruho Co. Ltd., AbbVie GK, Janssen Pharmaceutical K.K., Kyowa Hakko Kirin Co. Ltd., and UCB Japan Co., Ltd. Shinya Sakurai and Naoki Hoshii are employees of UCB Japan Co., Ltd. Hidemi Nakagawa has received consulting agreements, honoraria and/or speaker
fees from Japan Tobacco Inc., LEO Pharma, Maruho Co. Ltd., Kyowa Hakko Kirin Co. Ltd., AbbVie GK, Mitsubishi-Tanabe Pharma, Torii Pharmaceuticals Co. Ltd., Janssen Pharmaceuticals K.K., Novartis Pharma K.K., Eli Lilly Japan K.K., Bristol-Myers Squibb, and UCB Japan Co., Ltd.

**Compliance with Ethics Guidelines.** The study was carried out in accordance with the applicable regulatory and International Council for Harmonization-Good Clinical Practice requirements, and the Helsinki Declaration of 1964, and its later amendments. The study protocol was reviewed and approved by an institutional review board prior to implementation. Written informed consent was obtained from all patients.

**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 use of the data, proposals 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 pre-specified time, typically 12 months, on a password-protected portal.

**Open Access.** This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc/4.0/.

**REFERENCES**

1. Kubota K, Kamijima Y, Sato T, et al. Epidemiology of psoriasis and palmoplantar pustulosis: a nationwide study using the Japanese national claims database. BMJ Open. 2015;5(1):e006450.

2. Napolitano M, Caso F, Scarpa R, et al. Psoriatic arthritis and psoriasis: differential diagnosis. Clin Rheumatol. 2016;35(8):1893–901.

3. National Psoriasis Foundation: Plaque Psoriasis. 2019. https://www.psoriasis.org/about-psoriasis/types/plaque. Accessed 4 Sept 2019.

4. Grozdev I, Korman N, Tsankov N. Psoriasis as a systemic disease. Clin Dermatol. 2014;32(3):343–50.

5. Ryan C, Kirby B. Psoriasis is a systemic disease with multiple cardiovascular and metabolic comorbidities. Dermatol Clin. 2015;33(1):41–55.

6. Ito T, Takahashi H, Kawada A, Iizuka H, Nakagawa H, Research JSFP. Epidemiological survey from 2009 to 2012 of psoriatic patients in Japanese Society for Psoriasis Research. J Dermatol. 2018;45(3):293–301.

7. Belinchón I, Vanaclocha F, De La Cueva-Dobao P, et al. Metabolic syndrome in Spanish patients with psoriasis needing systemic therapy: prevalence and association with cardiovascular disease in PSORISK, a cross-sectional study. J Dermatol Treat. 2015;26(4):318–25.

8. Honma M, Shibuya T, Iwasaki T, et al. Prevalence of coronary artery calcification in Japanese patients with psoriasis: a close correlation with bilateral diagonal earlobe creases. J Dermatol. 2017;44(10):1122–8.

9. Takahashi H, Tsuji H, Takahashi I, Hashimoto Y, Ishida-Yamamoto A, Iizuka H. Erratum to "Prevalence of obesity/adiposity in Japanese psoriasis patients: adiposity is correlated with the severity of psoriasis"[J Dermatol Sci 2009; 54: 61–3]. J Dermatol Sci. 2009;55(1):74–6.
10. Takahashi H, Takahashi I, Honma M, Ishida-Yamamoto A, Iizuka H. Prevalence of metabolic syndrome in Japanese psoriasis patients. J Dermatol Sci. 2010;57(2):143–4.

11. Budu-Aggrey A, Brumpton B, Tyrrell J, et al. Evidence of a causal relationship between body mass index and psoriasis: a mendelian randomization study. PLoS Med. 2019;16(1):e1002739.

12. Borska L, Kremlacek J, Andrys C, et al. Systemic inflammation, oxidative damage to nucleic acids, and metabolic syndrome in the pathogenesis of psoriasis. Int J Mol Sci. 2017;18(11):2238.

13. Kimball A, Gieler U, Linder D, Sampogna F, Warren R, Augustin M. Psoriasis: is the impairment to a patient’s life cumulative? J Eur Acad Dermatol. 2010;24(9):989–1004.

14. Mabuchi T, Yamaoka H, Kojima T, Ikoma N, Akasaka E, Ozawa A. Psoriasis affects patient’s quality of life more seriously in female than in male in Japan. Tokai J Exp Clin Med. 2012;37(3):84–8.

15. Ohtsuki M, Terui T, Ozawa A, et al. Japanese guidance for use of biologics for psoriasis (the 2013 version). J Dermatol. 2013;40(9):683–95.

16. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008;58(5):826–50.

17. National Institute for Health and Care Excellence. Psoriasis Management. 2019. https://bnf.nice.org.uk/treatment-summary/psoriasis.html. Accessed 19 Mar 2019.

18. Silfvast-Kaiser A, Paek SY, Menter A. Anti-IL17 therapies for psoriasis. Expert Opin Biol Th. 2019;19(1):45–54.

19. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020;82(6):1445–86.

20. Mariette X, Förger F, Abraham B, et al. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIIB, a prospective, postmarketing, pharmacokinetic study. Ann Rheum Dis. 2018;77(2):228–33.

21. Weir N, Athwal D, Brown D, et al. A new generation of high-affinity humanized PEGylated Fab' fragment anti-tumor necrosis factor-α monoclonal antibodies. Therapy. 2006;3(4):535–46.

22. US Food and Drug Administration. Certolizumab Pegol Prescribing Information. 2019. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed 15 Nov 2019.

23. European Medicines Agency. Certolizumab Pegol Summary of Product Characteristics. https://www.ema.europa.eu/en/documents/product-information/cimzia-epar-product-information_en.pdf. Accessed 15 Nov 2019.

24. Certolizumab Pegol Product Information. https://www.swissmedicinfo.ch/?Lang=EN. Accessed 15 Nov 2019.

25. Pharmaceuticals and Medical Devices Agency. https://www.info.pmda.go.jp/go/interview/1/820110_3999437G1022_1_014_1F.pdf. Accessed 15 Nov 2019.

26. Lebwohl M, Blauvelt A, Paul C, et al. Certolizumab pegol for the treatment of chronic plaque psoriasis: results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept-and placebo-controlled study (CIMPACT). J Am Acad Dermatol. 2018;79(2):266–76.e5.

27. Gottlieb AB, Blauvelt A, Thaci D, et al. Certolizumab pegol for the treatment of chronic plaque psoriasis: results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). J Am Acad Dermatol. 2018;79(2):302-14.e6.

28. Blauvelt A, Reich K, Lebwohl M, et al. Certolizumab pegol for the treatment of patients with moderate-to-severe chronic plaque psoriasis: pooled analysis of week 16 data from three randomized controlled trials. J Eur Acad Dermatol. 2018;79(2):266–76.

29. Criteria Committee of the New York Heart Association. Diseases of the heart and blood vessels: nomenclature and criteria for diagnosis. 6th ed. Boston: Little, Brown and Co.; 1964.

30. Kimball A, Naegeli A, Edson-Heredia E, et al. Psychometric properties of the Itch Numeric Rating Scale in patients with moderate-to-severe plaque psoriasis. Brit J Dermatol. 2016;175(1):157–62.

31. Asahina A, Nakagawa H, Etoh T, Ohtsuki M, Group JUS. Efficacy and safety of ustekinumab in Japanese patients with moderate-to-severe plaque-type psoriasis: long-term results from a phase 2/3 clinical trial. J Dermatol. 2012;39(3):242–52.
33. Nakagawa H, Niiro H, Ootaki K, Group JBS. Brodalumab, a human anti-interleukin-17-receptor antibody in the treatment of Japanese patients with moderate-to-severe plaque psoriasis: efficacy and safety results from a phase II randomized controlled study. J Dermatol Sci. 2016;81(1):44–52.

34. Imafuku S, Torisu-Itakura H, Nishikawa A, Zhao F, Cameron GS, Group JU-S. Efficacy and safety of ixekizumab treatment in Japanese patients with moderate-to-severe plaque psoriasis: subgroup analysis of a placebo-controlled, phase 3 study (UNCOVER-1). J Dermatol. 2017;44(11):1285–90.

35. Ohtsuki M, Kubo H, Morishima H, Goto R, Zheng R, Nakagawa H. Guselkumab, an anti-interleukin-23 monoclonal antibody, for the treatment of moderate to severe plaque-type psoriasis in Japanese patients: efficacy and safety results from a phase 3, randomized, double-blind, placebo-controlled study. J Dermatol. 2018;45(9):1053–62.

36. Ohtsuki M, Morita A, Abe M, et al. Secukinumab efficacy and safety in Japanese patients with moderate-to-severe plaque psoriasis: subanalysis from ERASURE, a randomized, placebo-controlled, phase 3 study. J Dermatol. 2014;41(12):1039–46.

37. Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based multinational assessment of psoriasis and psoriatic arthritis survey. J Am Acad Dermatol. 2014;70(5):871–8130.

38. Dattola A, Balato A, Megna M, et al. Certolizumab for the treatment of psoriasis and psoriatic arthritis: a real-world multicentre Italian study. J Eur Acad Dermatol Venereol. 2020;34(12):2839–45.