Certolizumab Pegol in Japanese Patients with Moderate to Severe Plaque Psoriasis: Effect of Demographics and Baseline Disease Characteristics on Efficacy

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ABSTRACT

Introduction: We present certolizumab pegol (CZP) efficacy data across patient demographic and baseline disease characteristic subgroups from a phase 2/3 trial investigating CZP treatment in Japanese patients with moderate to severe plaque psoriasis (PSO; ClinicalTrials.gov identifier: NCT03051217).

Methods: Patients were randomised 1:2:2 to placebo once every 2 weeks (Q2W), CZP 400 mg Q2W and CZP 200 mg Q2W (400 mg weeks 0, 2 and 4) for 16 weeks. Patients who achieved ≥ 50% reduction in their baseline Psoriasis Area and Severity Index (PASI 50) score at week 16 continued therapy to week 52.

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PASI 75/90 (75% and 90% reduction, respectively) and Physician's Global Assessment (PGA) 0/1 responder rates at weeks 16 and 52 were reported for patient demographic and baseline disease characteristic subgroups, including body mass index (BMI), PASI, disease duration and prior biologic use. Non-responder imputation was used.

Results: Of the randomised patients, 2/26 patients in the placebo group, 47/53 patients in the CZP 400 mg Q2W group and and 39/48 patients in the CZP 200 mg Q2W group completed week 52. In the subgroups evaluated, week 16 efficacy was generally maintained through week 52. At week 52, PASI 75 was achieved by 84.2, 85.7 and 80.0% of patients receiving CZP 400 mg Q2W in the low $(15.0–23.7 \text{ kg/m}^2)$/intermediate $(> 23.7–27.4 \text{ kg/m}^2)$/high $(> 27.4–47.0 \text{ kg/m}^2)$ BMI subgroups, respectively, and by 77.8, 70.6 and 69.2%, respectively of patients treated with CZP 200 mg Q2W. PASI 75 at week 52 was achieved by 92.9, 75.0 and 84.2% of patients receiving CZP 400 mg Q2W in the low $(12.0–18.0)$/intermediate $(> 18.0–27.0)$/high $(> 27.0–67.2)$ baseline PASI subgroups, respectively, and by 85.0, 58.3 and 68.8% of patients receiving CZP 200 mg Q2W, respectively. Similar responses were observed across other subgroups evaluated for both CZP doses in PASI 75/90 and PGA 0/1.

Conclusion: Clinically meaningful improvements in signs and symptoms of PSO were

maintained through week 52 for CZP dosed at 400 mg Q2W or 200 mg Q2W, across patient subgroups. In general, a numerically greater response was observed for patients receiving CZP 400 mg Q2W versus those receiving CZP 200 mg Q2W across patient subgroups.

Trial Registration: ClinicalTrials.gov identifier, NCT03051217.

Keywords: Anti-tumour necrosis factor; BMI; Certolizumab pegol; Japan; Plaque psoriasis

Key Summary Points

Why carry out this study?

In a Japanese phase 2/3 trial, certolizumab pegol (CZP) treatment showed clinically meaningful improvements in Japanese patients with moderate to severe plaque psoriasis (PSO) over 52 weeks.

The efficacy of biologic treatment for PSO may be influenced by patient demographics and baseline disease characteristics.

Here, we report the efficacy of CZP in Japanese patients with PSO from the same trial, across patient demographic and baseline disease characteristic subgroups.

What was learned from the study?

The clinically meaningful improvements seen with CZP treatment at week 16 were maintained through week 52. Improvements were seen across evaluated patient subgroups, including body mass index (BMI), baseline Psoriasis Area and Severity Index (PASI), disease duration and prior biologic exposure.

Generally, a numerically greater response was observed for CZP 400 mg (every 2 weeks) versus CZP 200 mg Q2W across patient subgroups.

INTRODUCTION

Psoriasis is a common, chronic inflammatory disease with a prevalence of 0.34% in Japan [1]. Of all psoriasis cases in Japan, 86% are plaque psoriasis (PSO) cases, and 53% of these involve moderate to severe disease [2].

The treatment options for PSO depend on disease severity. Patients with moderate to severe PSO may be managed with biologic agents administered as monotherapy or in combination with topical therapies, phototherapy or other systemic therapies. Biologic therapies, such as anti-tumour necrosis factor (anti-TNF) and anti-interleukin (anti-IL-12/-23p40, -IL-23 and -IL-17), are the recommended treatment options for the management of moderate to severe PSO [3, 4].

Certolizumab pegol (CZP) is a unique Fc-free PEGylated anti-TNF biologic. PEGylation increases the half-life of CZP to 14 days [5]. In Japan, CZP is currently approved for the treatment of rheumatoid arthritis, PSO, psoriatic arthritis, generalised pustular psoriasis and erythrodermic psoriasis [6]. CZP dosed at 400 mg once every 2 weeks (Q2W) and 200 mg Q2W over 52 weeks demonstrated clinically meaningful improvements in Japanese patients with moderate to severe PSO, with no new safety signals identified compared with previously reported data in patients with PSO [7, 8].

Despite the availability of several recommended treatment options for PSO, it has been reported that a proportion of patients discontinue their treatments due to the lack of effectiveness [9, 10]. Evidence indicates that demographics and baseline disease characteristics may influence the treatment efficacy of biologics in PSO [11, 12]. Indeed, it has been suggested that body mass index (BMI), baseline Psoriasis Area and Severity Index (PASI) score, prior biologic exposure at baseline, gender and smoking status are factors that may affect clinical response to treatments [11–17]. For example, obese patients tend to have reduced response to anti-TNFs and anti-IL-17 used in the treatment of PSO [12, 17–20]. Patients with higher PASI score at baseline were observed to have higher response rates compared with

patients who had a lower baseline PASI score [11, 21]. Response rates have also also observed to be higher in patients who had no prior biologic exposure compared with those who were previously treated with biologics [11, 14–16].

CZP demonstrated clinically meaningful improvements across several patient subgroups (such as age, weight, BMI, baseline PASI score, baseline body surface area [BSA], disease duration, prior biologic exposure and prior anti-TNF exposure at baseline) in three global phase 3 trials (CIMPASI-1, CIMPASI-2 and CIMPACT) in North America and Europe [22–24]. The efficacy of CZP across patient demographic and baseline disease characteristic subgroups has not been assessed in Japanese patients with PSO. Here, we present the efficacy of CZP dosed at 400 mg and 200 mg Q2W in Japanese patients with moderate to severe PSO over 52 weeks of treatment, across patient demographic and baseline disease characteristic subgroups.

METHODS

Study Design

This was a post-hoc analyses of a phase 2/3, double-blind, placebo-controlled, multicentre, randomised trial conducted in Japan (NCT03051217) [7, 8]. Enrolled patients were randomised 1:2:2 to placebo Q2W, CZP 400 mg Q2W and CZP 200 mg Q2W (400 mg weeks 0, 2 and 4), for 16 weeks of treatment. Patients who achieved at least a 50% reduction in PASI score from baseline (PASI 50) at week 16 continued therapy through to week 52. At week 16, patients initially randomised to CZP 200 mg Q2W were re-randomised (1:1) to CZP 200 mg Q2W or CZP 400 mg Q4W (once every 4 weeks), while patients initially randomised to placebo or CZP 400 mg Q2W continued in the same treatment group. Patients who did not achieve a PASI 50 response at week 16 escaped from double-blind treatment and entered the open-label escape arm and received CZP treatment (CZP 400 mg Q2W as three loading doses for the first three visits, followed by CZP 200 mg Q2W). The design and methods of the full study have been reported previously [7, 8].

All double-blind CZP and placebo treatments were administered subcutaneously at the study site by trained site personnel not involved in any other study procedures. This study protocol was reviewed by the institutional review board (IRB) of each institution prior to implementation. Written informed consent was obtained from all patients. 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.

Study Participants

Full inclusion and exclusion criteria have been published previously [7]. Briefly, included patients were ≥ 20 years of age, with moderate to severe PSO for ≥ 6 months duration, with baseline PASI score ≥ 12, affected BSA of ≥ 10% and Physician's Global Assessment (PGA) ≥ 3 on a 5-point scale. Patients were also candidates for systemic psoriasis therapy, phototherapy or chemophototherapy. Excluded patients were those who had a history of primary failure to any biologic (i.e. no response within the first 12 weeks of treatment), secondary failure to > 2 biologics (i.e. patient initially responded then discontinued treatment due to loss of response after 12 weeks of treatment) or a diagnosis of any inflammatory arthritis other than psoriatic arthritis, guttate, drug-induced, erythrodermic or pustular psoriasis.

Efficacy Evaluations Across Subgroups

The primary efficacy endpoint of the study and other secondary outcomes (efficacy and safety) over 52 weeks of CZP treatment have been reported previously [7, 8]. In the present post-hoc analysis, subgroup analyses were conducted for patient demographic and baseline disease characteristics, such as: baseline BMI (kg/m^2; classified by tertiles), baseline PASI (classified by tertiles), duration of disease (years; classified as ≤ median or > median) and prior biologic exposure (classified as presence or absence).

Efficacy outcomes evaluated across subgroups included: PASI 75, PASI 90 (percentage

of patients who achieved ≥ 75%, ≥ 90% reduction in PASI score from baseline, respectively) and PGA 0/1 ("clear" or "almost clear" with ≥ 2-point improvement from baseline) response at weeks 16 and 52.

Statistical Analyses

Subgroup analyses at week 16 were pre-specified in the protocol, and subgroup analyses at week 52 were conducted post-hoc. Responder rates in the full analysis set were summarised descriptively according to patients' originally randomised treatment group at week 0. Escapers were treated as non-responders from the time of escape onwards. Missing data were imputed using non-responder imputation. No statistical tests were performed. A subgroup analysis was not performed if any of the categories within the subgroup included < 10% of all patients.

RESULTS

Patient Disposition and Baseline Characteristics

Of the 168 patients screened, 127 patients were randomised to: placebo (n = 26), CZP 400 mg Q2W (n = 53) and CZP 200 mg Q2W (n = 48) [7]. Of the randomised patients, 23/26 placebo-treated patients, 51/53 patients treated with CZP 400 mg Q2W and 46/48 of patients treated with CZP 200 mg Q2W completed week 16; 2/26 placebo-treated patients, 47/53 patients treated with CZP 400 mg Q2W and 39/48 patients treated with CZP 200 mg Q2W completed week 52 [8]. Three placebo-treated patients, three patients treated with CZP 400 mg Q2W and one patient treated with CZP 200 mg Q2W withdrew due to adverse events (AEs) [8].

Demographics and baseline characteristics were similar across CZP treatment groups, and have been published previously [7]. Briefly, mean (standard deviation [SD]) baseline BMI was 26.0 (4.3), 26.0 (5.5) and 27.3 (5.1) kg/m^2 for the CZP 400 mg Q2W, CZP 200 mg Q2W and placebo groups, respectively [7]. The mean
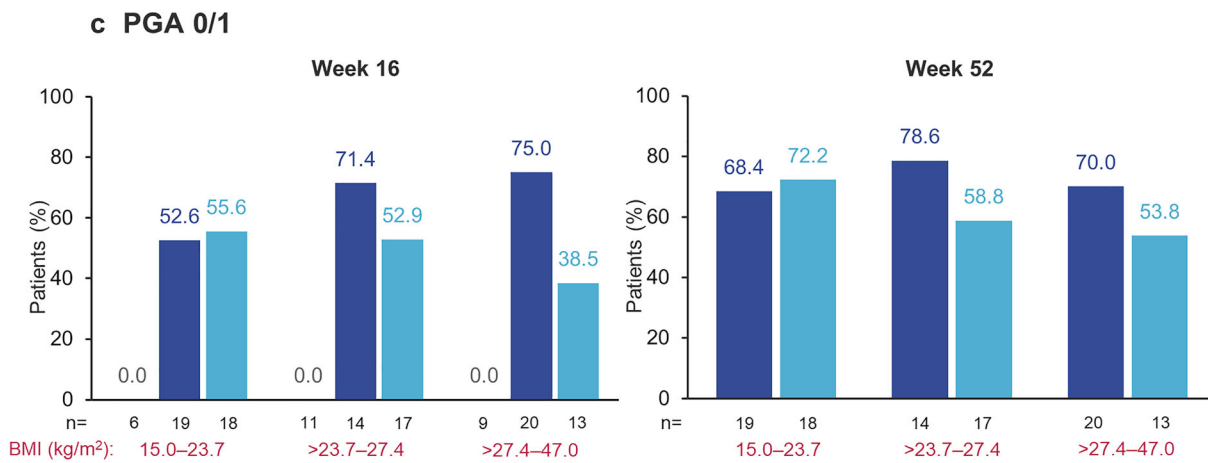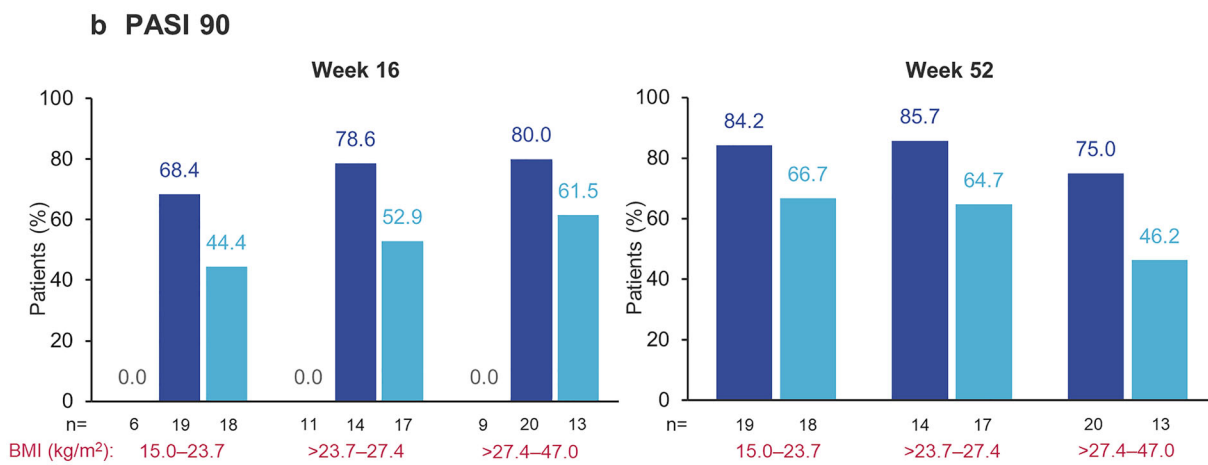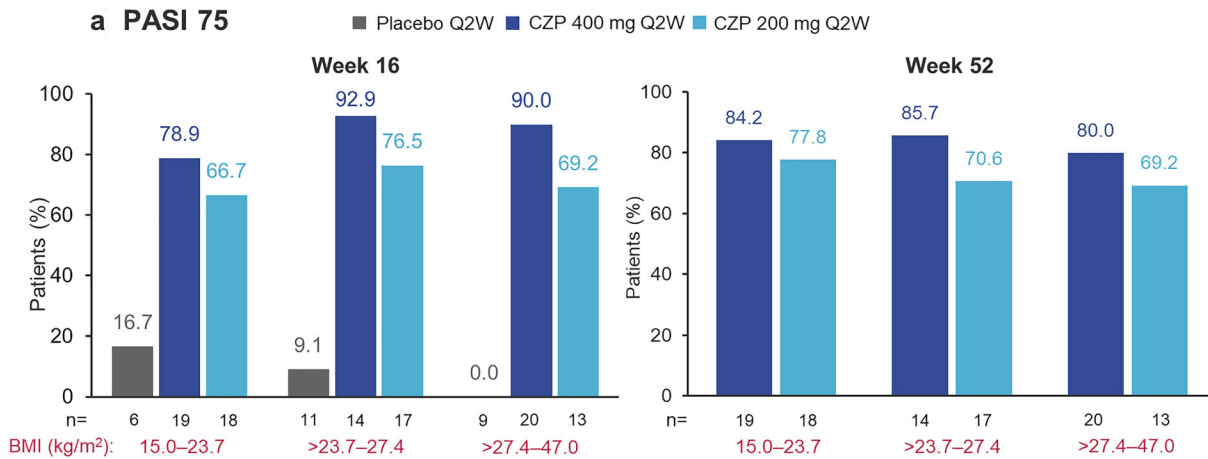
(SD) baseline PASI score was 26.5 (11.0), 24.5 (12.6) and 24.5 (10.4) for the CZP 400 mg Q2W, CZP 200 mg Q2W and placebo groups, respectively [7]. The mean (SD) duration of disease was 13.2 (9.3) years for the CZP 400 mg Q2W group, 12.7 (10.1) years for the CZP 200 mg Q2W group and 12.7 (8.6) years for the placebo group [7].

Efficacy Evaluations Across Subgroups

Response by Baseline BMI

Patients were classified into tertiles based on baseline BMI values: 15.0–23.7 kg/m^2 (low), > 23.7–27.4 kg/m^2 (intermediate) and > 27.4–47.0 kg/m^2 (high). Week 16 PASI 75 responder rates in the low, intermediate and high BMI subgroups were 78.9, 92.9 and 90.0%, respectively, for the CZP 400 mg Q2W group, 66.7, 76.5 and 69.2%, respectively, for the CZP 200 mg Q2W group and 16.7, 9.1 and 0.0%, respectively, for the placebo group (Fig. 1a). Week 16 PASI 90 responder rates in the low, intermediate and high BMI subgroups were 68.4, 78.6 and 80.0%, respectively, for the CZP 400 mg Q2W group, 44.4, 52.9 and 61.5%, respectively, for the CZP 200 mg Q2W group and 0.0, 0.0 and 0.0%, respectively, for the placebo group (Fig. 1b). Week 16 PGA 0/1 responder rates in the low, intermediate and high BMI subgroups were 52.6, 71.4 and 75.0%, respectively, for the CZP 400 mg Q2W group, 55.6, 52.9 and 38.5%, respectively, for the CZP 200 mg Q2W group and 0.0, 0.0 and 0.0%, respectively, for the placebo group (Fig. 1c).

Efficacy achieved at week 16 was generally maintained through week 52. PASI 75 at week 52 was achieved by 84.2, 85.7 and 80.0 of patients receiving CZP 400 mg Q2W in the low, intermediate and high BMI subgroups, respectively, and by 77.8, 70.6 and 69.2% of patients receiving CZP 200 mg Q2W, respectively (Fig. 1a). PASI 90 at week 52 was achieved by 84.2, 85.7 and 75.0% of patients receiving CZP 400 mg Q2W in the low, intermediate and high BMI subgroups, respectively, and by 66.7, 64.7 and 46.2% of patients receiving CZP 200 mg Q2W, respectively (Fig. 1b). PGA 0/1 at week 52 was achieved by 68.4, 78.6

a PASI 75   ■ Placebo Q2W ■ CZP 400 mg Q2W ■ CZP 200 mg Q2W

Week 16

Patients (%)

- 16.7 | 78.9 | 66.7
- 9.1 | 92.9 | 76.5
- 0.0 | 90.0 | 69.2

n= 6 19 18 | 11 14 17 | 9 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

Week 52

Patients (%)

- 84.2 | 77.8
- 85.7 | 70.6
- 80.0 | 69.2

n= 19 18 | 14 17 | 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

b PASI 90

Week 16

Patients (%)

- 0.0 | 68.4 | 44.4
- 0.0 | 78.6 | 52.9
- 0.0 | 80.0 | 61.5

n= 6 19 18 | 11 14 17 | 9 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

Week 52

Patients (%)

- 84.2 | 66.7
- 85.7 | 64.7
- 75.0 | 46.2

n= 19 18 | 14 17 | 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

c PGA 0/1

Week 16

Patients (%)

- 0.0 | 52.6 | 55.6
- 0.0 | 71.4 | 52.9
- 0.0 | 75.0 | 38.5

n= 6 19 18 | 11 14 17 | 9 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

Week 52

Patients (%)

- 68.4 | 72.2
- 78.6 | 58.8
- 70.0 | 53.8

n= 19 18 | 14 17 | 20 13
BMI (kg/m²): 15.0–23.7 | >23.7–27.4 | >27.4–47.0

◀ **Fig. 1** Response by baseline BMI. Non-responder imputation. Escapers were treated as non-responders from the time of escape onwards. Statistical significance between groups was not tested. n = number of patients in the subgroup at baseline. Patients were classified into tertiles based on baseline BMI values: 15.0–23.7, > 23.7–27.4 and > 27.4–47.0 kg/m². Only 2 patients continued placebo treatment to week 52; therefore placebo data are not shown for week 52. *BMI* Body mass index, *CZP* certolizumab pegol, *PASI* Psoriasis Area and Severity Index, *PASI 75/90* at least 75%/90% improvement from baseline PASI, *PGA* Physician's Global Assessment, *Q2W* once every 2 weeks

and 70.0% of patients receiving CZP 400 mg Q2W in the low, intermediate and high BMI subgroups, respectively, and by 72.2, 58.8 and 53.8% of patients receiving CZP 200 mg Q2W, respectively (Fig. 1c).

Response by Baseline PASI

Patients were classified into tertiles based on baseline PASI values: 12.0–18.0 (low), > 18.0–27.0 (intermediate) and > 27.0–67.2 (high). Week 16 PASI 75 responder rates in the low, intermediate and high baseline PASI subgroups were 85.7, 90.0 and 84.2%, respectively, for the CZP 400 mg Q2W group, 80.0, 58.3 and 68.8%, respectively, for the CZP 200 mg Q2W group and 0.0, 22.2 and 0.0%, respectively, for the placebo group (Fig. 2a). Week 16 PASI 90 responder rates in the low, intermediate and high baseline PASI subgroups were 57.1, 80.0 and 84.2%, respectively, for the CZP 400 mg Q2W group, 50.0, 41.7 and 62.5%, respectively, for the CZP 200 mg Q2W group, and 0.0, 0.0 and 0.0%, respectively, for the placebo group (Fig. 2b). Week 16 PGA 0/1 responder rates in the low, intermediate and high baseline PASI subgroups were 64.3, 70.0 and 63.2%, respectively, for the CZP 400 mg Q2W group, 65.0, 33.3 and 43.8%, respectively, for the CZP 200 mg Q2W group, and 0.0, 0.0 and 0.0%, respectively, for the placebo group (Fig. 2c).

Efficacy achieved at week 16 was generally maintained through week 52. PASI 75 at week 52 was achieved by 92.9, 75.0 and 84.2 of patients receiving CZP 400 mg Q2W in the low, intermediate and high baseline PASI subgroups,

respectively, and by 85.0, 58.3 and 68.8% of patients receiving CZP 200 mg Q2W, respectively (Fig. 2a). PASI 90 at week 52 was achieved by 85.7, 75.0 and 84.2% of patients receiving CZP 400 mg Q2W in the low, intermediate and high baseline PASI subgroups, respectively, and by 70.0, 41.7 and 62.5% of patients receiving CZP 200 mg Q2W, respectively (Fig. 2b). PGA 0/1 at week 52 was achieved by 85.7, 65.0 and 68.4% of patients receiving CZP 400 mg Q2W in the low, intermediate and high baseline PASI subgroups, respectively, and by 80.0, 50.0 and 50.0% of patients receiving CZP 200 mg Q2W, respectively (Fig. 2c).

Response by Baseline Disease Duration

Patients were classified based on the baseline median disease duration: ≤ 10.7 years and > 10.7 years. Week 16 PASI 75 responder rates in patients with ≤ 10.7 years and > 10.7 years disease duration were 84.6% and 88.9%, respectively, for the CZP 400 mg Q2W group, 68.0% and 73.9%, respectively, for the CZP 200 mg Q2W group and 15.4% and 0.0%, respectively, for the placebo group (Fig. 3a). Week 16 PASI 90 responder rates in patients with ≤ 10.7 years and > 10.7 years disease duration were 73.1% and 77.8%, respectively, for the CZP 400 mg Q2W group, 48.0% and 56.5%, respectively, for the CZP 200 mg Q2W group and 0.0% and 0.0%, respectively, for the placebo group (Fig. 3b). Week 16 PGA 0/1 responder rates in patients with ≤ 10.7 years and > 10.7 years disease duration were 69.2% and 63.0%, respectively, for the CZP 400 mg Q2W group, 48.0% and 52.2%, respectively, for the CZP 200 mg Q2W group, and 0.0% and 0.0%, respectively, for the placebo group (Fig. 3c).

Efficacy achieved at week 16 was generally maintained through week 52. PASI 75 at week 52 was achieved by 84.6% and 81.5% of patients receiving CZP 400 mg Q2W with ≤ 10.7 years and > 10.7 years disease duration, respectively, and by 72.0% and 73.9% of patients receiving CZP 200 mg Q2W, respectively (Fig. 3a). PASI 90 at week 52 was achieved by 80.8% and 81.5% of patients receiving CZP 400 mg Q2W with ≤ 10.7 years and > 10.7 years disease duration, respectively, and by 52.0% and 69.6% of

a **PASI 75**   ■ Placebo Q2W ■ CZP 400 mg Q2W ■ CZP 200 mg Q2W

b **PASI 90**

c **PGA 0/1**
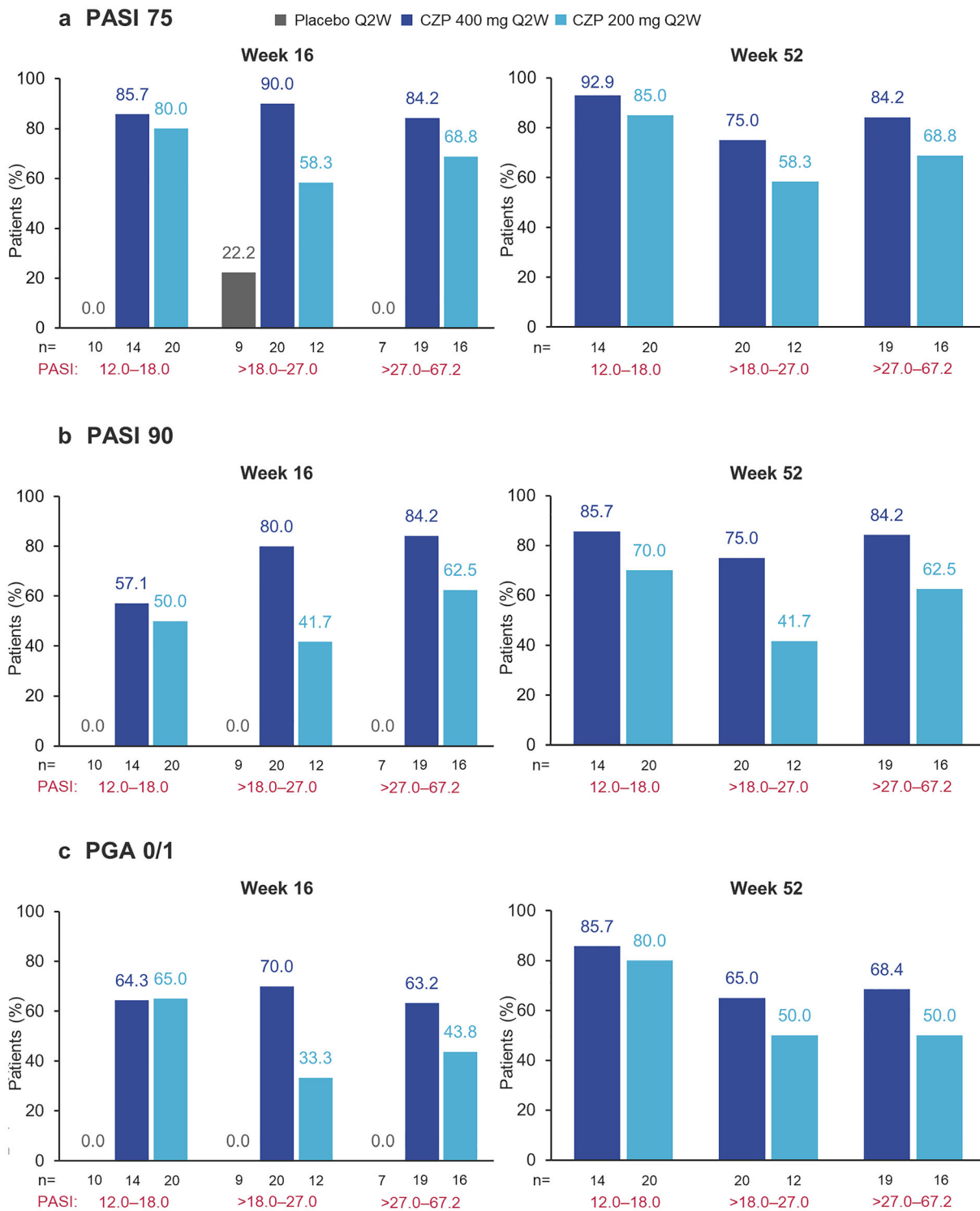
◄**Fig. 2** Response by baseline PASI. Non-responder imputation. Escapers were treated as non-responders from the time of escape onwards. Statistical significance between groups was not tested. n = number of patients in the subgroup at baseline. Patients were classified into tertiles based on baseline PASI values: 12.0–18.0, > 18.0–27.0 and > 27.0–67.2. Only 2 patients continued placebo treatment to week 52; therefore placebo data are not shown for week 52

patients receiving CZP 200 mg Q2W, respectively (Fig. 3b). PGA 0/1 at week 52 was achieved by 73.1% and 70.4% of patients receiving CZP 400 mg Q2W with ≤ 10.7 years and > 10.7 years disease duration, respectively, and by 60.0% and 65.2% of patients receiving CZP 200 mg Q2W, respectively (Fig. 3c).

Response by Prior Biologic Exposure

Patients were classified based on the presence or absence of prior biologic exposure at baseline. Week 16 PASI 75 responder rates in patients with and without prior biologic exposure were 94.7% and 82.4%, respectively, for the CZP 400 mg Q2W group, 64.3% and 73.5%, respectively, for the CZP 200 mg Q2W group and 0.0% and 11.1%, respectively, for the placebo group (Fig. 4a). Week 16 PASI 90 responder rates in patients with and without prior biologic exposure were 78.9% and 73.5%, respectively, for the CZP 400 mg Q2W group, 42.9% and 55.9%, respectively, for the CZP 200 mg Q2W group and 0.0% and 0.0%, respectively, for the placebo group (Fig. 4b). Week 16 PGA 0/1 responder rates in patients with and without prior biologic exposure were 63.2% and 67.6%, respectively, for the CZP 400 mg Q2W group, 42.9% and 52.9%, respectively, for the CZP 200 mg Q2W group and 0.0% and 0.0%, respectively, for the placebo group (Fig. 4c).

Efficacy achieved at week 16 was generally maintained through week 52. PASI 75 was achieved by 84.2% and 82.4% of patients receiving CZP 400 mg Q2W with and without prior biologic exposure, respectively, and by 71.4% and 73.5% of patients receiving CZP 200 mg Q2W, respectively (Fig. 4a). PASI 90 at week 52 was achieved by 84.2% and 79.4% of patients receiving CZP 400 mg Q2W with and

without prior biologic exposure, respectively, and by 64.3% and 58.8% of patients receiving CZP 200 mg Q2W, respectively (Fig. 4b). PGA 0/1 was achieved by 68.4% and 73.5% of patients receiving CZP 400 mg Q2W with and without prior biologic exposure, respectively, and by 64.3% and 61.8% of patients receiving CZP 200 mg Q2W, respectively (Fig. 4c).

Response by Other Patient Demographic and Baseline Disease Characteristic Subgroups

For other patient demographic and baseline disease characteristic subgroups, responder rates were generally similar between the categories within each subgroup (see Electronic Supplementary Material [ESM] Tables 1–3). Among the subgroup of low, intermediate and high body weight, efficacy achieved at week 16 was generally maintained through week 52. Similar trends were observed for PASI 90 and PGA 0/1 (ESM Supplementary Fig. 1).

DISCUSSION

In this phase 2/3 Japanese trial, CZP treatment resulted in clinically meaningful improvements in the signs and symptoms of PSO at week 16, which were maintained through week 52 across evaluated patient subgroups. In general, a numerically greater response was observed for CZP 400 mg Q2W versus CZP 200 mg Q2W across patient subgroups. High efficacy levels were observed with the CZP 400 mg Q2W dose irrespective of baseline patient factors.

Several studies have reported an increased risk of PSO in patients who are obese [25, 26], and patients with severe PSO have been found to be more likely to be obese, compared with those with mild PSO [27]. Similar trends were observed in a Japanese population, where higher prevalence of obesity and higher mean BMI were reported in patients with PSO compared to healthy controls [28]. Patients who are overweight or obese have an increased amount of visceral fat, which contributes to a higher systemic inflammatory burden [19]. An increase in body weight may also alter drug distribution and lead to elevated drug clearance [19, 29, 30]. Since most systemic treatment strategies for

a PASI 75   ■ Placebo Q2W ■ CZP 400 mg Q2W ■ CZP 200 mg Q2W

b PASI 90

c PGA 0/1
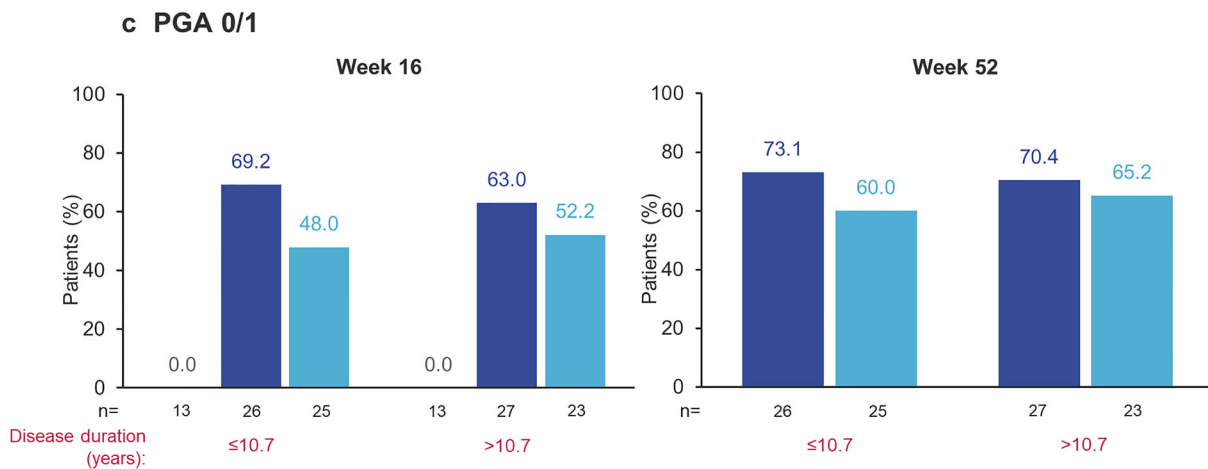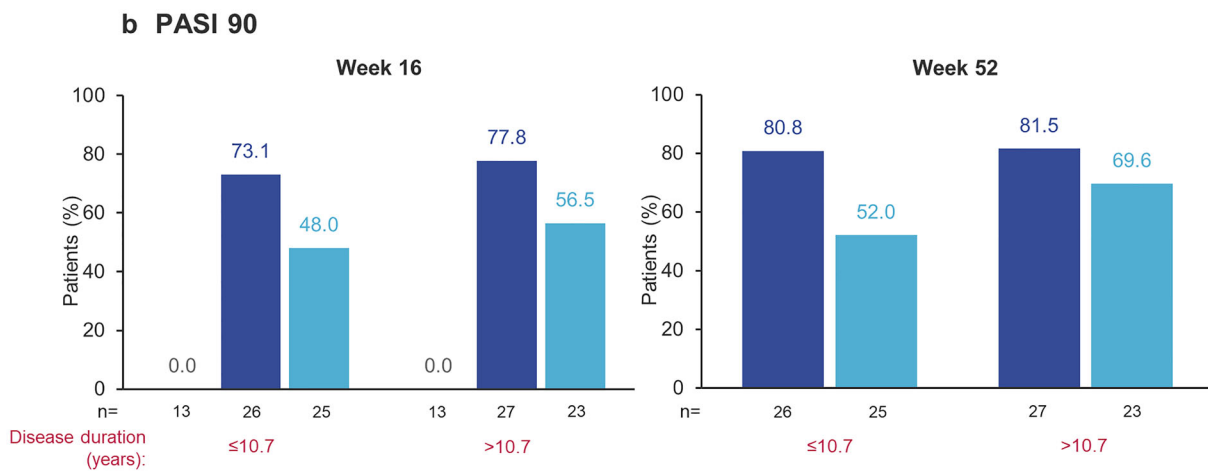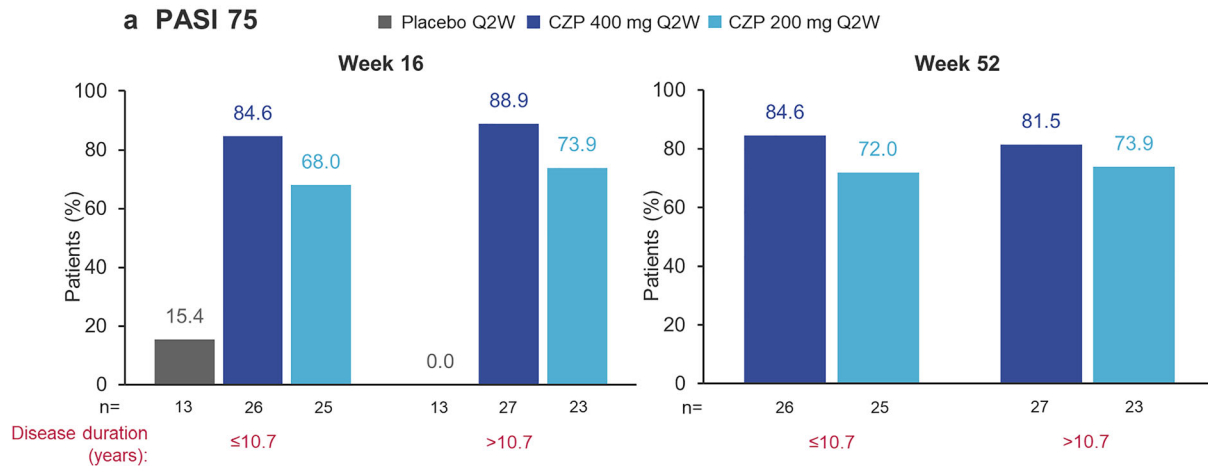
◀ **Fig. 3** Response by baseline disease duration. Non-responder imputation. Escapers were treated as non-responders from the time of escape onwards. Statistical significance between groups was not tested. n = number of patients in the subgroup at baseline. Patients were classified based on the baseline median disease duration: ≤ 10.7 years and > 10.7 years. Only 2 patients continued placebo treatment to week 52; therefore placebo data are not shown for week 52

PSO do not rely on weight-based dosing, the administered dose may be inadequate for patients with a higher BMI, thus causing a reduced response in this patient subpopulation [31]. Indeed, BMI has been shown to affect clinical response to PSO treatments, where obese patients tend to have reduced response to some anti-TNFs (such as infliximab, adalimumab and etanercept) [12, 19, 20] and some anti-IL-17s (such as secukinumab and brodalumab) [17, 18]. In patients with psoriasis treated with adalimumab, the PASI 75 response at week 16 in the BMI < 25, 25 to < 30 and ≥ 30 kg/m² subgroups was reported to be 85.0, 85.7 and 61.3%, respectively [32]; the PASI 90 response in these patients was 70.0, 53.6 and 35.5%, respectively [32]. In patients treated with etanercept, the PASI 75 response at week 12 in the BMI ≤ 35 and > 35 kg/m² subgroups was 73.7% and 61.2%, respectively [33]. In the current study, CZP response was comparable across BMI subgroups for the 400 mg Q2W dose. At week 52, 84.2, 85.7 and 80.0% of patients receiving CZP 400 mg Q2W, in the low, intermediate and high BMI subgroups, respectively, achieved a PASI 75 response, and 84.2, 85.7 and 75.0%, respectively, achieved a PASI 90 response.

Some studies have suggested that a high baseline PASI predicts the achievement of PASI 90 response at week 24 [11, 21]. In this study, PASI 75 response was similar across baseline PASI subgroups. In terms of PASI 90 response in the group treated with CZP 400 mg Q2W, although the week 16 response was 57.1% in patients with low baseline PASI and 84.2% in those with high baseline PASI, the week 52 response rates were similar (85.7% and 84.2%, respectively). Additionally,

CZP response was generally comparable among patients with different disease duration and prior biologic treatment histories at baseline. These findings suggests that CZP provides a clinical benefit independent of disease duration and prior biologic treatment history.

The efficacy observed across all subgroups at weeks 16 and 52 was similar to the overall study population [7, 8]. In general, PASI 75 and PASI 90 responder rates were higher in the CZP 400 mg Q2W group versus the CZP 200 mg Q2W group across patient subgroups, including BMI, baseline PASI, disease duration and prior biologic exposure. A numerically greater response was also observed for the CZP 400 mg Q2W group versus the CZP 200 mg Q2W group in the overall study population. These findings suggest that additional benefits may be obtained from the higher dose.

The results of this Japanese study are comparable to those of the larger global phase 3 studies of CZP in PSO. In the subgroup analysis of the pooled data from the CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) trials, efficacy measured by PASI 75, PASI 90 and PGA 0/1 was observed for both the CZP 400 mg Q2W and CZP 200 mg Q2W doses over 48 weeks of treatment across subgroups, including baseline BMI, baseline disease duration, baseline PASI and prior anti-TNF biologic use [22, 24]. The PASI 75, PASI 90 and PGA 0/1 responder rates in the pooled CIMPASI-1 and CIMPASI-2 analysis were also greater for the CZP 400 mg Q2W group versus the CZP 200 mg Q2W group across most subgroups at week 48 [22, 24].

Limitations of this trial include the lack of an active comparator and the exclusion of patients with a history of primary failure to biologic therapy. As all clinical trials have strict inclusion and exclusion criteria which may affect the generalisability of these results to clinical practice, there is a need to use real-world data in registries to monitor efficacy of CZP over the longer term. Sample sizes for many of the subgroups were relatively small and caution should be used when interpreting these results. However, the results here are comparable with those from the larger global studies of CZP in PSO patients.

a PASI 75

■ Placebo Q2W ■ CZP 400 mg Q2W ■ CZP 200 mg Q2W

Week 16

Patients (%)

94.7 | 64.3 | 0.0 | 11.1 | 82.4 | 73.5

n= 8 19 14 18 34 34

Prior biologic exposure: Yes No

Week 52

Patients (%)

84.2 | 71.4 | 82.4 | 73.5

n= 19 14 34 34

Yes No

b PASI 90

Week 16

Patients (%)

78.9 | 42.9 | 0.0 | 0.0 | 73.5 | 55.9

n= 8 19 14 18 34 34

Prior biologic exposure: Yes No

Week 52

Patients (%)

84.2 | 64.3 | 79.4 | 58.8

n= 19 14 34 34

Yes No

c PGA 0/1

Week 16

Patients (%)

63.2 | 42.9 | 0.0 | 0.0 | 67.6 | 52.9

n= 8 19 14 18 34 34

Prior biologic exposure: Yes No

Week 52

Patients (%)

68.4 | 64.3 | 73.5 | 61.8

n= 19 14 34 34

Yes No

◀**Fig. 4** Response by prior biologic exposure at baseline. Non-responder imputation. Escapers were treated as non-responders from the time of escape onwards. Statistical significance between groups was not tested. n = number of patients in the subgroup at baseline. Patients were grouped based on prior biologic exposure: never used/No or used/ Yes (≥ 1 therapy). Only 2 patients continued placebo treatment to week 52; therefore placebo data are not shown for week 52

CONCLUSION

Overall, these data provide evidence to support the efficacy of CZP in Japanese patients with moderate to severe PSO, across patient demographic and baseline disease characteristic subgroups, over 52 weeks of treatment.

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