CLINICAL STUDY REPORT SYNOPSIS: PS0005 (CIMPASI-1)

Name of company: UCB Biopharma, SPRL	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia	**Volume**: Not applicable	
Name of active ingredient: Certolizumab pegol	**Page:** Not applicable	

Title of study: A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Study Followed by a Dose-Blind Period and Open-Label Follow-Up to Evaluate the Efficacy and Safety of Certolizumab Pegol in Subjects with Moderate to Severe Chronic Plaque Psoriasis

Investigators: Thirty Investigators enrolled subjects in this study.

Study sites: The study was conducted at 30 sites located in North America (United States and Canada) and Europe (Czech Republic, Hungary, and Germany).

Publications (references): none

Study period: Approximately 3 years and 10 months **First subject enrolled:** 16 Dec 2014 **Last subject completed:** 24 Oct 2018	**Phase of development:** Phase 3

Objectives: The primary objective of the study was to demonstrate the efficacy of certolizumab pegol (CZP) administered subcutaneously (sc) at the doses of CZP 400mg every 2 weeks (Q2W) and CZP 200mg Q2W after a loading dose of CZP 400mg at Weeks 0, 2, and 4 in the treatment of moderate to severe chronic plaque psoriasis (PSO). The secondary objectives of the study were to:

- Assess the optimal initial treatment dose for the treatment of moderate to severe chronic plaque PSO
- Assess durability of the clinical response with continued treatment
- Assess the safety and tolerability of CZP
- Improvement of skin-related quality of life (Dermatology Life Quality Index [DLQI]).

The other objectives of the study were to demonstrate the effects of CZP on aspects of the disease:

- Improvement of general Health Related Quality of Life (HRQoL – Short Form 36-Item Health Survey [SF-36®])
- Depression and anxiety
- Work productivity and activity impairment
- Subject's health status
- Psoriatic nail disease in subjects with nail disease at Baseline
- Assess the safety and efficacy of long-term use of CZP

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Methodology: This was a Phase 3, randomized, double-blind, placebo-controlled multicenter study to demonstrate the efficacy and safety of CZP over placebo. The study population included adults with moderate to severe chronic plaque PSO, including both subjects who had received previous biologic treatment as well as those who were biologic treatment naïve. The study included 5 periods: Screening, Initial Treatment (double-blind, placebo-controlled), Maintenance Treatment (dose-blind), Open-label Treatment, and Safety Follow-up (SFU). The completed initial double-blind treatment period of 16 weeks was used to demonstrate the efficacy of CZP over placebo. Further blinded treatment from Weeks 16 to 48 was intended to collect information on dosing beyond initial treatment. Open-label treatment for an additional 96 weeks provided long-term safety data on the use of CZP for moderate to severe chronic plaque PSO.

During the 16-week Initial Treatment Period, subjects were randomized in a 2:2:1 ratio to receive either:

- CZP 200mg Q2W: CZP administered sc at the dose of CZP 400mg at Baseline, and Weeks 2 and 4, followed by CZP 200mg Q2W (starting at Week 6)
- CZP 400mg Q2W: CZP administered sc at the dose of CZP 400mg Q2W
- Placebo: placebo administered sc Q2W

Subjects who achieved at least a 50% reduction from Baseline in Psoriasis Area and Severity Index (PASI) response (PASI50) at Week 16 continued therapy as follows:

- Subjects randomized to CZP 200mg Q2W continued to receive CZP 200mg Q2W.
- Subjects randomized to CZP 400mg Q2W continued to receive CZP 400mg Q2W.
- Subjects randomized to placebo who achieved a PASI50 but not a 75% reduction from Baseline in PASI (PASI75) response at Week 16 received CZP 400mg at Weeks 16, 18, and 20 (loading doses) followed by CZP 200mg Q2W (starting at Week 22).
- Subjects randomized to placebo who achieved a PASI75 response at Week 16 continued to receive placebo.
- During the dose-blind Maintenance Treatment Period, subjects continued to receive study medication in a dose-blind fashion and were assessed at Week 32 through Week 48 for continued PASI50 response. Subjects who did not achieve a PASI50 response at Week 32 or a later time point were withdrawn from the study.

Subjects who did not achieve a PASI50 response at Week 16 escaped from blinded treatment and received treatment as described below:

- Escape treatment: Subjects who entered the escape arm of the study received open-label CZP 400mg Q2W. Subjects who received unblinded CZP 400mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.

All subjects who completed the Maintenance Treatment Period through Week 48 (with a PASI50 response at Week 48) received open-label treatment for up to an additional 96 weeks.

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During this period, subjects who completed the Week 48 Visit with a PASI50 response in a dose-blind group received CZP 200mg Q2W.

All subjects who completed the Week 48 Visit in the escape arm continued to receive CZP 400mg Q2W or may have, at the discretion of the Investigator, had their dose decreased to CZP 200mg Q2W if they achieved a PASI75 response at Week 48.

Subjects who received CZP 200mg Q2W and did not achieve a PASI50 response at Weeks 60, 72, 84, 96, 108, 120, or 132 received CZP 400mg Q2W for at least 12 weeks. Subjects who received CZP 400mg Q2W for at least 12 weeks and did not achieve a PASI50 response were withdrawn from the study.

Subjects who received CZP 200mg Q2W and achieved a PASI50 response but not a PASI75 response at Weeks 60, 72, 84, 96, 108, 120, or 132 may have had their CZP dose increased to 400mg Q2W, at the discretion of the Investigator.

Subjects who received CZP 400mg Q2W for at least 12 weeks and achieved a PASI75 response at Weeks 48, 60, 72, 84, 96, 108, 120, or 132 may have been switched to CZP 200mg Q2W, at the discretion of the Investigator.

Number of subjects (planned and analyzed): A total of 225 subjects were planned, and 234 subjects were randomized: 95 subjects randomized to the CZP 200mg Q2W group, 88 subjects randomized to the CZP 400mg Q2W group, and 51 subjects randomized to the placebo group. For the Initial Treatment Period, all 234 subjects in the Randomized Set (RS) were included in the Safety Set (SS) and a total of 219 subjects were included in the Per Protocol Set (PPS).

A total of 226 subjects were included in the Treated with CZP Set (TCS), 224 subjects were included in the Maintenance Safety Set (MSS), 223 subjects were included in the Maintenance Set, and 188 subjects were included in the Treated with Blinded CZP Set (TBCS).

A total of 223 of 234 subjects in the RS started the Maintenance Treatment Period, 159 subjects remained on blinded treatment and 64 subjects escaped to open-label treatment. For those subjects on blinded treatment, 79 subjects received CZP 200mg Q2W (including 5 subjects from the placebo group during the Initial Treatment Period), 77 subjects received CZP 400mg Q2W, and 3 subjects received placebo.

A total of 200 of 234 subjects in the RS started the Open-label Treatment Period; 147 subjects entered from the blinded arm and 53 subjects entered from the escape arm. A total of 200 subjects were included in the Open-label Extension Set (OLS), including 3 subjects in the Placebo/CZP 200mg Q2W group, 74 subjects in the CZP 200mg Q2W/CZP 200mg Q2W group, 70 subjects in the CZP 400mg Q2W/CZP 200mg Q2W group, and 53 subjects in the Escape CZP 400mg Q2W/CZP 400mg Q2W group. For safety summaries, the OLS included 169 subjects in the CZP 200mg Q2W group, 99 subjects in the CZP 400mg Q2W group, and 200 subjects in the All CZP group.

For the Combined Initial, Maintenance, and Open-label Treatment Period, 229 subjects were included in the TCS, including 188 subjects in the CZP 200mg Q2W group and 167 subjects in the CZP 400mg Q2W group.

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Diagnosis and main criteria for inclusion: The study population included adults (≥18 years of age) with moderate to severe chronic plaque PSO for ≥6 months, defined as a Baseline PASI ≥12 and body surface area (BSA) ≥10% and Physician's Global Assessment (PGA) score ≥3, including both subjects who have received previous biologic treatment as well as those who were biologic treatment naïve. Subjects must not have been primary failures to any prior biologic therapy (primary failure defined as no response within the first 12 weeks of treatment with the biologic) and may have been a secondary failure (ie, subject initially responded to therapy and then stopped treatment due to loss of response after Week 12) to no more than 1. Subjects with erythrodermic, guttate, or generalized pustular form of PSO were excluded.

Test product, dose(s) and mode of administration, batch number(s): Certolizumab pegol is an engineered humanized monoclonal antibody Fab' fragment with specificity for human tumor necrosis factor alpha (TNFα), manufactured in *Eschericia. coli*. The antibody fragment is subsequently purified and conjugated with high molecular weight polyethylene glycol (40kDa).

Certolizumab pegol was supplied as a sterile, clear, colorless to slightly yellow liquid solution with a pH of approximately 4.7 in a 1mL single-use, glass prefilled syringe (PFS) with a 25G ½-inch thin-wall needle for sc injection. Each syringe contained an injectable volume of 1mL at a concentration of 200mg/mL of CZP in 10mM sodium acetate buffer and 125mM sodium chloride as a tonicity agent.

Batch numbers: BX1012364, BX1012248, BX1012252, BX1012292, BX1012761, BX1012372, BX1012550, BX1012551, BX1012693, BX1012694, BX1013148, BX1013023, BX1013147, BX1013266, BX1013421, BX1013265, BX1013724, BX1012849, BX1013704, BX1013880, BX1014578, BX1014579, BX1014774, BX1014854, 227849, 236497

Duration of treatment: The duration of the study for each subject was up to 157 weeks, consisting of:

- Screening Period of up to 5 weeks
- Initial Treatment Period of 16 weeks (Week 0 to Week 16)
- Maintenance Treatment Period of 32 weeks (Week 16 to Week 48)
- Open-label Treatment Period of 96 weeks (Week 48 to Week 144)
- SFU Period of 8 weeks (Week 144 to Week 152). Note: Ten (10) weeks since final dose.

Reference therapy, doses and mode of administration, batch numbers: Placebo (0.9% saline) was supplied as a sterile solution in a single-use glass PFS with a 25G ½-inch thin-wall needle for sc injection, containing an injectable volume of 1mL.

Batch numbers: BX1012252, BX1012292, BX1012372, BX1012550, BX1012693, BX1012849, BX1013147, BX1013023, BX1012761, BX1013265

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Criteria for evaluation:

Efficacy: The coprimary efficacy variables were:

- PASI75 at Week 16
- PGA Clear or Almost clear (with at least 2-category improvement) at Week 16

The secondary efficacy variables were:

- At least 90% reduction from Baseline in PASI (PASI90) at Week 16
- PGA Clear or Almost clear (with at least 2-category improvement) at Week 48
- PASI75 at Week 48
- Change from Baseline in DLQI at Week 16

The other efficacy variables are listed below and were evaluated at all scheduled visits. This excluded the primary and secondary variables.

- PASI50, PASI90, and 100% reduction from Baseline in PASI (PASI100)
- PASI75
- PGA Clear or Almost clear (with at least 2-category improvement)
- Absolute and percent change from Baseline in PASI score
- PGA score distribution
- Time to onset of action, defined as the time to PASI50
- Time to onset of action, defined as the time to PASI75
- Time to onset of action, defined as the time to PASI90
- Absolute and percent change from Baseline in the BSA affected by PSO
- Change from Baseline in modified Nail Psoriasis Severity Index
- Change from Baseline in SF-36 all domains, and physical and mental component summary scores, and percent of subjects achieving the minimal clinically important difference (MCID)
- Change from Baseline in DLQI, percent of subjects achieving MCID, and percent achieving DLQI Remission
- Change from Baseline in Hospital Anxiety and Depression Scale for anxiety (HADS-A) and Hospital Anxiety and Depression Scale for depression (HADS-D) scores, percent of subjects with scores below 8 in HADS-A and HADS-D (subjects with normal scores)
- Change from Baseline in Work Productivity and Activity Impairment Questionnaire–Specific Health Problem (WPAI-SHP) v2.0 adapted to PSO scores
- Responses to the European Quality of Life 5 dimensions, 3 levels (EQ-5D-3L™) questionnaire,

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absolute and changes from Baseline in EQ-5D-3L visual analogue scale scores

- Direct medical resource use: number of concomitant medical procedures, number of health care provider consultations not foreseen by the protocol, number of hospitalizations, number of emergency room visits, and length of hospital stay
- Socio-professional status (educational level, professional status, and assistance in the usual activities)

The following variables were considered key efficacy variables for the open-label extension analysis:

- PASI75, PASI90, and PASI100
- PGA Clear or Almost Clear (with at least 2-category improvement)
- Change from Baseline in DLQI and percent achieving DLQI remission

The 6 key efficacy variables listed above were summarized for the Open-label Treatment Period only and for the Combined Initial, Maintenance, and Open-label Treatment Period. Efficacy variables that were not defined as key were only summarized for the Open-label Treatment Period.

Pharmacokinetics: All subjects provided samples for pharmacokinetic evaluation at Baseline; Weeks 2, 4, 16, 24, 32, 48, 72, 96, 120, and 144; the Early Withdrawal Visit; and the SFU Visit (10 weeks after final dose of CZP).

Immunogenicity: Plasma samples for the measurement of anti-CZP antibodies were collected at Baseline; Weeks 2, 4, 16, 24, 32, 48, 72, 96, 120, and 144; the Early Withdrawal Visit; and the SFU Visit (10 weeks after final dose of CZP).

Safety: Safety variables assessed were:

- Adverse events (AEs)
- Blood pressure
- Physical examination
- Clinical laboratory values (hematology, biochemistry, and urinalysis)
- Interferon-gamma release assay test for tuberculosis

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Statistical methods: This final clinical study report presents the complete analysis of results through the end of the study. Descriptive statistics were displayed to provide an overview of the study results. For categorical variables, the number and percentage of subjects in each category was presented. The denominator for percentages was based on the number of subjects appropriate for the purpose of analysis for the respective treatment group, subset, and period.

A Baseline value for a subject was defined as the latest measurement for that subject up to and including the day of administration of first study medication, unless otherwise stated. If a Baseline value was missing or not collected, and a Screening value was available, the Screening value was utilized as the Baseline value. Baseline values for composite scores were computed using components from the same visit when the relevant measurements were recorded prior to dosing. For example, if the Screening Visit had all of the components, but the Baseline Visit was missing one or more components, the Baseline value for the component score was calculated using the Screening Visit values.

All efficacy analyses were performed using the RS. The PPS was used for a sensitivity analysis on the primary endpoints only. For the final efficacy analyses of key and other efficacy endpoints, the RS and OLS were used for the Combined Initial, Maintenance, and Open-label Treatment Period and the OLS was used for the Open-label Treatment Period. Safety summaries were performed using the SS, TCS, TBCS, MSS, or OLS.

The statistical analysis of the coprimary efficacy variables and secondary efficacy variables accounted for multiplicity and controlled the familywise type I error rate at a 2-sided alpha level of 0.05 by using a fixed-sequence testing procedure.

The hypotheses were mapped into 2 sets (H1, H3, H5, and H7) and (H2, H4, H6, and H8) such that the hypotheses within each set corresponded to the same CZP dose. The type I error was split equally between CZP 400mg Q2W and CZP 200mg Q2W, such that each dose was tested at a 2-sided alpha level of 0.025.

The first 2 hypotheses for each dose (H1 and H3 for CZP 400mg Q2W, and H2 and H4 for CZP 200mg Q2W) tested whether the given CZP dose was superior to placebo for PASI75 response and PGA response at Week 16. These were the hypothesis tests corresponding to the coprimary endpoints. If both were rejected at a 2-sided alpha level of 0.025, that alpha was passed to the next test in the sequence, allowing the testing procedure to proceed.

The hypotheses associated with the subsequent tests were for the secondary efficacy endpoints and were based on testing for superiority relative to placebo. See Figure 1 for details on this fixed-sequence testing procedure.

If all hypotheses within 1 set of hypotheses (either CZP 400mg Q2W or CZP 200mg Q2W) were rejected, the corresponding type I error probability was passed on to the other set of hypotheses and that set was retested, if necessary, at a 2-sided alpha level of 0.05.

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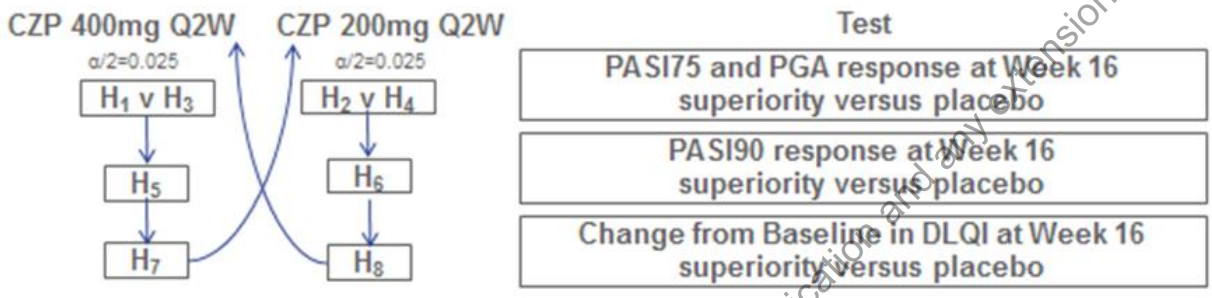
Figure 1: Fixed-sequence testing procedure



CZP=certolizumab pegol; DLQI=Dermatology Life Quality Index; H=hypothesis; PASI75=at least 75% reduction from Baseline in Psoriasis Area and Severity Index; PASI90=at least 90% reduction from Baseline in Psoriasis Area and Severity Index; PGA=Physician's Global Assessment; Q2W=every 2 weeks

Analysis of the coprimary efficacy variables. The first coprimary efficacy variable, PASI75 at Week 16, was based on the PASI score, which scores for each body part and the percentage of skin covered with PSO. The PASI75 response is based on at least 75% improvement (reduction) from Baseline in the PASI score. The second coprimary efficacy variable was a static PGA for PSO to assess disease activity during the study. The Investigator assessed the overall severity of PSO using a 5-point scale. Subjects were classified as responders at Week 16 if they achieved a PGA score of 0 or 1, and had at least a 2-category improvement from Baseline. The primary analyses for these variables were based on logistic regression for the RS. The odds ratio of the responder rate at Week 16 was estimated and tested between randomized treatment groups using a logistic regression model with factors of treatment group, geographic region, and prior biologic exposure (yes/no). The odds ratio, associated confidence interval (CI), and p-value were presented. The Markov Chain Monte Carlo method for multiple imputation was used to account for missing values in the primary analysis of PGA and PASI75 at Week 16. This is a commonly used method for handling intermittent or monotonic missing data under the assumption of a missing at random pattern of missingness. The multiple imputation procedure for PGA response was based on the observed score on a scale from 0 to 4 (as opposed to the binary response). Similarly, for PASI75, the multiple imputation procedure was based on the actual PASI score.

Analysis of the secondary efficacy variables. The PASI90 response at Week 16 was calculated and analyzed in the same manner described for the primary analysis of PASI75 response at Week 16. The analysis of the DLQI was based on the change from Baseline at Week 16 for the RS. Randomized treatment group comparisons for each CZP treatment group vs placebo were performed using an analysis of covariance model with treatment group, geographic region, and prior biologic exposure as factors, and Baseline DLQI score as a covariate. The least squares (LS) means and standard errors (SE) derived from the model were presented for each treatment group. Additionally, adjusted mean treatment differences, corresponding CIs, and p-values were reported. Missing values were imputed using last observation carried forward. The analysis of the PASI75 responder rate at Week 48 and PGA Clear or Almost clear (with at least 2-category improvement) at Week 48 was based on the RS and was summarized only for the

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CZP 200mg Q2W and CZP 400mg Q2W randomized treatment groups. Missing data were handled based on a combination of nonresponder imputation (NRI) and multiple imputation.

Summary and conclusions:

Subject disposition: A total of 234 randomized subjects started the Initial Treatment Period; 95 subjects randomized to the CZP 200mg Q2W group, 88 subjects randomized to the CZP 400mg Q2W group, and 51 subjects randomized to the placebo group. Overall, 225 subjects (96.2%) completed the Initial Treatment Period; the percentages of subjects who completed the Initial Treatment Period were higher in the CZP 200mg Q2W (96.8%) and CZP 400mg Q2W (98.9%) groups compared with the placebo group (90.2%) groups. A total of 9 subjects (3.8%) discontinued during the Initial Treatment Period (prior to Week 16); overall, the most frequently reported primary reasons for discontinuation were consent withdrawn (5 subjects [2.1%]) and lost to follow-up (2 subjects [0.9%]). The single subject in the CZP 400mg Q2W group who discontinued the Initial Treatment Period did so due to a serious and non-fatal AE. Of the 225 subjects who completed the Initial Treatment Period, 2 subjects (0.9%) did not enter the Maintenance Treatment Period; of these 2 subjects, 1 completed the Week 16 visit and was dosed at Week 16, but subsequently died due to a motor vehicle accident (ie, a serious adverse event (SAE) of multiple injuries).

A total of 223 subjects started the Maintenance Treatment Period, and 202 subjects (90.6%) completed Week 48. A total of 21 subjects (9.4%) discontinued during the Maintenance Treatment Period (prior to Week 48; 10 of the 159 subjects who were in the Blinded Maintenance group and 11 of the 64 subjects who were in the Escape Maintenance group). Overall, the most frequently reported primary reasons for discontinuation were consent withdrawn and other: mandatory withdrawal due to not achieving a PASI50 response (7 subjects each [3.1%]). The single subject who discontinued the Maintenance Treatment Period due to an AE did so due to a non-serious and non-fatal AE.

A total of 200 subjects started the Open-label Treatment Period, and 152 subjects (76.0%) completed Week 144. A total of 48 subjects (24.0%) discontinued during the Open-label Treatment Period (prior to Week 144); overall, the most frequently reported primary reasons for discontinuation were lost to follow up (15 subjects [7.5%]), other (13 subjects [6.5%]), and consent withdrawn (10 subjects [5.0%]). Twelve of the 13 subjects who discontinued the study due to "other" did so for mandatory withdrawal due to a PASI50 nonresponse; the remaining subject discontinued due to study medication noncompliance.

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Efficacy results:

Efficacy during the Initial Treatment Period

The statistical analysis of the coprimary efficacy variables (PASI75 and PGA responder rates) and selected secondary efficacy variables (PASI90 responder rate and change from Baseline in DLQI) at Week 16 were evaluated using a fixed-sequence testing procedure. Based on this procedure, data from PS0005 demonstrate that treatment with CZP 200mg Q2W and CZP 400mg Q2W resulted in clinically meaningful and statistically significant improvements compared with placebo in PSO area and severity (as assessed by PASI75 and PASI90 responder rates) as well as global physician-assessment of disease activity (via PGA responder rates of 0 or 1). In addition, CZP 200mg Q2W and CZP 400mg Q2W resulted in clinically meaningful and statistically significant improvements in patients' HRQoL (as assessed by the mean change from Baseline at Week 16 in DLQI) compared with placebo.

The results of the coprimary endpoints were supported and confirmed by similar findings from all sensitivity analyses.

Psoriasis area and severity

- Statistically significant and clinically meaningful differences in PSO area and severity, as measured by the PASI75 and PASI90 responder rates, were observed for CZP-treated subjects compared with placebo-treated subjects. At Week 16, the PASI75 responder rates were significantly greater in both the CZP 200mg Q2W group (66.5%) and CZP 400mg Q2W group (75.8%) compared with the placebo group (6.5%; $p<0.0001$ for both comparisons). This analysis for the coprimary endpoint was supported by the predefined sensitivity analyses and the analysis using the PPS. Similarly, PASI90 responder rates were significantly greater in both the CZP 200mg Q2W group (35.8%) and CZP 400mg Q2W group (43.6%) compared with the placebo group (0.4%; $p<0.0001$ for both comparisons).
- During the Initial Treatment Period, PASI50, PASI75, PASI90, and PASI100 responder rates in both the CZP 200mg Q2W and CZP 400mg Q2W groups consistently increased over time through Week 16.
- In general, the improvements in PASI responder rates occurred rapidly following the initiation of treatment with CZP. Clinically meaningful differences versus placebo were observed for PASI50 responder rates at Week 2 for the CZP 200mg Q2W group and at Week 4 for the CZP 400mg Q2W group; at Week 4 for PASI75 responder rates for both CZP groups; and at Week 8 for PASI90 responder rates for both CZP groups. For PASI100 responder rates, clinically meaningful improvements were seen at Week 16.
- Clinically meaningful differences in time to achieving a PASI50, PASI75, and PASI90 response were observed for CZP-treated subjects compared with placebo-treated subjects during the Initial Treatment Period. The median times to achieving PASI50 responses were 54.0 days and 31.0 days for the CZP 200mg Q2W and CZP 400mg Q2W groups, respectively. The median times to achieving

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PASI75 responses were 83.0 and 84.0 days, respectively, for the CZP 200mg Q2W and CZP 400mg Q2W groups. The median times to achieving PASI90 responses were 115.0 days and 114.0 days for the CZP 200mg Q2W and CZP 400mg Q2W groups, respectively. The differences versus placebo for the CZP 200mg Q2W and 400mg Q2W groups resulted in nominal p-values <0.0001 for all comparisons.

- Numerically greater improvements in those endpoints assessing PSO area and severity were generally seen in the CZP 400mg Q2W group compared with the CZP 200mg Q2W group during the Initial Treatment Period. PASI50, PASI75, and PASI90 responder rates and mean percent improvement from Baseline in PASI score were numerically higher in the CZP 400mg Q2W group as compared to the CZP 200mg Q2W group at Weeks 12 and 16. No differences were observed between the CZP 200mg Q2W and CZP 400mg Q2W groups for PASI100 responder rates.

Physician's Global Assessment of disease activity

- At Week 16 (the coprimary endpoint), PGA responder rates were significantly higher in both the CZP 200mg Q2W group (47.0%) and CZP 400mg Q2W group (57.9%) compared with the placebo group (4.2%; p<0.0001 for both comparisons).
- The improvements in PGA responder rates occurred rapidly following the initiation of treatment with CZP; clinically meaningful differences versus placebo were observed for both CZP groups beginning at Week 4 and at all subsequent time points through Week 16.
- PGA responder rates in both the CZP 200mg Q2W and CZP 400mg Q2W groups consistently increased through Week 16.
- PGA responder rates at Week 12 and Week 16 were numerically higher in the CZP 400mg Q2W group compared with the CZP 200mg Q2W group.

Subgroup analyses of the coprimary endpoints

- All subgroups had a clinically meaningful difference from placebo in PGA and PASI75 responder rates at Week 16 for both CZP groups. Subgroup analyses of the coprimary endpoints revealed that BMI in the CZP 400mg Q2W group; geographic region in the 200mg Q2W group; and gender in both the CZP 200mg Q2W and 400mg Q2W groups appeared to have influences on PASI75 and PGA responder rates. For the CZP 400mg Q2W group, subjects in the highest 2 quintiles of BMI had lower responder rates compared with subjects in the lower quintiles; subjects in North America had better responder rates than subjects in Europe in the CZP 200mg Q2W group; and male subjects had better responder rates than female subjects in both CZP dose groups for PASI75 and in the 400mg Q2W group for PGA. In addition, PASI75 and PGA responder rates in the CZP 400mg Q2W and CZP 200mg Q2W groups were similar in subjects from North America but were numerically higher in the

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CZP 400mg Q2W group compared with the CZP 200mg Q2W group in subjects from Europe.

- It should be noted that the results of the subgroup analyses should be interpreted with caution given that the sample sizes of many of the subgroup categories were relatively small. In addition, potential interactions between subgroup categories may have influenced the results and cannot be adequately explored in this individual study due to the small group sizes. Of note, with the exception of subjects positive for anti-CZP antibodies, in those subgroups in which PASI75 and PGA responder rates were comparatively lower, the responder rates in the CZP 200mg Q2W and 400mg Q2W groups were still clinically meaningfully greater than the responder rates observed in the corresponding placebo group across subgroups.

Health-related quality of life

- At Week 16, the LS mean (SE) decrease (ie, improvement) from Baseline in DLQI using LOCF was -9.3 (0.58) points for the CZP 200mg Q2W group and -10.2 (0.60) for the CZP 400mg Q2W compared with -3.3 (0.69) points for the placebo group ($p<0.0001$ for both comparisons).
- Subjects in the CZP 200mg Q2W and CZP 400mg Q2W groups had similar and clinically meaningful improvements in patients' HRQoL (as assessed by the mean change from Baseline in the DLQI) compared with the placebo group. Consistently larger decreases from Baseline in the DLQI score were observed over time from Weeks 2 through 8 for the CZP 200mg Q2W group and from Weeks 2 through 12 for the CZP 400mg Q2W group, and these decreases were subsequently maintained at Week 16.
- The percentages of subjects who were DLQI MCID responders (defined as a ≥4-point change in the DLQI score) in both the CZP 200mg Q2W and CZP 400mg Q2W groups were higher than placebo at each time point. At Week 16, 66.3% of subjects in the CZP 200mg Q2W group and 78.4% of subjects in the CZP 400mg Q2W group were DLQI MCID responders compared with 41.2% of subjects in the placebo group. The percentage of subjects who were DLQI MCID responders was numerically higher in the CZP 400mg Q2W group compared with the CZP 200mg Q2W group at Weeks 12 and 16.
- Generally similar and increasingly larger percentages of subjects in both the CZP 200mg Q2W and CZP 400mg Q2W groups achieved DLQI remission as compared with placebo at each time point. At Week 16, 47.4% of subjects in the CZP 200mg Q2W group and 45.5% of subjects in the CZP 400mg Q2W group had achieved DLQI remission compared with 5.9% of subjects in the placebo group.
- Results of the DLQI were supported by clinically meaningful improvements versus placebo in overall health status (as assessed by the EQ-5D-3L VAS), physical functioning (as assessed by the SF-36 PCS), mental health (as assessed by the SF-36 MCS) as well as anxiety and depression (as assessed by the HADS-A and HADS-D) following treatment with CZP 200mg Q2W and CZP 400mg Q2W during the Initial Treatment Period. Impairment while working and in daily activities due to PSO (as

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assessed by the WPAI-SHP) was reduced in the CZP treatment groups over placebo as early as Week 4 (first assessment) and the reduction in impairment was sustained through the Initial Treatment Period. Improvements observed in these PRO measures in the CZP 400mg Q2W group were comparable to and, in some cases, greater than those improvements seen in the CZP 200mg Q2W group.

Efficacy during the Maintenance Treatment Period

- PASI75 responder rates at Week 16 were 66.5% for the CZP 200mg Q2W group and 75.8% for the CZP 400mg Q2W group. Compared with Week 16, PASI75 responder rates among subjects in the RS were maintained at Week 48 in the CZP 200mg Q2W group (67.2%) and continued to increase through Week 48 in the CZP 400mg Q2W group (87.1%).
- PGA responder rates at Week 16 were 47.0% for the CZP 200mg Q2W group and 57.9% for the CZP 400mg Q2W group. Compared with Week 16, PGA responder rates among subjects in the RS continued to improve in both the CZP 200mg and 400mg Q2W groups at Week 48 (52.7% and 69.5%, respectively), with greater numerical improvements observed in the CZP 400mg Q2W group.
- In those subjects who were PASI75 or PGA responders at Week 16, responder rates for each generally remained high at Week 48.
- During the Maintenance Treatment Period (based on either randomized treatment group or maintenance treatment group), the improvements observed across the collection of efficacy endpoints assessed during the Initial Treatment Period (based on PSO severity and/or area; PSO-specific HRQoL; and PRO measurements) were, at a minimum, consistently maintained through 48 weeks of treatment. In general, the improvements that were observed were numerically larger in the CZP 400mg Q2W group compared with the CZP 200mg Q2W group.
- For the CZP 400mg Q2W group, treatment longer than the initial 16 weeks resulted in further improvements through Week 48 for some endpoints, and these improvements were generally larger than those observed in the CZP 200mg Q2W group. Specifically, in the CZP 400mg Q2W group, consistent increases (relative to Week 16) were observed through Week 48 in PASI75 and PGA responder rates. For PASI90 and PASI100 responder rates, further improvements in both the CZP 200mg Q2W and CZP 400mg Q2W groups were observed through Week 28, and these improvements were maintained through Week 48.
- For those placebo-treated subjects who did not achieve a PASI50 response by Week 16, treatment with open-label CZP 400mg Q2W in the Maintenance Treatment Period resulted in improvements across the spectrum of efficacy endpoints assessed that resembled a pattern of improvement similar to those subjects who were originally randomized to blinded CZP treatment in the Initial Treatment Period. There were too few subjects in the CZP 200mg Q2W/Esc CZP 400mg Q2W and CZP 400mg

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Q2W/Esc CZP 400mg Q2W escape maintenance groups to allow for meaningful conclusions to be made.

Efficacy during the Combined Initial, Maintenance, and Open-label Treatment Period

The focus of this summary is on the RS. The OLS is primarily used to summarize escapers (ie, subjects who received continuous open-label CZP 400mg Q2W for ~2.5 years) and nonadjusters (ie, subjects who entered the Open-label Treatment Period and did not subsequently have a dose adjustment).

Efficacy results for the CZP 200mg Q2W group

- Across the spectrum of efficacy endpoints assessed, CZP 200mg Q2W treatment up to 3 years demonstrated improvements that were generally maintained through Week 144.
  - PASI75, PGA, PASI90, and PASI100 responder rates (RS) increased consistently over time through Week 16 and were generally maintained through Week 48. PASI75, PGA, PASI90, and PASI100 responder rates were maintained during the Open-label Treatment Period through Week 144.
  - Evaluation of maintenance of response in subjects who were responders at Week 16 (RS) demonstrated that PASI75, PGA, and PASI90 responder rates were maintained in >95%, >75%, and >75%, respectively from Week 20 to Week 48 and >75%, >60%, and >65%, respectively, from Weeks 60 to 144.
  - Improvements from Baseline in the DLQI that were achieved during the Initial Treatment Period (by Week 16) were maintained through the Maintenance Period (through Week 48) and the Open-label Treatment Period (through Week 144). DLQI remission rates increased through Week 16 and were maintained through Week 48 and Week 144, with 44.7% of subjects achieving DLQI remission at Week 144.
  - For the subjects who entered the Open-label Treatment Period (OLS), trends were generally similar compared with the RS. For subjects who remained on CZP 200mg Q2W throughout the Open-label Treatment Period (nonadjusters), PASI75, PASI90, and PGA responder rates were generally maintained through Week 144. PASI100 responder rates for nonadjusters in the CZP 200mg Q2W/CZP 200mg Q2W group gradually declined over time through Week 144.

Efficacy results for the CZP 400mg Q2W group

- Across the spectrum of efficacy endpoints assessed, CZP 400mg Q2W treatment demonstrated improvements that were maintained through Week 48. Following the dose down adjustment to CZP 200mg Q2W at Week 48, some loss of responses were generally observed during the Open-label Treatment Period, with a magnitude and time to decline that was endpoint-specific. Some regain in efficacy was observed during the Open-label Treatment Period, which could be due to dose

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readjustments back to CZP 400mg Q2W.

- PASI75, PGA, PASI90, and PASI100 responder rates (RS) increased consistently over time through Week 16 and were maintained through Week 48. During the Open-label Treatment Period, some declines in PASI75, PGA, and PASI90 were observed through Week 84, which then stabilized through Week 144; PASI100 responder rates were maintained through Week 144.
- Evaluation of maintenance of response in subjects who were responders at Week 16 (RS) demonstrated PASI75, PGA, and PASI90 responder rates were maintained in >95%, >85%, and >80%, respectively, from Week 20 to Week 48. Following the dose down adjustment to CZP 200mg Q2W at Week 48, PASI75, PGA, and PASI90 responder rates were >75%, >50%, and >55%, respectively, from Weeks 60 to 144.
- Improvements from Baseline in the DLQI and DLQI remission rates achieved by Week 16 were maintained through Week 48. Following the dose down adjustment to CZP 200mg Q2W at Week 48, improvements from Baseline in the DLQI were maintained, but DLQI remission rates declined with 47.1% of subjects achieving DLQI remission at Week 144.
- For the subjects who entered the Open-label Treatment Period (OLS), trends were generally similar compared with the RS. All subjects who dosed down at Week 48 and remained on CZP 200mg Q2W throughout the Open-label Treatment Period (nonadjusters) were PASI75 responders at Week 48. For these subjects, PASI75 rates were maintained through Week 144; PASI90, PASI100, and PGA responder rates generally declined after Week 48 with some regain in response late in the study.

Efficacy results for the Escape CZP 400 mg Q2W/CZP 400mg Q2W group

- Although the data in this section are for open-label CZP treatment, this treatment group represents the longest, continuous exposure to CZP 400mg Q2W for up to 128 weeks (~2.5 years). Improvements across the spectrum of efficacy endpoints assessed were observed up to Week 32 (ie, up to 16 weeks of CZP treatment) and maintained through Weeks 60 and 144 (ie, up to 40 and 128 weeks of CZP treatment, respectively). This pattern of improvement was similar to those subjects who were originally randomized to blinded CZP 400mg Q2W treatment in the Initial and Maintenance Treatment Periods (Table 1).

Table 1: PGA, PASI75, PASI90, and PASI100 responder rates over time – Combined Initial, Maintenance, and Open-label Treatment Period

Parameter Statistic	OLS (MCMC) Escape CZP 400mg Q2W/ CZP 400mg Q2W [a] N=53			RS (MCMC) CZP 400mg Q2W [b] N=88		
	Week 32 (ie, Week 16 of open-label CZP treatment)	Week 60 (ie, Week 44 of open-label CZP treatment)	Week 144 (ie, Week 128 of open-label CZP treatment)	Week 16	Week 48 [b]	Week 144
PGA responder rates over time						
Responder rate (%)	63.7	69.2	69.7	58.2	69.9	48.7
PASI75 responder rates over time						
Responder rate (%)	72.7	89.7	81.8	76.4	86.6	69.9
PASI90 responder rates over time						
Responder rate (%)	48.1	69.1	61.1	44.7	60.4	41.8
PASI100 responder rates over time						
Responder rate (%)	17.9	32.4	31.9	12.1	24.0	24.6

CI=confidence interval; CZP=certolizumab pegol; MCMC=Markov Chain Monte Carlo; OLS=Open-label Set; PASI50/75/90/100=at least 50%/75%/90%/100% reduction from Baseline in Psoriasis Area and Severity Index; PGA=Physician's Global Assessment; Q2W=every 2 weeks; RS=Randomized Set

Note: PGA responders=Clear or Almost clear (with at least 2-category improvement from Baseline).

Note: Dose adjustments after Week 48 were not considered in this table.

Note: Estimates of the responder rate and CIs were based on using a logistic regression model with factors for treatment, region, and prior biologic exposure (yes/no) on the multiply imputed data sets where missing data were imputed using the MCMC method. The responder rates were the adjusted predicted probabilities from the logistic regression model. Subjects who should have been withdrawn at Week 32 or later due to lack of PASI50 response or subjects on CZP 400mg Q2W (for at least 12 weeks) during the Open label Treatment Period who did not achieve a PASI50 response during the Open-label Treatment Period and should have been mandatorily withdrawn were treated as nonresponders for subsequent time points. All other missing data were imputed using multiple imputation based on MCMC methodology. In cases where no data were missing at a visit, the logistic regression was performed on the observed data.

[a] In the Escape CZP 400mg Q2W/CZP 400mg Q2W group, subjects escaped from their randomized treatment (eg, CZP 200mg Q2W, CZP400mg Q2W, or placebo) at Week 16.

[b] Subjects in the CZP 400mg Q2W group had a protocol-mandated dose down to CZP 200mg Q2W at Week 48.

Pharmacokinetics results:

The observed plasma concentrations of CZP were consistent with the dosing regimens for the different treatment groups.

The lower plasma concentrations of CZP observed in subjects who were anti-CZP antibody positive were as expected.

Immunogenicity results:

During the Combined Initial and Maintenance Treatment Period, as expected, the percentage of subjects who were anti-CZP antibody positive was higher in the CZP 200mg Q2W group than in the CZP 400mg Q2W group. In the CZP 200mg Q2W group, the percentages of subjects who were anti-CZP antibody positive at Weeks 16 and 48 were, respectively, 11.6% and 14.7%, (11 and 14 of 95 subjects, respectively) while the corresponding percentages of subjects in the CZP 400mg Q2W group who were anti-CZP antibody positive at Weeks 16 and 48 were, respectively, 4.5% and 9.1% (4 and 8 of 88 subjects). Both groups included subjects who escaped from their initial treatment to 400mg Q2W at Week 16.

The percentage of subjects who were anti-CZP antibody positive at any time during treatment was 14.9% (10 of 67 subjects) in the CZP 200mg Q2W to CZP 200mg Q2W at Week 16 to CZP 200mg Q2W at Week 48 group. The percentage of subjects who were anti-CZP antibody positive at any time during treatment was 8.8% (6 of 68 subjects) in the CZP 400mg Q2W to CZP 400mg Q2W at Week 16 to CZP 200mg Q2W at Week 48 group. In the placebo to Escape CZP 400mg Q2W at Week 16 to CZP 400mg Q2W at Week 48 group, the percentage of subjects who were anti-CZP antibody positive at any time during treatment was 15.4% (4 of 26 subjects).

It was noted that the incidence of anti-CZP antibody positivity at Week 144 was sometimes higher or lower than the corresponding incidence at Week 48. The reason for this is that there were 2 sources for the change in the incidence of anti-CZP antibody positivity between Weeks 48 and 144. The first was that not all subjects included in the assessment at Week 48 continued into the Open-label Treatment Period, so anti-CZP antibody-positive subjects could leave the study or enter the Open-label Treatment Period (randomly), thus either lowering or raising the proportion of anti-CZP antibody-positive subjects remaining in the group of subjects who entered the Open-label Treatment Period. The second source was that of new first occurrences of anti-CZP antibody positivity in the subjects during the Open-label Treatment Period, which would increase the incidence of anti-CZP antibody positivity.

While persistent high anti-CZP antibody responses with resulting falls in CZP concentration were observed in some subjects, in other subjects the anti-CZP antibody responses were transient and often associated with only transient falls in the CZP concentration.

Safety results:

- The safety profile was comparable between CZP treatment and placebo during the 16-week Initial Treatment Period with the exception of higher incidences with CZP treatment (particularly CZP 400mg Q2W) of Infections and infestations (driven by a higher percentage of subjects with nasopharyngitis) as well as higher incidences of Respiratory, thoracic, and mediastinal disorders and Gastrointestinal disorders (neither driven by a particular preferred term), as would be expected for an anti-TNFα agent.
- The mean duration of exposure for the study in the All CZP group was 807.7 days. The duration of exposure was higher in the CZP 200mg Q2W group (mean: 562.0 days) compared with the CZP 400mg Q2W group (mean: 474.9 days), which is expected given that most subjects remained on or were switched to CZP 200mg Q2W at Week 48 (unless they were in the escape arm) per the dosing schedule. The total subject exposure years at risk was 538.93 years in the All CZP group, 307.00 years in the CZP 200mg Q2W group, and 231.93 years in the CZP 400mg Q2W group.

- The exposure-adjusted incidence rate (IR)of treatment-emergent adverse events (TEAEs) in the All CZP group was 330.78/100 subject-years (subject-yrs) in the Initial Treatment Period, 237.67/100 subject-yrs in the Combined Initial and Maintenance, and 93.94/100 subject-yrs in the Open-label Treatment Period, suggesting that there was no increased risk of TEAEs after longer or higher CZP exposure.
- During the Initial Treatment Period, the incidence and exposure-adjusted IR of TEAEs was lower in the CZP 200mg Q2W group compared with the CZP 400mg Q2W group (54.7% vs 64.8%, respectively; 292.33 and 375.87/100 subject-yrs, respectively); this imbalance was attributed primarily to a higher incidence of TEAEs in the Infections and infestations SOC in the CZP 400mg Q2W group. During the Open-label Treatment Period, similar proportions of subjects in the CZP 200mg Q2W and CZP 400mg Q2W groups had at least 1 TEAE during the Open-label Treatment Period (64.5% and 67.7%, respectively); however, the exposure-adjusted IR was slightly lower for the CZP 200mg Q2W group compared with the CZP 400mg Q2W group (94.35 vs 113.03/100 subject-yrs, respectively).
- Overall, the exposure-adjusted IR of any SAE in the All CZP group during the entire study was low (6.39/100 subject-yrs). The exposure-adjusted IR of any SAE in the All CZP group was 12.69/100 subject-yrs during the Initial Treatment Period, 8.28/100 subject-yrs during the Combined Initial and Maintenance Treatment Period, and 5.04/100 subject-yrs during the Open-label Treatment Period, suggesting no increase in risk after longer or higher CZP exposure.
- During the Combined Initial, Maintenance, and Open-label Treatment Period, 11 TEAEs leading to permanent study medication discontinuation were reported by 11 subjects (4.8%) in the All CZP group; the incidence was similar between the CZP 200mg and CZP 400mg Q2W groups (1.6% and 4.8%, respectively).
- Overall, most TEAEs were mild or moderate in intensity and were not considered by the Investigator as related to study medication.
- Regarding AEs of interest, the incidence of serious infections, malignancies, serious cardiovascular events, and serious bleeding events was low in the All CZP group during the Combined Initial, Maintenance, and Open-label Treatment Period and similar in the CZP 200mg Q2W and CZP 400mg Q2W groups; there were no events of demyelination, hematopoietic cytopenia, lupus or lupus-like illness, or serious skin reactions reported during the study.
- Maintaining CZP treatment at either dose (200mg Q2W or 400mg Q2W) for up to an additional 128 weeks beyond the Initial Treatment Period of 16 weeks was not associated with an increased safety risk compared with the Initial Treatment Period in the PSO population in this study.
- The safety profile for up to 144 weeks of CZP treatment, including the type and incidence of TEAEs, was consistent with that expected in subjects with moderate to severe chronic plaque PSO receiving an anti-TNFα agent and with previous studies of CZP. No new safety signals were identified following review of AEs, biochemistry values, hematology values, or vital signs at either the 200mg Q2W dose or the 400mg Q2W dose that have not been previously observed in other studies with CZP in PSO subjects or other indications (ie, rheumatoid arthritis, Crohn's disease, axial spondyloarthritis, and psoriatic arthritis).

Table 2 CIMPASI-1: Comparison of incidence and exposure-adjusted IRs across treatment periods for select safety parameters

Category Period	CZP 200mg Q2W			CZP 400mg Q2W			All CZP		
	N	n (%)	IR	N	n (%)	IR	N	n (%)	IR
TEAEs									
Initial (Weeks 0 to16) [a]	95	52 (54.7)	292.33	88	57 (64.8)	375.87	183	109 (59.6)	330.78
Combined Initial and Maintenance (Weeks 0 to 48) [b]	100	72 (72.0)	217.45	144	111 (77.1)	257.63	226	175 (77.4)	237.67
Open-label (Weeks 48 to 144) [c]	169	109 (64.5)	94.35	99	67 (67.7)	113.03	200	147 (73.5)	93.94
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	137 (72.9)	124.19	167	137 (82.0)	221.87	229	200 (87.3)	172.34
SAEs									
Initial (Weeks 0 to16) [a]	95	2 (2.1)	6.93	88	5 (5.7)	19.02	183	7 (3.8)	12.69
Combined Initial and Maintenance (Weeks 0 to 48) [b]	100	4 (4.0)	5.32	144	11 (7.6)	10.38	226	15 (6.6)	8.28
Open-label (Weeks 48 to 144) [c]	169	9 (5.3)	4.03	99	8 (8.1)	6.89	200	17 (8.5)	5.04
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	14 (7.4)	4.80	167	19 (11.4)	8.78	229	32 (14.0)	6.39
Serious infections									
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	2 (1.1)	0.65	167	3 (1.8)	1.31	229	5 (2.2)	0.93
Malignancies									
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	0	--	167	2 (1.2)	0.87	229	2 (0.9)	0.37
Serious cardiovascular events (MACE)									
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	1 (0.5)	0.33	167	0	--	229	1 (0.4)	0.19

Category Period	CZP 200mg Q2W			CZP 400mg Q2W			All CZP		
	N	n (%)	IR	N	n (%)	IR	N	n (%)	IR
Serious bleeding events									
Combined Initial, Maintenance, and Open-label (Weeks 0 to 144) [b]	188	1 (0.5)	0.33	167	0	--	229	1 (0.4)	0.19

CZP=certolizumab pegol; IR=incidence rate; MACE=major adverse cardiac event; Q2W=every 2 weeks; SAE=serious adverse event; TEAE=treatment-emergent adverse event

[a] Analyzed for Safety Set.
[b] Analyzed for the Treated with CZP Set.
[c] Analyzed for the Open-label Set.

Conclusions:

Treatment with CZP 200mg Q2W and CZP 400mg Q2W resulted in clinically meaningful and statistically significant improvements in PSO area and severity, global physician-assessment of disease activity, and patients' HRQoL through 16 weeks of treatment, and these improvements were, at a minimum, consistently maintained through Week 48 and continued to be maintained through Week 144.

Overall, these results demonstrate that efficacy is maintained while receiving continuous CZP 200mg Q2W treatment for up to 3 years. Based on the dose-down study design, full 3-year exposure to CZP 400mg Q2W is not available in this study; however, maintenance of efficacy has been shown for continuous open-label CZP 400mg Q2W treatment for up to ~2.5 years (ie, based on CZP 400mg Q2W exposure in the Escape CZP 400mg Q2W/CZP 400mg Q2W group).

For subjects receiving CZP 400mg Q2W who dosed down to CZP 200mg Q2W, some decline in the clinical response was observed over time for some subjects; however, durability of efficacy response was observed in a subset of subjects who were PASI75 responders at Week 48 (ie, nonadjusters). Further exploration is needed to identify who may require continuous CZP 400mg Q2W treatment.

The safety profile for CZP in subjects with moderate to severe chronic plaque PSO in PS0005 was similar to that observed in previous studies with CZP and was consistent with that expected in subjects receiving anti-TNFα therapy. No notable differences were observed in the safety profile between CZP 200mg Q2W and CZP 400mg Q2W, with no apparent dose response over long-term CZP exposure. No new safety signals have been identified following CZP treatment for up to 144 weeks.

Overall, considering both efficacy and safety results, this study demonstrated a positive benefit-risk balance of CZP treatment with CZP 200mg Q2W and CZP 400mg Q2W in subjects with moderate to severe PSO.

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