

CLINICAL STUDY REPORT SYNOPSIS: PSA001

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| Name of company: UCB BIOSCIENCES GmbH | Individual study table referring to part of the dossier: Not applicable | <i>(For National Authority Use Only)</i> |
| Name of finished product: Cimzia | Volume: Not applicable | |
| Name of active ingredient: Certolizumab pegol | Page: Not applicable | |
| Title of study: Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Certolizumab Pegol in Subjects with Adult-Onset Active and Progressive Psoriatic Arthritis (PsA) | | |
| Investigators: 92 centers enrolled subjects | | |
| Study sites: This was a multicenter study involving 92 sites located in [REDACTED] and [REDACTED] | | |
| Publication(s) (reference[s]): none | | |
| Studied period: 2001 days First subject enrolled: 02 Mar 2010 Last subject completed date: 24 Aug 2015 | | Phase of development: Phase 3 |
| <p>Objectives: The primary objectives of the study were to demonstrate the efficacy of certolizumab pegol (CZP) administered subcutaneously (sc) at the dose of 200mg every 2 weeks (Q2W) or 400mg every 4 weeks (Q4W) after loading with 400mg at Weeks 0, 2, and 4 on the signs and symptoms of active PsA and on the inhibition of progression of structural damage in adults with active PsA.</p> <p>The secondary objectives of the study were to assess the effects on safety and tolerability and to demonstrate the effects of CZP on:</p> <ul style="list-style-type: none"> • Health outcomes • Psoriatic skin disease in the subgroup of affected subjects (>3% body surface area [BSA]) at Baseline • Dactylitis in all subjects and the subgroup of subjects with dactylitis at Baseline • Enthesitis in the subgroup of subjects with enthesitis at Baseline • Axial involvement in the subgroup of affected subjects (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] \geq4) at Baseline | | |

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| <p>The other objectives of the study were to assess the effect of CZP treatment on:</p> <ul style="list-style-type: none"> • Psoriatic nail disease in the subgroup of subjects with psoriatic nail disease at Baseline • Direct medical resources utilization • Subject's health status • Disease Activity Score-28 joint count (DAS28) | | |
| <p>Methodology: This was a 3-part study in subjects with adult-onset active PsA consisting of a 24-week Double-Blind Treatment Period followed by a 24-week Dose-Blind Treatment Period and then a 156-week Open-Label Treatment Period. This final report provides an evaluation of efficacy and safety results from the combined Double-Blind, Dose-Blind, and Open-Label Treatment Periods. During the Dose-Blind Treatment Period, subjects originally randomized to CZP treatment continued to receive the same treatment regimen. Subjects originally randomized to placebo and not rerandomized to escape treatment on Week 16 were rerandomized in a 1:1 ratio to receive 3 loading doses of CZP 400mg at Weeks 24, 26, and 28 followed by either CZP 200mg Q2W from Week 30 onward or CZP 400mg Q4W from Week 32 onward. Study treatments (including placebo) were administered by dedicated, unblinded, trained study center personnel from Weeks 0 to 28; subjects then self-administered study medication at home Q4W starting from Week 30.</p> <p>After the completion of the Open-Label Treatment Period of the last subject, the database was locked, and the final clinical study report (CSR; this report) was written.</p> | | |
| <p>Number of subjects (planned and analyzed): The planned number of subjects was 130 subjects per treatment group. The actual number of subjects analyzed was 138 subjects in the Week 0 (Wk0) CZP 200mg Q2W group, 135 subjects in the Wk0 CZP 400mg Q4W group, 198 subjects in the All CZP 200mg Q2W group, and 195 subjects in the All CZP 400mg Q4W group.</p> | | |

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| <p>Diagnosis and main criteria for inclusion: This study included adult subjects, male and females, ≥ 18 years of age, with a diagnosis of adult-onset active PsA of at least 6 months duration who had failed 1 or more disease-modifying antirheumatic drug (DMARDs). Subjects must not have received any nonbiological therapy for PsA within or outside a clinical study in the 3 months or within 5 half-lives prior to Baseline (whichever was longer). Subjects may not have been exposed to more than 1 tumor necrosis factor alpha (TNFα) antagonist prior to the Baseline Visit and may not have been a primary failure to any TNFα antagonist therapy (defined as no response within the first 12 weeks of treatment with the TNFα antagonist). Subjects with active infections, high risk of infections, or a recent vaccination were excluded.</p> | | |
| <p>Test product, doses and mode of administration, batch numbers: Certolizumab pegol was supplied as a sterile, clear, and 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 1/2-inch thin-wall needle for sc injection. Each syringe contained an extractable volume of 1mL at a concentration of 200mg/mL of CZP in 10mM sodium acetate buffer and 125mM sodium chloride as a tonicity agent.</p> <p>Injections were given sc in the lateral abdominal wall or upper outer thigh. During each dosing visit, if 2 injections were being administered (ie, CZP 400mg as 2 injections of 200mg each, CZP 200mg as 1 injection of CZP and 1 injection of placebo, or placebo as 2 injections of saline) each of the 2 injections were to be administered at a separate injection site.</p> <p>Batch numbers: [REDACTED]</p> | | |
| <p>Duration of treatment: up to 216 weeks (this final CSR covers the Double-Blind, Dose-Blind, and Open-Label Treatment Periods)</p> | | |
| <p>Reference therapy, dose, and mode of administration, batch numbers: Placebo was supplied in a PFS with a 25G 1/2-inch thin-wall needle, containing an injectable volume of 1mL 0.9% saline for single use. Injections were given sc in the lateral abdominal wall or upper outer thigh.</p> <p>Batch numbers: [REDACTED]</p> | | |

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| <p>Criteria for evaluation:</p> <p>Only measurements for assessment of efficacy variables in the combined Treatment Period (ie, including the Double-Blind, Dose-Blind, and Open-Label Treatment Periods through Week 216) are described in this final CSR. The variables up to Weeks 24 and 48 were included in the analysis of the Double-Blind and Dose-Blind Treatment Periods, which were reported in the first and second interim CSRs, respectively; these variables are included mainly to support the interpretation of the outcomes from the combined Treatment Period and are displayed in italics.</p> <p>Efficacy: There were 2 primary efficacy variables:</p> <ul style="list-style-type: none"> • <i>American College of Rheumatology 20% response criteria (ACR20) responder at Week 12</i> • <i>Change from Baseline in modified total Sharp score (mTSS) at Week 24</i> <p>The key secondary variables included:</p> <ul style="list-style-type: none"> • <i>ACR20 responder at Week 24</i> • <i>Change from Baseline in Health Assessment Questionnaire–Disability Index (HAQ-DI) at Week 24</i> • <i>Change from Baseline in mTSS at Week 48</i> • <i>Psoriasis Area and Severity Index 75% response (PASI75) responder at Week 24</i> <p>Other secondary efficacy variables included:</p> <ul style="list-style-type: none"> • <i>ACR20 responder at Weeks 1, 2, 4, 8, 16, 18, 20, and 24</i> • <i>American College of Rheumatology 50% response criteria (ACR50) responder at Weeks 1, 2, 4, 8, 12, 16, 18, 20, and 24</i> • <i>American College of Rheumatology 70% response criteria (ACR70) responder at Weeks 1, 2, 4, 8, 12, 16, 18, 20, and 24</i> • <i>Change from Baseline in all individual ACR core components at Weeks 1, 2, 4, 8, 12, 16, 18, 20, and 24</i> <ul style="list-style-type: none"> – <i>Swollen joint count (66 joints)</i> – <i>Tender joint count (68 joints)</i> – <i>HAQ-DI (except for Week 24, which is a key secondary variable)</i> | | |

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| <ul style="list-style-type: none"> - <i>Patient's Assessment of Arthritis Pain (PtAAP)-visual analog scale (VAS)</i> - <i>Patient's Global Assessment of Disease Activity (PtGADA)-VAS</i> - <i>Physician's Global Assessment of Disease Activity (PhGADA)-VAS</i> - <i>C-reactive protein (CRP)</i> • <i>Change from Baseline in HAQ-DI at Week 48</i> • <i>Change from Baseline in mTSS at Weeks 12, 96, 168, and 216</i> • <i>mTSS responder at Weeks 24 and 48</i> • <i>Change from Baseline in the erosion score of mTSS at Weeks 12, 24, 48, 96, 168, and 216</i> • <i>Change from Baseline in the joint space narrowing (JSN) score of mTSS at Weeks 12, 24, 48, 96, 168, and 216</i> • <i>PASI75 responder at Weeks 1, 2, 4, and 12 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline</i> • <i>Psoriasis Area and Severity Index 90% response (PASI90) responder at Weeks 1, 2, 4, 12, and 24 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline</i> • <i>Physician's Global Assessment of Psoriasis (PhGAP) responder at Weeks 12 and 24 in the subgroup of subjects with PSO involving at least 3% BSA at Baseline</i> • <i>Changes from Baseline in Leeds Dactylitis Index (LDI) at Weeks 12 and 24 for subjects with dactylitis at Baseline</i> • <i>Change from Baseline in the Leeds Enthesitis Index (LEI) at Weeks 12 and 24 for subjects with enthesitis at Baseline</i> • <i>Change from Baseline in the Fatigue Assessment Scale (FASCA) at Weeks 12 and 24</i> • <i>Change from Baseline in Short-Form 36-item Health Survey (SF-36) Physical Component Summary (PCS) at Weeks 4, 8, 12, 16, 20, 24, 28, 36, and 48</i> • <i>Change from Baseline in SF-36 Physical Function domain Weeks 4, 8, 12, 16, 20, 24, 28, 36, and 48</i> • <i>Change from Baseline in SF-36 Mental Component Summary (MCS) at Weeks 4, 12, and 24</i> • <i>Change from Baseline in Psoriatic Arthritis Quality of Life (PsAQoL) at Weeks 12 and 24</i> | | |

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| <ul style="list-style-type: none"> • <i>Change from Baseline in BASDAI at Weeks 1, 2, 4, 8, 12, 16, 18, 20, 24, 26, 28, 36, and 48 in all subjects and in the subgroup of subjects with BASDAI Q2 ≥4 at Baseline</i> • <i>BASDAI 50% response criteria (BASDAI50) at Weeks 1, 2, 4, 8, 12, 16, 18, 20, 24, 26, 28, 36, and 48 in all subjects and in the subgroup of subjects with BASDAI Q2 ≥4 at Baseline</i> • <i>Scores of individual questions of the Work Productivity Survey (WPS) at Weeks 4, 12, and 24</i> <p>Other efficacy variables included:</p> <ul style="list-style-type: none"> • ACR20 responder at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • ACR50 responder at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • ACR70 responder at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 | | |

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| <ul style="list-style-type: none"> • Change from Baseline in all individual ACR core components at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216: <ul style="list-style-type: none"> – Swollen joint count (66 joints) – Tender joint count (68 joints) – HAQ-DI – PtAAP – PtGADA-VAS – PhGADA-VAS • HAQ-DI responder at Weeks 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 24, 28, 32, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • PtAAP responder at Weeks 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 24, 26, 28, 32, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • PtGADA-VAS responder at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • Change from Baseline in CRP at Weeks 6, 10, 14, 26, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • mTSS response rate at Weeks 96, 168, and 216 • PASI75 responder at Weeks 8, 16, 20, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • PASI90 responder at Weeks 8, 16, 20, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline | | |

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| <ul style="list-style-type: none"> • PhGAP response (by category) at Weeks 1, 2, 4, 8, 16, 20, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • Change from Baseline in the LDI at Weeks 1, 2, 4, 8, 16, 20, 28, 36, 48, 60, 72, 80, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 for subjects with dactylitis at Baseline • Change from Baseline in the LEI at Weeks 1, 2, 4, 8, 16, 20, 28, 36, 48, 60, 72, 80, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 for subjects with enthesitis at Baseline • Change from Baseline in the FASCA at Weeks 1, 2, 4, 6, 8, 10, 16, 18, 20, 26, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • FASCA responder at Weeks 1, 2, 4, 6, 8, 10, 12, 16, 18, 20, 24, 26, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in SF-36 (PCS) at Weeks 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • SF-36 (PCS) responder at Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in SF-36 Physical Function domain at Weeks 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in SF-36 (MCS) at Weeks 8, 16, 20, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • SF-36 (MCS) responder at Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in SF-36 domains at Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in PsAQoL at Weeks 1, 2, 4, 8, 16, 18, 20, 26, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in BASDAI at Weeks 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in all subjects and in the subgroup of subjects with BASDAI Q2 \geq 4 at Baseline | | |

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| <ul style="list-style-type: none"> • BASDAI50 responder at Weeks 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in all subjects and in the subgroup of subjects with BASDAI Q2\geq 4 at Baseline • Scores of the individual questions of the WPS at Weeks 8, 16, 20, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • Psoriatic Arthritis Response Criteria (PsARC) responder at Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • DAS28(CRP) at Weeks 1, 2, 4, 8, 12, 16, 18, 20, 24, 26, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216: <ul style="list-style-type: none"> – Change from Baseline – Disease activity classification – European League Against Rheumatism (EULAR) response • DAS28(CRP) Low Disease Activity (LDA)/Remission at Week 1, 2, 4, 8, 12, 16, 18, 20, 24, 26, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • <i>Escape criteria fulfilled (yes/no)</i> • Resources utilization: concomitant medical procedures, health care provider consultations not foreseen by the protocol, hospitalizations, and emergency room visits • EuroQoL Health Status Questionnaire (EQ-5D-3L) dimensions at Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in EQ-5D-3L VAS Score at Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Change from Baseline in psoriatic BSA (%) at Weeks 12, 16, 24, 48, 96, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • Change from Baseline in PASI at Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • PASI50 responder and PASI100 responder at Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup | | |

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| <p>of subjects with psoriasis involving at least 3% BSA at Baseline</p> <ul style="list-style-type: none"> • PASI100 responder at Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • Change from Baseline in Dermatology Life Quality Index (DLQI) at Weeks 2, 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in all subjects and in the subgroup of subjects with psoriasis involving at least 3% BSA at Baseline • Change from Baseline in modified Nail Psoriasis Severity Index (mNAPSI) score at Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 in the subgroup of subjects with nail disease at Baseline • Socioprofessional status at Baseline, and Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 168, 180, 192, 204, and 216 • Number of digits affected by dactylitis at Baseline, Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Presence of dactylitis at Baseline, Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, and 216 • Minimal disease activity at Baseline, Weeks 12, 16, 24, 48, 96, 156, 168, 180, 192, 204, and 216 | | |
| <p>Pharmacokinetics/pharmacodynamics: Plasma samples for the measurement of CZP concentrations were taken at Baseline; Weeks 1, 2, 4, 12, 16, 24, and thereafter every 24 weeks through to study Completion/Withdrawal Visit; Early Withdrawal; and the Safety Follow-Up Visit 10 weeks after the last dose of study medication.</p> | | |

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| <p>Immunology: Plasma samples for the measurement of anti-CZP antibodies were taken at Baseline; Weeks 1, 2, 4, 12, 16, 24, and thereafter every 24 weeks through to study Completion/Withdrawal Visit; Early Withdrawal; and the Safety Follow-Up Visit 10 weeks after the last dose of study medication.</p> <p>Safety: Safety variables to be assessed were:</p> <ul style="list-style-type: none"> • Adverse events (AEs) • Laboratory parameters (chemistry, hematology, and urinalysis) • Vital signs (blood pressure, pulse, respiration rate, and temperature) • Other: weight and tuberculosis (TB) testing (chest x-ray and purified protein derivative [PPD] testing) | | |
| <p>Statistical methods:</p> <p>For quantitative data in general, summary statistics (n [number of available measurements], arithmetic mean, standard deviation [SD], median, minimum, and maximum) were presented by treatment group. For selected variables also quartiles (Q1 and Q3) were presented. Mean, SD, and median were displayed to 1 more decimal place than collected in the case report form or than the rounded calculated variable.</p> <p>For descriptive statistics of continuous variables, change from Baseline and the actual value at each time point itself were displayed.</p> <p>Frequency tables (frequency counts and percentages) were presented for categorical data. If there were missing values, either a missing category was included in the display or the number of nonmissing results was used for calculations.</p> <p>In case imputation was performed, summary statistics did not utilize the “n” (number of available measurements).</p> <p>In general, percentages were calculated based on the utilized analysis set; however, in case only subsets were affected, the N of the subset was used as denominator (eg, suspected axial involvement, psoriatic BSA).</p> <p>Unless stated otherwise, all statistical tests were 2-sided and conducted at the 0.05 alpha level. All exploratory statistical testing was done applying the same figures. P-values were presented to 3 decimal places.</p> <p>The Open-Label Treatment Period began at the Week 48 Visit, at the time of first open-label study medication administration (inclusive) and ended at the Week 216 Visit. For subjects early</p> | | |

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terminating, the Safety Follow-Up Visit represented the end of the Open-Label Treatment Period, and the last non-Safety Follow-Up Visit (ie, Withdrawal Visit) was used for the end of Open-Label Treatment Period measurements.

The study protocol had 6 subject sets for analyses: Enrolled Set (ES), Randomized Set (RS), Full Analysis Set (FAS), Per-Protocol Set (PPS), and 2 different Completer Sets (CS) (First Completer Set [CS1] and Second Completer Set [CS2]). Not all these analysis sets are relevant for the objectives and scope of the Open-Label Treatment Period analyses.

All the efficacy analyses were descriptive and do not compare CZP groups to placebo. In general, descriptive analyses were presented with all randomized subjects. Tables relating to primary and key secondary endpoints were repeated in all subjects that entered the Open-Label Treatment Period (Open-Label Set [OLS]). The safety analyses were based on the set of subjects treated with CZP (using the Treated with CZP Set [TCS]).

Summary and conclusions:

Subject disposition: At Week 0, a total of 273 subjects were randomized to CZP (138 subjects to the CZP 200mg Q2W group and 135 subjects to the CZP 400mg Q4W group), and 136 subjects were randomized to placebo. Of the 136 subjects who were randomized to placebo, 120 subjects completed the Double-Blind Treatment Period and switched to CZP at either Week 16 or 24; this resulted in 60 subjects each who were re-randomized to either the CZP 200mg Q2W group or the CZP 400mg Q4W group. By the end of the study, a total of 198 subjects received CZP 200mg Q2W and a total of 195 subjects received CZP 400mg Q4W.

A total of 368 subjects (90.0%) completed the Double-Blind Treatment Period (up to Week 24) and entered the Dose-Blind Treatment Period. A total of 350 subjects (85.6%) completed the Dose-Blind Treatment Period (up to Week 48) and entered the Open-Label Treatment Period; a total of 264 subjects (64.5%) completed the Open-Label Treatment Period.

Of the 393 subjects randomized to the All CZP Treatment Group (ie, all subjects who received CZP in either the Double-Blind, Dose-Blind, or Open-Label Periods), 129 subjects (32.8%) discontinued over the combined Treatment Period (ie, Weeks 0 to 216). The most common reasons for discontinuation were AEs (13.2%) and consent withdrawn (9.9%).

Efficacy results:

Primary and key secondary efficacy variables

The results of the primary analysis for ACR20 responders at Week 12 were robust and demonstrated the efficacy of CZP for the treatment of signs and symptoms in subjects with active PsA. Clinically meaningful results were obtained for the change from Baseline in mTSS at Week 24 that demonstrated the inhibition of the progression of structural damage. Moreover, the

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results showed CZP to have consistent and clinically relevant efficacy across subgroups. All secondary analyses supported the primary analysis.

The results of the key secondary analyses were also robust and demonstrated the efficacy of CZP for the treatment of signs and symptoms (ACR20 responders at Week 24), improvement in physical function (change from Baseline in HAQ-DI at Week 24), and improvement of skin manifestations of PsA (PASI75 responder at Week 24) in subjects with active PsA. The progression of structural damage was inhibited in CZP-treated subjects up to 48 weeks compared with placebo in subjects with structural damage at Baseline (mTSS >6).

Long-term inhibition of structural damage progression

Low or no progression of structural damage was observed in the All CZP group (as measured by mean change from Baseline in mTSS) at Weeks 96, 168, and 216 using the RS (OC) and mixed effect models for repeated measures (MMRM) analysis using the RS. The majority of subjects ($\geq 70.5\%$ in the All CZP group) were mTSS responders from Weeks 96 to 216. The annualized rate of radiographic progression while on CZP treatment was minimal (0.09 points per 48 weeks); this annualized rate of radiographic progression is lower than the rate extrapolated for adalimumab (0.4 to 0.5 points per 48 weeks) in a 10-year follow-up study on subjects with rheumatoid arthritis (RA) (Landewe et al, 2015).

Changes from Baseline in the erosion score and JSN through Week 216 were minimal, indicating that long-term (up to 216 weeks) CZP treatment stabilized or slowed further joint erosion and JSN in subjects with active PsA who remained in the study.

Taken together, these results indicate that the efficacy of CZP treatment in inhibiting the progression of structural damage in subjects with active PsA, who remained in the study, was sustained with long-term (up to 216 weeks) CZP treatment.

Long-term treatment of signs and symptoms

The percentage of ACR20 responders in the All CZP group using OC data increased from Baseline to Week 48 (77.9%) and was maintained through Week 216 (83.1%); similar trends were seen for the percentage of ACR50 and ACR70 responders. All improvements in ACR components from Baseline that were achieved at Week 48 were maintained through Week 216.

Additional assessments of CZP treatment on the signs and symptoms of PsA in the All CZP group using OC data included LDI, LEI, PsARC, DAS28(CRP), BASDAI, and minimal disease activity. Subjects treated with CZP achieved clinically meaningful decreases in LDI and the presence of dactylitis at Week 48 that were maintained through Week 216. Subjects treated with CZP also showed improvement in enthesitis at Week 48 that was maintained through Week 216. The majority of subjects (89.6%) achieved the PsA response criteria (as measured by PsARC),

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which quantifies improvements in PtGADA, PhGADA, swollen joint count (SJC), and tender joint count (TJC), at Week 48 and this was maintained through Week 216 (90.8%). The mean decrease (ie, improvement) from Baseline in DAS28[CRP] achieved at Week 48 was maintained through Week 216 (-2.18 points and -2.58 points, respectively). The percentage of subjects with a EULAR response of “good” achieved at Week 48 was maintained through Week 216 (64.1% and 74.6%, respectively). The percentage of subjects with minimal disease activity achieved at Week 48 was maintained through Week 216 (44.4% and 58.1%, respectively). Subjects with suspected axial involvement at Baseline achieved a mean improvement in BASDAI at Week 48 that was maintained through Week 216 (-2.71 points and -2.96 points, respectively) and the mean increase in the percentage of BASDAI50 responders achieved at Week 48 was also maintained through Week 216 (48.7% and 51.5%, respectively). Taken together, these OC observations indicate that the efficacy of CZP treatment in effectively reducing signs and symptoms of active PsA in subjects who remain in the study is sustained with long-term (up to 216 weeks) CZP treatment.

Multiple imputations were used in addition to no imputation (OC) to analyze these efficacy data. For categorical (responder-type) variables these results were also analyzed using nonresponder imputation (NRI) and, in the case of ACR responders, NRI/ Last Observation Carried Forward (LOCF) post-hoc hybrid imputation methods which both support the long-term efficacy observed using OC data. However, it should be noted that the percentage of ACR20 and PsARC responders exhibited a decreasing trend (>10%) from Week 48 to Week 216 using NRI; this decreasing trend was ameliorated for ACR20 using the NRI/LOCF hybrid imputation method.

Long-term improvement in physical function and health-related outcomes

Subjects treated with CZP had relief of pain (PtAAP) and tiredness/fatigue (FASCA) and reduction in their disease activity (PhGADA and PtGADA). These improvements were clinically meaningful and improvements achieved at Week 48 were maintained through Week 216. CZP-treated subjects also had improvements in physical function (HAQ-DI, SF-36 PCS, and SF-36 Physical Functioning domain) that were maintained through Week 216.

Improvements in health-related quality of life achieved by Week 48 in CZP-treated subjects, as measured by both PsA-specific and psoriasis-specific measures (PsAQoL and DLQI) and by generic measures (SF-36 PCS, SF-36 MCS, and all domains) maintained through Week 216. Increased productivity within and outside the home (WPS) achieved at Week 48 were also maintained through Week 216.

Taken together, these observations indicate that the efficacy of CZP treatment in improving physical function and health-related outcomes in subjects with active PsA who remain in the study is sustained with long-term (up to 216 weeks) CZP treatment.

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Multiple imputations were used in addition to no imputation (OC) to analyze these efficacy data. For categorical (responder-type) variables these results were also analyzed using NRI which supports the long-term efficacy observed using OC data.

Long-term effect on other patient-reported outcomes

Subjects receiving CZP also achieved improvements in outcomes measured by the EQ-5D-3L dimensions (mobility, self-care, pain/discomfort, anxiety/depression, and ability to perform usual activities) that were achieved at Week 48 and were maintained through Week 216. Based on questions regarding socioprofessional status, the percentage of subjects reporting no need for help in usual activities was also maintained through Week 216.

The majority of subjects did not have any hospitalizations or emergency room visits and approximately one-third of subjects had no concomitant medical procedures or additional healthcare provider consultations not foreseen by the protocol with onset during the combined Treatment Period (DB1+DB2+DB3). Although the percentage of subjects with hospitalizations, emergency room visits, concomitant medical procedures, and additional healthcare provider consultations not foreseen by the protocol increased from Week 48, this is not unexpected given the long-term (216 week) duration of this study.

Long-term skin effects

Clinically meaningful improvements with CZP treatment were observed in psoriasis area and severity (as measured by PASI). For subjects with at least 3% psoriasis BSA at Baseline, the percentage of PASI50 responders in the All CZP group using OC data achieved at Week 48 was maintained through Week 216 (92.5% and 90.1%, respectively). Similar trends were observed for the percentage of PASI75, PASI90, and PASI100 responders. Improvements in psoriatic BSA achieved at Week 48 were also maintained through Week 216. The percentage of subjects whose psoriasis was rated as “clear” or “almost clear” (PhGAP responder) at Week 48 was maintained through Week 216 (84.9% and 77.5%, respectively). Improvements in psoriatic nail disease (mNAPSI) achieved at Week 48 was maintained through Week 216 (-2.3 points and -2.9 points, respectively).

Taken together, these observations indicate that the efficacy of CZP treatment in improving the skin effects of psoriasis for the subgroup of subjects with psoriasis, involving at least 3% BSA at Baseline who remain in the study, is sustained with long-term (up to 216 weeks) CZP treatment.

Multiple imputations were used in addition to no imputation (OC) to analyze these efficacy data. For categorical (responder-type) variables these results were also analyzed using NRI which supports the long-term efficacy observed using OC data.

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| Name of active ingredient: Certolizumab pegol | Page: Not applicable | |
| <i>Subgroup analyses of the change from Baseline in mTSS</i> | | |
| <p>No differences in mTSS progression or mTSS responders through Week 216 were observed based on baseline mTSS score or baseline CRP in subjects originally randomized to CZP or placebo.</p> | | |
| <i>Subgroup analysis of ACR20, ACR50, and ACR70 responders</i> | | |
| <p>No difference in ACR20, ACR50, or ACR70 responders through Week 216 was observed based on duration of disease, concomitant use of allowed DMARDs at Baseline, prior use of sDMARDs, prior anti-TNFα therapy, Baseline CRP values, or anti-CZP antibody status in the All CZP group. Differences were observed in ACR responders based on age and gender. The percentage of ACR20, ACR50, and ACR70 responders was consistently greater in younger subjects (<45 years) and males compared with older subjects (\geq45 years) and females.</p> | | |
| <i>Subgroup analysis of change from Baseline in HAQ-DI</i> | | |
| <p>No difference in the change from Baseline in HAQ-DI through Week 216 was observed based on age, gender, duration of disease, geographic region, concomitant use of allowed DMARDs at Baseline, prior use of sDMARDs, prior TNFα therapy, or anti-CZP antibody status in the All CZP group.</p> | | |
| <i>Overall long-term efficacy conclusions</i> | | |
| <p>In summary, these results indicate that the improvement of signs and symptoms of PsA (including enthesitis, patient and physician assessment of disease activity, SJC, TJC, and disease activity), improvement in physical function and health-related outcomes (including relief of pain and tiredness/fatigue and improvement in workplace and household productivity and HRQoL), and improvement of skin and nail manifestations within the first 6 months of treatment were sustained with long-term (up to 216 weeks) CZP treatment.</p> | | |
| Pharmacokinetics/pharmacodynamics results: | | |
| <ul style="list-style-type: none"> • As expected, the CZP plasma trough concentrations from Week 12 to Week 216 were lower in the subjects treated with CZP 400mg Q4W compared with subjects treated with CZP 200mg Q2W because of the longer dose interval. • Subjects who were positive for anti-CZP antibodies had lower mean (geometric) CZP plasma trough concentrations between Week 12 and 216 compared with subjects who were negative for anti-CZP antibodies; similar trends were observed between the 2 dosing regimens. | | |

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| Immunology results: <ul style="list-style-type: none"> • During the combined Treatment Period (DB1+DB2+DB3) the overall percentage of subjects who were anti-CZP antibody positive was 17.3% (68 of 393 subjects) in combining both All CZP groups; 17.7% (35 of 198 subjects) in the All CZP 200mg Q2W group and 16.9% (33 of 195 subjects) in the All CZP 400mg Q4W group. • However, there was no difference in ACR20, ACR50, or ACR70 responders or change from Baseline in HAQ-DI based on anti-CZP antibody status. • The first occurrence of anti-CZP antibodies was most frequent at Week 12 in the Wk0 CZP 200mg Q2W group and the Wk0 CZP 400mg Q4W group (6.5% [9 of 138 subjects] and 8.1% [11 of 135 subjects], respectively). • Concomitant DMARD use at Baseline did not appear to affect the first occurrence of anti-CZP antibodies or the overall anti-CZP antibody status for either dosing regimen. • Of the 68 anti-CZP antibody positive subjects in the All CZP group, equal numbers showed transient and persistent anti-CZP antibody responses; 8.7% (34 of 393 subjects) in the All CZP treatment group had transient appearance of antibodies and 8.7% (34 of 393 subjects) had persistent appearance of anti-CZP antibodies. • The overall percentage of subjects who were anti-CZP antibody positive with a persistent reduction in CZP plasma trough concentrations was estimated to be 11.5% (45 of 393 subjects). | | |
| Safety results: Exposure A total of 198 subjects received CZP 200mg Q2W and 195 subjects received CZP 400mg Q4W. The median number of doses received was 100.0 for the All CZP 200mg Q2W group and 51.0 for the All CZP 400mg Q4W group. The median duration of exposure as determined in the narrow sense (ie, last injection date–first injection date+14 [or+28] days) was 195.0 weeks for the All CZP 200mg Q2W group and 194.9 weeks for the All CZP 400mg Q4W group. The patient-years (pt-yrs) of exposure for the All CZP group was 1320.8 pt-yrs; 674.4 pt-yrs for the All CZP 200mg Q2W group and 646.4 pt-yrs for the All CZP 400mg Q4W group. Adverse events The incidence of treatment-emergent adverse events (TEAEs) was 93.4% (IR=161.9 per 100 pt-yrs) in the All CZP group. The most commonly reported TEAEs (by PT) in the All CZP | | |

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group were upper respiratory tract infection (23.7% [IR=8.5 per 100 pt-yrs]) and nasopharyngitis (22.1% [IR=8.0 per 100 pt-yrs]). The incidence of severe TEAEs was 18.1% in the All CZP group. The incidence of TEAEs leading to permanent study medication discontinuation was 13.7% in the All CZP group. Most severe TEAEs and TEAEs that led to permanent study medication discontinuation were reported by <2.0% of subjects.

The incidence of drug-related TEAEs was 50.6% in the All CZP group. The most commonly reported drug-related TEAEs (by preferred term [PT]) in the All CZP group were upper respiratory tract infection (7.9%), nasopharyngitis (7.4%), pharyngitis (6.4%), and bronchitis (5.9%).

The incidence of serious adverse events (SAEs) was 25.4% (IR=8.7 per 100 pt-yrs) in the All CZP group. The most common SAE (by PT) in the All CZP group was psoriatic arthropathy (2.0% [IR=0.6 per 100 pt-yrs]); all other SAEs (by PT) were reported by ≤1% of subjects.

Six deaths were reported during the combined Treatment Period (DB1+DB2+DB3); 2 subjects died during the Double-Blind Treatment Period (cardiac arrest and sudden death), 1 subject died during the Dose-Blind Period (breast cancer) and 3 subjects died during the Open-Label Period (pneumonia and sepsis, myocardial infarction, and lymphoma). Only the fatal TEAEs pneumonia and sepsis (both reported in 1 subject) were considered related to study medication.

The incidence of TEAEs in subjects who were anti-CZP antibody positive was similar to the incidence in subjects who were anti-CZP negative (91.2% and 93.8%, respectively); incidences of severe TEAEs, drug-related TEAEs, SAEs, discontinuation due to TEAEs, and death were also similar regardless of anti-CZP antibody status.

There were 3 pregnancies reported by female subjects and 2 pregnancies of male partners reported during the study. One pregnancy by the subject was carried full-term with no birth defects and the outcomes of the other 2 pregnancies are unknown despite repeated attempts by the Investigator to follow up with these subjects. One partner pregnancy was carried full-term with no birth defects and the other partner pregnancy was spontaneously aborted at 10 weeks gestation; no follow-up information could be obtained.

Adverse events of interest

Anti-TNFα medications carry an increased risk of infections. The incidence of TEAEs in the Infections and infestations system organ class (SOC) was 75.1% in the All CZP group.

The incidences of opportunistic and serious infections were low (0.5% [IR=0.2 per 100 pt-yrs] and 5.9% [IR=1.8 per 100 pt-yrs], respectively) in the All CZP group. There were no rare infections reported over the combined Treatment Period (DB1+DB2+DB3). All opportunistic infections (by PT) were reported for ≤1 subject and had an incidence of <1.0%. Of the

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29 subjects who had TEAEs related to TB (PTs of mycobacterium TB complex test positive, latent TB, immunology test, and tuberculin test positive), only 1 subject had a serious TB-related TEAE; there were no subjects with confirmed TB.

Malignancies were rare during the combined Treatment Period (DB1+DB2+DB3); a total of 7 subjects (1.8% [IR=0.5 per 100 pt-yrs]) in the All CZP group had any malignancy.

Subjects in this study, like the general population of PsA patients (Husted et al, 2011; Gladman et al, 2009), had high cardiovascular comorbidity. The incidence of cardiac events (ie, TEAEs in the Cardiac disorders SOC) was low in the All CZP group (5.1% [IR=1.6 per 100 pt-yrs]); there were no events of or related to congestive heart failure. The incidence of vascular events (ie, TEAEs in the Vascular disorders SOC) was 16.5% (IR=5.6 per 100 pt-yrs) in the All CZP group. Hypertension (including new onset or worsening of hypertension), which was reported in the medical history of 33.5% of all subjects, was the most commonly reported vascular event (46 subjects; 11.7% [IR=3.8 per 100 pt-yrs] in the All CZP group). Serious cardiovascular events in subjects receiving CZP included coronary artery thrombosis, myocardial infarction, acute myocardial infarction, cerebrovascular accident, and transient ischemic attack.

Hepatic disorders were typically related to liver function parameters, particularly alanine aminotransferase (ALT) increased (8.1% [IR=2.6 per 100 pt-yrs]), aspartate aminotransferase (AST) increased (5.1% [IR=1.6 per 100 pt-yrs]), and gamma-glutamyltransferase (GGT) increased (5.1% [IR=1.6 per 100 pt-yrs]); in most instances, these events were for elevations of <2x upper limit of normal (ULN). The incidence of treatment-emergent hepatic disorder TEAEs was 17.3% (IR=6.0 per 100 pt-yrs) in the All CZP group. The incidence of drug-related hepatic disorder TEAEs was not affected by Baseline weight or use of concomitant DMARDs at Baseline.

There were no TEAEs suggestive of demyelinating disorders or notable neurological SAEs reported during the 48-week combined Double-Blind and Dose-Blind Treatment Period. There were 3 subjects who had TEAEs of autoimmune disorders (lupus-like syndrome, pustular psoriasis, and Crohn's disease; only lupus-like syndrome was considered related to study medication. There were 4 subjects who had serious bleeding events (hematoma, uterine hemorrhage, haemoptysis, and metrorrhagia); all 4 events were considered serious and none were considered related to study medication. Reports of leukopenia, neutropenia, and thrombocytopenia were rare (<3.0% each in the All CZP group); all of these events were nonserious and mild or moderate in intensity.

The incidence of acute systemic hypersensitivity injection reactions was low (0.8% [IR=0.2 per 100 pt-yrs]) in the All CZP group; all subjects with acute hypersensitivity injection reactions were in the All CZP 200mg Q2W group (1.5% [IR=0.4 per 100 pt-yrs]). The incidence of

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delayed systemic hypersensitivity injection reactions was low in the All CZP group (1.5% [IR=0.5 per 100 pt-yrs]). Injection site reaction was the most common local injection reaction, and the incidence was 2.0% (IR=0.6 per 100 pt-yrs) in the All CZP group.

Clinical laboratory evaluations and vital signs

Mean CRP values were elevated for the All CZP group at Screening and Baseline, which is expected in a population with active PsA. Notably, CZP treatment provided rapid and sustained improvement in CRP values, demonstrating improvement in systemic inflammation. Mean CRP values were within the normal range by Week 1 and remained within the normal range throughout the study.

During the combined Treatment Period (DB1+DB2+DB3), small mean increases from Baseline at Week 216 were observed for AST (3.4U/L) and ALT (2.4U/L) values in the All CZP group. The frequency of shifts from normal or low at Baseline to markedly elevated ($\geq 2xULN$) post-Baseline values (corresponding to the maximum post-Baseline value) for ALT and AST was low in CZP-treated subjects. Very high elevations ($\geq 10xULN$) of AST and ALT were observed in only 2 subjects (0.5%), both in the All CZP 200mg Q2W group; no elevations of AST or ALT were $\geq 20xULN$. Based on revised laboratory reference ranges, 1 subject fell within the category of bilirubin $\geq 2xULN$ and AST or ALT $\geq 3xULN$; the reported AE of Liver Enzyme Elevation in this subject was assessed as nonserious, moderate in intensity, and unlikely related to study drug. These results are consistent with other anti-TNF α medications (eg, infliximab [IFX] and adalimumab [ADA]), which have shown elevations in AST and ALT in patients with PsA.

The most common hematology parameters with shifts from Baseline to abnormal maximum/minimum post-Baseline values were shifts to high values for monocytes (38.8%) and shifts to low values for hematocrit (27.3%) and erythrocytes (22.7%). No subject had a markedly abnormal post-Baseline leukocyte value. The incidence of markedly abnormal hematology values in the All CZP group was low for hemoglobin, platelets, and neutrophils (<5% each); the incidence was 8.7% for lymphocytes but only 1 subject had a lymphocyte value of $< 500/\mu L$, which is the cutoff value for Rheumatology Common Toxicity Criteria (RCTC) Grade 3 provided in the Common Criteria for AEs (version 4.0). Similar to hematology parameters, markedly abnormal low values for lymphocytes were transient and returned to normal values spontaneously. Nine subjects had 10 infection-related TEAEs, 1 of which was serious (pneumonia), temporally associated (within ± 2 weeks) with a markedly abnormal low lymphocyte value. Lymphocyte counts for 8 of the 9 subjects returned to normal by the next study visit; lymphocyte count for 1 subject improved by the next study visit (Week 48). All of the infections resolved within a time frame that would be expected/reasonable.

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| No clinically meaningful adverse changes in biochemistry values, hematology values, urinalysis values, vital signs, or weight were observed. | | |
| <p>Overall safety conclusions</p> <p>During the combined Treatment Period (DB1+DB2+DB3) there were no new safety concerns, and long-term exposure did not increase the risk for AEs. The safety profile for patients with PsA treated with CZP for up to 216 weeks is consistent with the safety profile in RA and previous experience with CZP. Overall, most TEAEs were mild or moderate in intensity and were not described by the Investigator as drug-related. Overall, no safety signals were observed in biochemistry values, hematology values, urinalysis values, vital signs, or weight.</p> | | |
| <p>Conclusions:</p> <p>Certolizumab pegol 200mg Q2W and 400mg Q4W demonstrated robust improvement over 216 weeks in the treatment of signs and symptoms in subjects with active PsA who remained in the study. In addition, inhibition of the progression of structural damage was sustained with long-term (up to 216 weeks) CZP treatment in subjects with active PsA who remained in the study. There were no new safety concerns, and long-term exposure did not increase the risk for AEs. The safety profile for patients with PsA treated with CZP is consistent with the safety profile in RA and previous experience with CZP. Overall, considering both the efficacy and safety results, PsA001 demonstrated a positive benefit-risk ratio of CZP treatment in subjects with active PsA.</p> | | |
| <p>References:</p> <p>Gladman DD, Ang M, Su L, Tom BDM, Schentag CT, Farewell VT. Cardiovascular morbidity in psoriatic arthritis. <i>Ann Rheum Dis.</i> 2009;68:1131-5.</p> <p>Husted JA, Thavaneswaran A, Chandran V, Eder L, Rosen CF, Cook RJ, et al. Cardiovascular and other comorbidities in patients with psoriatic arthritis: a comparison with patients with psoriasis. <i>Arthritis Care and Res.</i> 2011;63(12):1729-35.</p> <p>Landewe R, Ostergaard M, Keystone EC, Florentinus S, Liu S, Van Der Heijde D. Analysis of Integrated Radiographic Data From Two Long-Term, Open-Label Extension Studies of Adalimumab for the Treatment of Rheumatoid Arthritis. 2015;67(2):180-6.</p> | | |
| <p>Report date: 19 Jul 2016</p> | | |