DOI: 10.1111/jdv.17486 JEADV

ORIGINAL ARTICLE

Three-year efficacy and safety of certolizumab pegol for the treatment of plaque psoriasis: results from the randomized phase 3 CIMPACT trial

R. B. Warren,[1,*] M. Lebwohl,[2] H. Sofen,[3] V. Piguet,[4,5] M. Augustin,[6] F. Brock,[7] C. Arendt,[8] F. Fierens,[8] A. Blauvelt[9]

[1]Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, The University of Manchester, Manchester, UK
[2]Icahn School of Medicine at Mount Sinai, New York, NY, USA
[3]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
[4]Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada
[5]Division of Dermatology, Department of Medicine, Women's College Hospital, Toronto, ON, Canada
[6]Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany
[7]UCB Pharma, Slough, UK
[8]UCB Pharma, Brussels, Belgium
[9]Oregon Medical Research Center, Portland, OR, USA
*Correspondence: R. B. Warren. E-mail: Richard.Warren@manchester.ac.uk

Abstract

Background Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-tumor necrosis factor biologic.

Objectives To report 3-year outcomes from the CIMPACT (NCT02346240) phase 3, CZP in moderate to severe plaque psoriasis, randomized controlled trial.

Methods Adults were randomized 3:3:3:1 to CZP 200 mg every other week (Q2W), CZP 400 mg Q2W, etanercept biweekly or placebo. At Week 16, CZP- and etanercept-treated PASI 75 responders were re-randomized to CZP 200 mg Q2W, CZP 400 mg Q4W, CZP 400 mg Q2W or placebo for maintenance treatment; PASI 75 non-responders entered an open-label escape CZP 400 mg Q2W arm. Patients entering the open-label extension (OLE; Weeks 48–144) from blinded treatment received CZP 200 mg Q2W.

Results Double-blinded results have been reported previously. 261 patients received 200 mg Q2W upon OLE entry. PASI 75 response was maintained in patients continuing 200 mg Q2W treatment through Weeks 16–144 (Week 144: 96.2%). In patients dosed down at Week 48 (double-blinded 400 mg to 200 mg Q2W), PASI 75 decreased (Week 48: 98.7%; Week 144: 85.9%). In patients who received placebo through Weeks 16–48, PASI 75 response decreased (Week 48: 60.4%), then increased following Week 48 switch to 200 mg Q2W (Week 144: 95.1%). 48 and 36 patients initially randomized to 200 and 400 mg Q2W, respectively, were Week 16 PASI 75 non-responders and entered the escape arm; at Week 144, 71.8% and 78.2% achieved PASI 75. No new safety signals were identified.

Conclusions Response to CZP was durable over three years; no new safety signals were identified.

Keywords: certolizumab pegol, clinical trial, long term, plaque psoriasis.
Received: 23 February 2021; revised: 21 May 2021; Accepted: 22 June 2021

Conflict of interest

RBW: Research grants and/or consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma. **ML:** Employee of Mount Sinai which receives research funds from AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, LEO Pharma, Ortho Dermatologics, Pfizer, and UCB Pharma; consultant for Aditum Bio, Allergan, Almirall, Arcutis, Avotres, BirchBioMed, BMD Skincare, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Evelo, Facilitate International Dermatologic Education, Foundation for Research and Education in Dermatology, Inozyme Pharma, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi Pharma, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Serono, Theravance, and Verrica. **HS:** Consulting fees from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira Inc., Eli Lilly, Janssen, Medimmune, Novartis, Pfizer, Sun

Pharma, UCB Pharma, and Valeant. **VP:** Consulting fees from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira Inc., Eli Lilly, Janssen, Medimmune, Novartis, Pfizer, Sun Pharma, UCB Pharma, and Valeant. **MA:** Consulting fees from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, GSK, Hexal, Janssen, LEO Pharma, Medac, Merck, MSD, Mundipharma, Novartis, Pfizer, Sandoz, UCB Pharma, and Xenoport. **FB, CA, FF:** Employees of UCB Pharma. **AB:** Served as a scientific adviser/clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte, Janssen, Landos, Leo, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma.

Funding

This study was funded by Dermira, Inc. in collaboration with UCB Pharma. UCB Pharma is the regulatory sponsor of certolizumab pegol in psoriasis. This article was based on the original study CIMPACT (NCT02346240) sponsored by Dermira, Inc. and UCB Pharma. Support for third-party writing assistance for this article, provided by Daniel Smith, of Costello Medical, Cambridge, UK, was funded by UCB Pharma in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Introduction

Plaque psoriasis (PSO) is an immune-mediated inflammatory disease that affects approximately 2–6% of adults in Western countries.[1–3] Biologic agents targeting tumor necrosis factor-alpha (TNF-α),[4] interleukin (IL)-12/23,[5] IL-23,[6] IL-17A[7] or IL-17RA[8] are now key to treatment.[9–12] PSO requires life-long management; therefore, it is important to understand long-term efficacy of treatments. Nearly half of patients discontinue treatment with their first biologic within three years.[13] Switching from one biologic to another has been associated with decreased efficacy.[14]

Certolizumab pegol (CZP) is an Fc-free, PEGylated, anti-TNF biologic approved for treatment of patients with moderate to severe PSO, as well as for rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis and Crohn's disease.[15,16] PEGylation increases the half-life of CZP to 14 days,[17] and because it is Fc-free, CZP does not bind to the neonatal Fc receptor for immunoglobulin G. Two prospective studies showed a lack of placental transfer of CZP from mothers to infants[18] and no to minimal transfer from plasma into breast milk.[19] Furthermore, a pharmacovigilance safety database analysis of pregnancy outcomes demonstrated no teratogenic effect of CZP compared to the general population in the US and EU, and no increased risk of fetal death.[20]

Efficacy of CZP in patients with moderate to severe PSO has been investigated in three phase 3 trials: CIMPASI-1 (NCT02326298), CIMPASI-2 (NCT02326272) and CIMPACT (NCT02346240).[21–23] Pooled three-year safety data from these trials, totalling 995 patients and 2231.3 patient-years (PY) of exposure, found no new safety signals for CZP in PSO as compared to previously reported data for CZP in other indications, and to other anti-TNF medications approved for PSO. Risk of treatment-emergent adverse events (TEAEs) did not increase with longer CZP exposure, and the safety profiles of high and low doses were similar.[24] Three-year efficacy outcomes have also been reported for the CIMPASI-1 and CIMPASI-2 trials.[25]

To date, 16- and 48-week efficacy outcomes have been reported from CIMPACT,[21] finding CZP to be efficacious compared with placebo[21–23] and etanercept (ETN) after 16 weeks of treatment,[21] with durability of initial responses through to Week 48.[21,26] Here, we present three-year efficacy and safety data from CIMPACT.

Methods

Study design

CIMPACT was a 144-week, phase 3, randomized, double-blinded, parallel-group, placebo- and active comparator-controlled, multicenter study conducted in North America and Europe, which was completed on 17th December 2018. The full study design and methods have been reported previously.[21]

Patients were randomized 3:3:3:1 to CZP 200 mg every other week (Q2W) (CZP 400 mg Q2W loading dose at Weeks 0, 2 and 4), CZP 400 mg Q2W, ETN 50 mg twice weekly or placebo (allocation ratio selected to minimize exposure to placebo). At Week 16, CZP- and ETN-treated patients who achieved a 75% improvement from baseline in their Psoriasis Area and Severity Index (PASI; PASI 75) were re-randomized to CZP 200 mg Q2W, CZP 400 mg every four weeks (Q4W), CZP 400 mg Q2W or placebo, depending on their initial treatment (Fig. 1). Week 16 PASI 75 responders who were initially randomized to placebo continued to receive double-blinded placebo.

Patients who achieved PASI 75 at Week 16 but did not achieve PASI 50 (50% improvement from baseline in PASI) at any visit after Week 16 until Week 48 of double-blinded treatment entered the 96-week open-label extension (OLE) at that visit. These patients received CZP 400 mg Q2W upon OLE entry.

PASI 75 non-responders at Week 16 entered an escape arm, in which they received open-label CZP 400 mg Q2W for up to 128 weeks.

At Week 48, patients in the double-blinded maintenance treatment arms entered the OLE and received open-label CZP

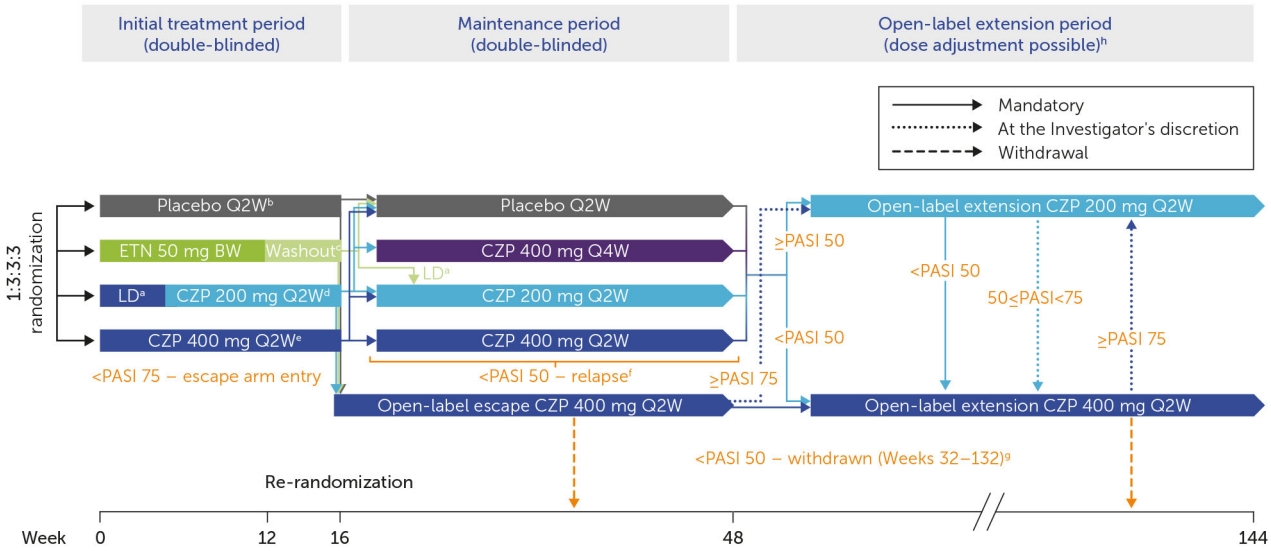

Figure 1 CIMPACT (NCT02346240) study design. Prior to Week 0, there was a screening period of up to 5 weeks to determine eligibility for study entry, obtain laboratory data, enable washout of medications not permitted for use during the study, and verify that doses of NSAIDs and other pain relievers were stable. [a]LD of CZP 400 mg Q2W at Weeks 0, 2 and 4 or Weeks 16, 18 and 20; [b]Placebo-treated Week 16 PASI 75 responders continued to receive placebo, while other Week 16 PASI 75 responders were re-randomized. PASI 75 non-responders from all initial treatment groups entered the open-label escape arm; [c]ETN-treated Week 16 PASI 75 responders, after a 4-week washout, were re-randomized 2:1 to CZP 200 mg Q2W (preceded by a CZP 400 mg LD at Weeks 16, 18 and 20) or placebo; [d]CZP 200 mg Q2W-treated Week 16 PASI 75 responders were re-randomized 2:2:1 to CZP 200 mg Q2W, CZP 400 mg Q4W, or placebo; [e]CZP 400 mg Q2W-treated Week 16 PASI 75 responders were re-randomized 2:2:1 to CZP 200 mg Q2W, CZP 400 mg Q2W, or placebo; [f]Patients receiving double-blinded maintenance treatment who did not achieve PASI 50 at any visit entered the OLE at that visit and initially received CZP 400 mg Q2W; [g]Patients who did not achieve PASI 50 having received CZP 400 mg Q2W for ≥16 weeks in the escape arm or ≥12 weeks in the OLE were withdrawn; [h]During open-label treatment (Weeks 48–144), patients receiving CZP 200 mg Q2W mandatorily dose escalated to CZP 400 mg Q2W if they did not achieve PASI 50; patients could also dose escalate at the investigator's discretion if they achieved 50≤PASI<75. Patients receiving open-label CZP 400 mg Q2W for ≥12 weeks could have their dose decreased from Week 48 onwards at the investigator's discretion if they achieved PASI 75. BW, twice weekly; CZP, certolizumab pegol; ETN, etanercept; LD, loading dose; NSAID, non-steroidal anti-inflammatory drug; PASI, Psoriasis Area and Severity Index; PASI 50/75, ≥50%/75% improvement from baseline in PASI; Q2W, every 2 weeks; Q4W, every 4 weeks.

200 mg Q2W (if they maintained ≥PASI 50 to Week 48), while patients in the escape arm continued to receive open-label CZP 400 mg Q2W. Dose adjustment was permitted at OLE study visits, based on PASI response and investigator discretion (Fig. 1).

Patients

Adult patients (≥18 years of age) with moderate or severe PSO for ≥6 months were enrolled. Full inclusion and exclusion criteria have been previously published.[21]

Efficacy outcomes

Week 16 and Week 48 data have been reported previously for the intent-to-treat population.[21] Here, we report efficacy data through 144 weeks among patients who entered the OLE and received CZP 200 mg Q2W at Week 48 after double-blinded maintenance treatment (Fig. 1). We also report Week 16–144 efficacy outcomes in patients randomized to placebo, CZP 200 mg Q2W or CZP 400 mg Q2W at Week 0 who did not achieve PASI 75 at Week 16 and entered the open-label escape arm. Patients who relapsed between Weeks 16 and 48 are not described.

Reported outcomes include the proportions of patients achieving PASI 75, 90% improvement from baseline in PASI (PASI 90), or Physician's Global Assessment score of 0 or 1 ('clear' or 'almost clear', with 2-point improvement from baseline; PGA 0/1). For efficacy analyses, patients were grouped according to their treatment group in the maintenance period and Week 48 dose allocation, irrespective of subsequent dose-switching.

Safety outcomes

Assessment of TEAEs is presented, defined as AEs occurring while treatment was ongoing or up to 70 days after the last CZP dose, regardless of the dose received. TEAEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 18.1. Serious TEAEs (SAEs) included all medical occurrences that were life-threatening or led to death, initial inpatient hospitalization, prolongation of hospitalization, congenital

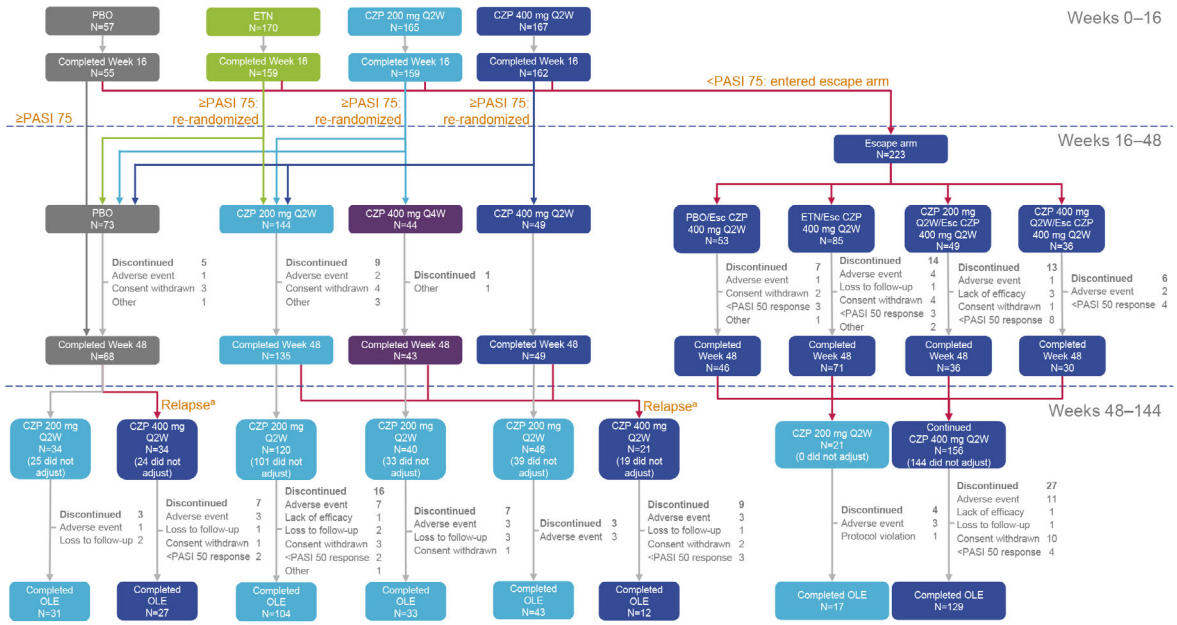

Figure 2 Patient disposition and discontinuations in the CIMPACT initial, maintenance and open-label treatment periods. N = 559 patients were randomized at Week 0. Weeks 0–16: initial treatment period; Weeks 16–48: maintenance treatment period; Weeks 48–144: OLE. Two patients who completed the initial treatment period did not continue to the maintenance treatment period, and six patients who completed the maintenance treatment period did not enter the OLE. [a]Did not achieve PASI 50 at a visit during the maintenance period; at Week 48, *n* = 2 patients who received double-blinded maintenance CZP 200 mg Q2W treatment, *n* = 1 who received CZP 400 mg Q4W, and *n* = 2 who received CZP 400 mg Q2W were mandated to receive CZP 200 mg Q2W upon OLE entry, but instead received CZP 400 mg Q2W. CZP, certolizumab pegol; Esc, escape; ETN, etanercept; OLE, open-label extension; PASI 50/75, ≥50%/75% improvement from baseline in Psoriasis Area and Severity Index; PBO, placebo; Q2W/Q4W, every 2/4 weeks.

anomalies or birth defects or resulted in persistent or significant disability. Events deemed medically significant by the investigator could also be recorded as SAEs, regardless of severity.

Safety data were analyzed for the combined CZP-treated group, and separately for the CZP 200 mg Q2W and 400 mg Q2W doses. Patients who received CZP 400 mg Q4W were combined with the CZP 200 mg Q2W group. Patients who switched dose could be counted in both CZP dose groups, but only once in the combined CZP group. Adverse events and exposure time were attributable to the dose most recently received. Exposure-adjusted incidence rates are incidences of new cases per 100 PY.

Statistical analysis

Estimates for responder rates and confidence intervals (CIs) were adjusted predicted probabilities from a logistic regression model with factors for treatment group, region and prior biologic exposure; due to the treatment groups included in these analyses, estimates may differ from those previously presented. Patients who were withdrawn having not achieved PASI 50, either at or after Week 32 in the escape arm or after ≥12 weeks' CZP 400 mg Q2W treatment in the OLE, were imputed as non-responders at subsequent time points. All other missing data were handled using the Markov Chain Monte Carlo (MCMC) method for multiple imputation. Patients who withdrew prior to Week 16 were not included. Results and associated 95% CIs are summarized alongside observed case (OC) data in Table S1.

Results

Patient disposition and baseline characteristics

At Week 0, 559 patients were randomized for initial treatment with CZP 200 mg Q2W, CZP 400 mg Q2W, ETN or placebo. At Week 16, 308 PASI 75 responders were re-randomized (Fig. 2); 144 to CZP 200 mg Q2W, 44 to CZP 400 mg Q4W, 49 to CZP 400 mg Q2W and 71 to placebo. Two patients who were randomized to placebo at Week 0 achieved PASI 75 at Week 16 and continued to receive placebo to Week 48. In total, 223 PASI 75 non-responders entered the escape CZP 400 mg Q2W arm at Week 16. Of the 559 patients randomized at Week 0, 24 discontinued prior to Week 16, and two did not continue having completed Week 16.

Table 1 Demographics and baseline characteristics by maintenance and open-label treatment groups

	Maintenance period treatment/open-label period treatment				
	PBO/CZP 200 mg Q2W (N = 34)	CZP 200 mg Q2W/CZP 200 mg Q2W (N = 122)	CZP 400 mg Q4W/CZP 200 mg Q2W (N = 41)	CZP 400 mg Q2W/CZP 200 mg Q2W (N = 48)	Esc CZP 400 mg Q2W/CZP 400 mg Q2W (N = 177)
Age (years), mean ± SD	45.7 ± 12.7	43.4 ± 12.4	49.5 ± 15.5	44.1 ± 12.6	47.3 ± 12.9
Male, *n* (%)	23 (67.6)	83 (68.0)	27 (65.9)	32 (66.7)	122 (68.9)
Caucasian, *n* (%)	34 (100)	120 (98.4)	40 (97.6)	46 (95.8)	169 (95.5)
BMI (kg/m^2), mean ± SD	29.2 ± 5.5	28.6 ± 5.3	28.8 ± 6.3	27.5 ± 5.1	30.2 ± 6.4
Weight (kg), mean ± SD	88.0 ± 20.1	86.0 ± 17.6	86.0 ± 23.1	81.7 ± 17.5	91.2 ± 22.0
PSO disease duration (years), mean ± SD	19.2 ± 13.9	18.0 ± 11.3	19.0 ± 14.2	17.7 ± 11.2	17.7 ± 11.4
Concurrent PsA (self-reported), *n* (%)	7 (20.6)	20 (16.4)	9 (22.0)	8 (16.7)	22 (12.4)
PASI, mean ± SD	20.4 ± 7.5	21.4 ± 8.7	20.5 ± 7.1	20.7 ± 6.9	20.6 ± 8.5
DLQI, mean ± SD	15.4 ± 8.1	13.3 ± 7.3	12.7 ± 6.4	15.4 ± 7.5	14.3 ± 7.4
BSA affected (%), median	17.5	23.0	24.0	24.5	21.0
PGA, *n* (%)					
3: moderate	22 (64.7)	85 (69.7)	31 (75.6)	33 (68.8)	120 (67.8)
4: severe	12 (35.3)	37 (30.3)	10 (24.4)	15 (31.3)	57 (32.2)
Any systemic PSO treatment, *n* (%)	20 (58.8)	88 (72.1)	31 (75.6)	37 (77.1)	128 (72.3)
Prior biologic therapy, *n* (%)					
0	27 (79.4)	86 (70.5)	26 (63.4)	35 (72.9)	133 (75.1)
1	4 (11.8)	28 (23.0)	14 (34.1)	12 (25.0)	35 (19.8)
2	3 (8.8)	8 (6.6)	1 (2.4)	1 (2.1)	9 (5.1)
Prior anti-TNF-α, n (%)	2 (5.9)	6 (4.9)	1 (2.4)	0	6 (3.4)

BSA, body surface area; BMI, body mass index; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; PGA, Physician's Global Assessment; PsA, psoriatic arthritis; PSO, psoriasis; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation; TNF, tumor necrosis factor.

At Week 48, 472 patients entered the OLE: 261 patients received CZP 200 mg Q2W upon OLE entry, 63 of whom adjusted their dose at least once (24.1%); 211 patients received CZP 400 mg Q2W upon OLE entry, 24 of whom adjusted their dose at least once (11.4%). Of these, 396 (83.9%) completed the OLE period. Demographics and baseline characteristics were balanced across OLE treatment groups (Table 1).

Durability of response in patients entering the open-label extension

Of the patients who completed Week 48 on double-blinded treatment and were mandated to receive CZP 200 mg Q2W upon OLE entry, 34 received placebo during Week 16–48 double-blinded maintenance treatment, 122 received CZP 200 mg Q2W, 41 received CZP 400 mg Q4W, and 48 received CZP 400 mg Q2W.

At the end of the double-blinded maintenance treatment period (Week 48), the PASI 75 responder rate was 93.2% among patients who received CZP 200 mg Q2W from Week 16, 92.7% for those receiving CZP 400 mg Q4W, and 98.7% for those receiving CZP 400 mg Q2W (Fig. 3a). At Week 144, after patients received CZP 200 mg Q2W in the OLE (with permitted dose adjustment), PASI 75 and PASI 90 responder rates were well maintained within the CZP 200 mg Q2W or CZP 400 mg Q4W-randomized patients, and declined following dose reduction in the CZP 400 mg Q2W-randomized group (Fig. 3a and b).

Responder rates improved from Week 48–144 in patients who received placebo between Weeks 16 and 48 and then received CZP 200 mg Q2W upon OLE entry; at Week 48, PASI 75 responder rates were 60.4%, increasing to 95.1% at Week 144 following CZP treatment during the OLE (Fig. 3a). The PASI 90 responder rate declined through Week 16–48 in these patients, from 62.1% to 23.4%, and increased again to 75.7% at Week 144 (Fig. 3b).

These trends were reflected in the PGA 0/1 responder rates (Table S1).

Long-term efficacy of CZP treatment in patients entering the open-label escape arm at Week 16

Continued CZP treatment in patients who entered the CZP 400 mg Q2W escape arm at Week 16 led to improved response rates at Weeks 48 and 144. Firstly, for patients who were initially randomized to CZP 200 mg Q2W, 48/165 (29.1%) did not achieve PASI 75 at Week 16 and entered the CZP 400 mg Q2W escape arm. After 32 weeks of treatment with CZP 400 mg

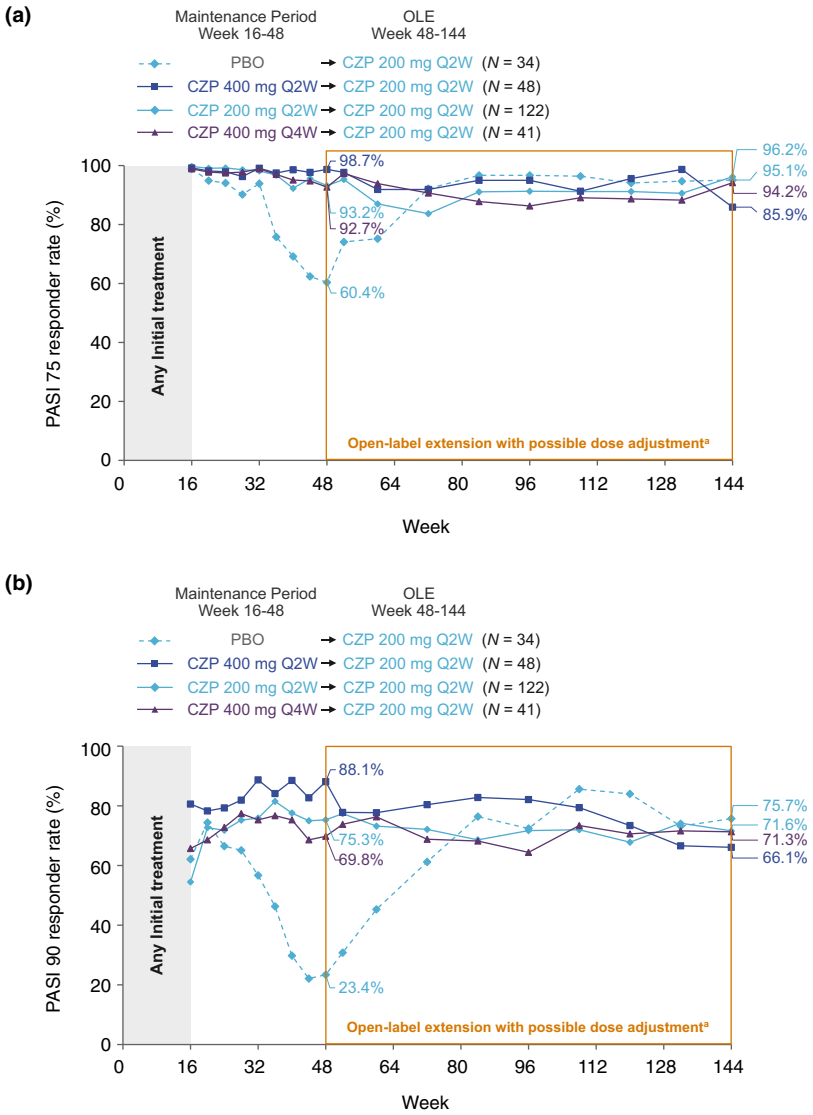

Figure 3 PASI 75 and PASI 90 response rates by maintenance treatment group to Week 144 in patients who received CZP 200 mg Q2W upon OLE entry: (a) PASI 75; (b) PASI 90. Patients were included irrespective of initial treatment period (both Figure 3a and b). Patients who achieved PASI 75 at Week 16, remained on double-blinded treatment through to Week 48, and were mandated to receive CZP 200 mg Q2W upon OLE entry were included. Patients who were withdrawn having not achieved PASI 50 from Week 32 onwards were imputed as non-responders at all subsequent time points. All other missing data were handled using the MCMC method for multiple imputation. [a]Dose adjustments were either mandatory or at investigator discretion, depending on PASI response. Two patients who received CZP 200 mg Q2W during maintenance treatment, one who received CZP 400 mg Q4W, and two who received CZP 400 mg Q2W and were mandated to receive CZP 200 mg Q2W upon OLE entry received CZP 400 mg Q2W instead. Of those patients who received CZP 200 mg Q2W upon OLE entry, 9/34 (26.5%) patients who received placebo from Week 16–48, 19/120 (15.8%) who received CZP 200 mg Q2W from Week 16–48, 7/40 (17.5%) who received CZP 400 mg Q4W from Week 16–48, and 7/46 (15.2%) who received CZP 400 mg Q2W from Week 16–48 adjusted their dose at least once during the OLE. CZP: certolizumab pegol; MCMC: Markov Chain Monte Carlo; OLE: open-label extension; PASI 75/90: ≥75%/90% improvement from baseline in Psoriasis Area and Severity Index; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

Q2W, 59.0% of these patients achieved PASI 75 and 28.8% achieved PASI 90. Following 128 weeks, 71.8% achieved PASI 75 and 42.7% achieved PASI 90 (Fig. 4, Table S1).

Secondly, for patients initially randomized to CZP 400 mg Q2W, 36/167 (21.6%) did not achieve PASI 75 at Week 16 and entered the CZP 400 mg Q2W escape arm. 79.7% of these

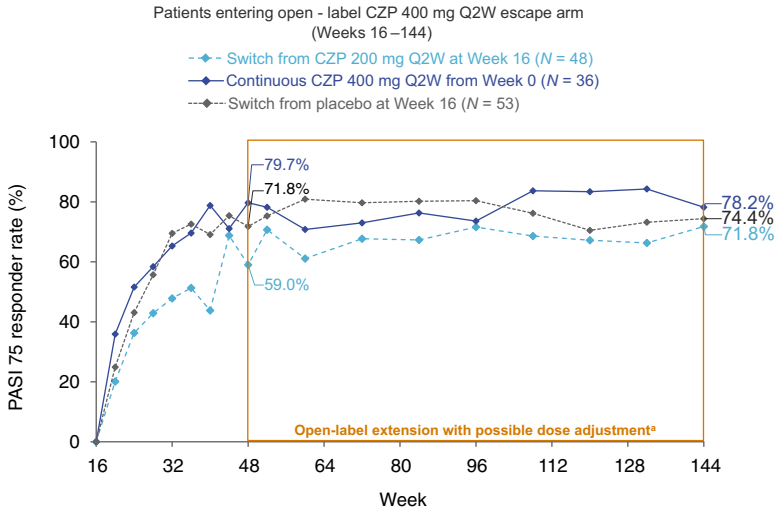

Figure 4 Evolution of PASI 75 responder rates to Week 144 in patients who entered the open-label CZP 400 mg Q2W escape arm as PASI 75 non-responders at Week 16. Patients included did not achieve PASI 75 at Week 16 and entered the open-label CZP 400 mg Q2W escape arm. Patients who were withdrawn having not achieved PASI 50 from Week 32 onwards were imputed as non-responders at all subsequent time points. All other missing data were handled using the MCMC method for multiple imputation. [a]Dose adjustments were either mandatory or at investigator discretion, depending on PASI response. 34 patients received CZP 200 mg Q2W to Week 16, entered the escape arm and then entered the OLE at Week 48 (14 did not enter the OLE), of whom 4 adjusted their dose at least once (11.8%). 29 patients received CZP 400 mg Q2W to Week 16, entered the escape arm and then entered the OLE at Week 48 (7 did not enter the OLE), of whom 6 adjusted their dose at least once (20.7%). 45 patients received PBO to Week 16, entered the escape arm and then entered the OLE at Week 48 (8 did not enter the OLE), of whom 11 adjusted their dose at least once (24.4%). CZP, certolizumab pegol; MCMC, Markov Chain Monte Carlo; OLE, open-label extension; PASI 50/75, ≥50%/75% improvement from baseline in Psoriasis Area and Severity Index; PBO, placebo; Q2W, every 2 weeks.

patients achieved PASI 75 after 32 additional weeks' CZP 400 mg Q2W treatment and 37.8% achieved PASI 90. This response was sustained through Week 144, with 78.2% achieving PASI 75 and 44.4% achieving PASI 90 after 128 additional weeks' CZP 400 mg Q2W treatment (Fig. 4, Table S1).

Of the 57 patients initially randomized to placebo, 53 (93.0%) did not achieve PASI 75 at Week 16 and entered the CZP 400 mg Q2W escape arm. After 32 weeks' CZP 400 mg Q2W treatment, 71.8% achieved PASI 75 and 52.8% achieved PASI 90. Following 128 weeks' CZP treatment, 74.4% achieved PASI 75 and 49.0% achieved PASI 90 (Fig. 4, Table S1).

These trends were reflected in the PGA 0/1 responder rates (Table S1).

In the subgroups of patients entering the escape arm who achieved <PASI 50 or 50≤PASI<75 at Week 16, PASI 75 response rates generally increased to Week 144 through 128 weeks of continued CZP treatment (Fig. S2).

Safety assessments

Through 144 weeks, 373 patients received ≥1 dose of CZP 200 mg Q2W and 412 patients received ≥1 dose of CZP 400 mg Q2W, totalling 632 and 592 PY of exposure, respectively; total exposure to CZP at any dose was 1224 PY (Table 2). During the study, 446 patients (81.8%) experienced at least one TEAE (Table 2), and 86 (15.8%) experienced a serious TEAE. Incidence rates of TEAEs did not increase over time as compared to previously reported data.[21] Three deaths occurred, all during the OLE: one case of acute myocardial infarction in a patient receiving CZP 200 mg Q2W, considered related to study treatment by the investigator in a patient with BMI ≥30 kg/m^2 at the time of the event, with pre-existing hypertension, atherosclerosis and ongoing tobacco use; two deaths considered unrelated to study treatment by the investigators, including one case of craniocerebral injury in a patient receiving CZP 400 mg Q2W and one case of chronic obstructive pulmonary disease in a patient receiving CZP 200 mg Q2W. Incidences of TEAEs were similar across the two dose groups (Table 2).

The most common TEAEs in patients receiving CZP were nasopharyngitis (20.4%), upper respiratory tract infection (13.8%) and hypertension (8.1%).

Opportunistic infections occurred in three patients (0.6%), including one case of active tuberculosis in a patient receiving escape CZP 400 mg Q2W (0.2%) during the maintenance period. One patient (0.2%) experienced primary progressive multiple sclerosis while receiving CZP 400 mg Q2W. Malignancies occurred in six patients (1.1%), including one case each of anaplastic oligodendroglioma, basal cell carcinoma, breast cancer, clear cell renal carcinoma, glioblastoma, Hodgkin's disease,

Table 2 Summary of TEAEs through the initial, maintenance and open-label periods (safety set)

Total exposure, PY	CZP 200 mg Q2W[a] (N = 373) 632		CZP 400 mg Q2W (N = 412) 592		All CZP (N = 545) 1224	
	n (%)	IR/100 PY (95% CI)	*n* (%)	IR/100 PY (95% CI)	*n* (%)	IR/100 PY (95% CI)
TEAEs overview						
All TEAEs	276 (74.0)	129.5 (114.6, 145.7)	299 (72.6)	132.7 (118.1, 148.7)	446 (81.8)	119.8 (109.0, 131.5)
TEAEs leading to death	2 (0.5)	0.3 (0.0, 1.1)	1 (0.2)	0.2 (0.0, 0.9)	3 (0.6)	0.2 (0.1, 0.7)
SAEs	37 (9.9)	6.3 (4.4, 8.7)	51 (12.4)	9.4 (7.0, 12.4)	86 (15.8)	7.7 (6.1, 9.5)
TEAEs leading to discontinuation	19 (5.1)	3.0 (1.8, 4.7)	27 (6.6)	4.6 (3.0, 6.7)	45 (8.3)	3.7 (2.7, 5.0)
Treatment-related TEAEs	77 (20.6)	14.2 (11.2, 17.8)	77 (18.7)	15.2 (12.0, 19.0)	136 (25.0)	13.5 (11.3, 16.0)
Selected TEAEs of interest						
System organ class						
Higher-level term						
Preferred term						
SIEs	8 (2.1)	1.3 (0.6, 2.5)	10 (2.4)	1.7 (0.8, 3.2)	18 (3.3)	1.5 (0.9, 2.4)
Opportunistic infections	1 (0.3)	0.2 (0.0, 0.9)	2 (0.5)	0.3 (0.0, 1.2)	3 (0.6)	0.2 (0.1, 0.7)
Active TB	0	0	1 (0.2)[b]	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Fungal esophagitis	1 (0.3)	0.2 (0.0, 0.9)	0	0	1 (0.2)	0.1 (0.0, 0.5)
Bacteremia[c]	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
All malignancies	4 (1.1)[d]	0.6 (0.2, 1.6)	4 (1.0)[e]	0.7 (0.2, 1.7)	6 (1.1)	0.5 (0.2, 1.1)
Malignancies excluding NMSC	4 (1.1)	0.6 (0.2, 1.6)	2 (0.5)	0.3 (0.0, 1.2)	5 (0.9)	0.4 (0.1, 1.0)
NMSC	0	0	2 (0.5)	0.3 (0.0, 1.2)	2 (0.4)	0.2 (0.0, 0.6)
MACE	2 (0.5)	0.3 (0.0, 1.1)	3 (0.7)	0.5 (0.1, 1.5)	5 (0.9)	0.4 (0.1, 1.0)
Cardiac failure	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Acute coronary syndrome	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Acute myocardial infarction	1 (0.3)	0.2 (0.0, 0.9)	0	0	1 (0.2)	0.1 (0.0, 0.5)
Angina pectoris	1 (0.3)	0.2 (0.0, 0.9)	0	0	1 (0.2)	0.1 (0.0, 0.5)
Extradural hematoma	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Demyelinating-like disorders	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Primary progressive multiple sclerosis	0	0	1 (0.2)[f]	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Serious psoriatic conditions	2 (0.5)	0.3 (0.0, 1.1)	2 (0.5)	0.3 (0.0, 1.2)	4 (0.7)	0.3 (0.1, 0.8)
Psoriasis	1 (0.3)	0.2 (0.0, 0.9)	0	0	1 (0.2)	0.1 (0.0, 0.5)
Erythrodermic psoriasis	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Guttate psoriasis	0	0	1 (0.2)	0.2 (0.0, 0.9)	1 (0.2)	0.1 (0.0, 0.5)
Pustular psoriasis	1 (0.3)	0.2 (0.0, 0.9)	0	0	1 (0.2)	0.1 (0.0, 0.5)
Serious bleeding events	1 (0.3)	0.2 (0.0, 0.9)	3 (0.7)	0.5 (0.1, 1.5)	4 (0.7)	0.3 (0.1, 0.8)
Hypersensitivity reactions and anaphylactic reactions	0	0	0	0	0	0
Injection site reactions	4 (1.1)	0.6 (0.2, 1.6)	6 (1.5)	1.0 (0.4, 2.2)	10 (1.8)	0.8 (0.4, 1.5)
Hepatic events	31 (8.3)	5.2 (3.6, 7.4)	36 (8.7)	6.5 (4.6, 9.0)	62 (11.4)	5.5 (4.2, 7.0)
Lupus and lupus-like events	0	0	0	0	0	0
Hematopoietic cytopenia	0	0	0	0	0	0

No cases of congenital anomalies/birth defects were reported.

CI, confidence interval; CZP, certolizumab pegol; IR, incidence rate; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancers; PY, patient-years; Q2W, every 2 weeks; SAE, serious TEAE; SIE, serious infection event; TB, tuberculosis; TEAE, treatment-emergent adverse event.

[a] Includes CZP 400 mg Q4W.

[b] One case of active TB reported in a patient who received etanercept during the initial 16-week period before escaping to CZP 400 mg Q2W (TB was diagnosed 172 days after etanercept initiation, 60 days after CZP initiation, and the patient was discontinued from the study; before study entry, the QuantiFERON TB GOLD test was negative and chest X-ray was normal; the patient lived in a country with a high prevalence of TB).

[c] Bacteremia secondary to *Eggerthella lenta*, did not lead to permanent discontinuation, was not considered related to study medication by the investigator, and was resolved.

[d] Includes one case of breast cancer, one case of glioblastoma, one case of Hodgkin's disease, and one case of laryngeal cancer.

[e] Includes one case of anaplastic oligodendroglioma, one case of clear cell renal carcinoma, one case of basal cell carcinoma, and one case of keratoacanthoma.

[f] The patient's medical history indicated that symptoms pre-dated study entry.

keratoacanthoma and laryngeal cancer (Table 2). No cases of hypersensitivity reactions, anaphylactic reactions, lupus or lupus-like events or hematopoietic cytopenia occurred.

Discussion

Over the course of three years' CZP treatment, improvements in signs and symptoms of moderate to severe PSO were well maintained. These data suggest that patients may be able to avoid treatment switching due to loss of efficacy over a longer time period, as is common with some biologic agents for treating PSO;[13,27] 21% of patients discontinue adalimumab within three years due to loss of efficacy, while 24% discontinue infliximab and 45% discontinue ETN within three years for the same reason.[13] The patient groups analyzed here included patients who responded to ETN treatment during the initial treatment period; high Week 48 PASI response rates have also been reported previously in the subgroup of patients who switched from ETN to CZP at Week 16.[21] This suggests prior treatment with ETN does not impact CZP efficacy.

The maintenance of response results seen in this trial are also consistent with the long-term efficacy reported for CZP in other indications (rheumatoid arthritis, psoriatic arthritis, Crohn's disease, axial spondyloarthritis),[26,28–30] and with those published for the CIMPASI-1 and CIMPASI-2 phase 3 trials.[25] Responder rates were high and numerically greater at Week 48 in patients receiving double-blinded CZP 400 mg Q2W than in patients receiving CZP 200 mg Q2W or CZP 400 mg Q4W (PASI 75: 98.7% versus 93.2% and 92.7%, respectively), suggesting that a higher CZP dose may be beneficial in some patients. Response rates were maintained through the OLE to Week 144 in patients originally treated with CZP 200 mg Q2W. In the group whose dose was lowered from CZP 400 mg Q2W to 200 mg Q2W upon OLE entry, some patients had a reduced response, suggesting that a proportion of patients may benefit from continued treatment at a higher dose. This was particularly notable when considering the higher response threshold of PASI 90. Because there are many approved therapies for psoriasis with different properties, many factors need to be considered when selecting the optimal therapy for an individual patient;[31,32] future research should aim to establish which subgroups most benefit from treatment with the 400 mg Q2W CZP dose.

Continuation of CZP treatment at the higher dose of 400 mg Q2W may also be a viable treatment strategy in patients who initially do not respond, or partially respond, to treatment. In this study, 59.0% of patients who did not achieve a PASI 75 response after 16 weeks' treatment with CZP dosed at 200 mg Q2W, and 79.7% of those dosed at 400 mg Q2W, achieved PASI 75 after 32 weeks' further treatment with CZP 400 mg Q2W. These responses were maintained or further improved to Week 144 (71.8% and 78.2%, respectively).

The three-year safety results presented here show that risk of TEAEs does not increase with longer exposure to CZP as compared to previously reported Week 48 data from the CIMPACT trial,[21] and no new safety signals were identified as compared to previously reported data for CZP, and to other anti-TNF medications approved for PSO.[33–35] This is consistent with a pooled safety analysis of the CIMPACT, CIMPASI-1 and CIMPASI-2 trials over three years of CZP treatment,[24] which also found no increased risk of TEAEs with increased exposure, and identified no new safety signals.

One limitation of this study was the possibility for patients to adjust dose during the OLE, and the implication of this on efficacy analyses of long-term dosing. Dose-switching could occur multiple times, based on PASI response and the investigator's discretion; 24.1% of patients who received CZP 200 mg Q2W upon OLE entry, as well as 11.4% who received CZP 400 mg Q2W, switched dose at least once. Although this complicates interpretation of long-term data, allowing dose adjustment reflects real-world clinical practice. Additionally, despite dose-switching, in all active treatment arms there was evidence of long-term durability of response. However, due to the specific restrictions and conditions associated with changes in CZP dose in this trial, the dose adjustments seen may not fully reflect all situations in which dose adjustment may occur in clinical treatment of patients with PSO. Therefore, results from this trial do not allow a conclusion to be drawn regarding which specific patients require increases and decreases in CZP dose. Re-randomization at Week 16, combined with the dose-switching and multiple treatment arms, also meant that each unique treatment path had a small sample size. This also complicates interpretation and analysis, although again this may reflect real-world treatment sequences, as disease flares and recedes. Finally, while PASI 75 was the standard response level used to define endpoints in PSO clinical trials when the CIMPACT study was designed, PASI 90 is now deemed more suitable as a robust response level to support treatment decisions. PASI 90 results are reported here; however, these were not the focus of the study and power calculations were based on PASI 75 rather than PASI 90 responses.

Overall, CZP offers long-term clinical efficacy in patients with moderate to severe PSO. Skin responses were durable in patients receiving either dose of CZP from Week 16 to Week 144, and no new safety signals were identified as compared to previously reported data.

Acknowledgements

The authors thank the patients, investigators and their teams who took part in this study. The authors acknowledge Susanne Wiegratz, MSc, UCB Pharma, for publication coordination, Sarah Kavanagh, MPH, for statistical analysis, and Daniel Smith, BA, Costello Medical, for medical writing and editorial assistance based on the authors' input and direction. This study was funded by UCB Pharma. Richard B. Warren is supported by the Manchester NIHR Biomedical Research Centre.

Authors' contributions

Substantial contributions to study conception and design: RBW, ML, HS, VP, MA, FB, CA, FF, AB; substantial contributions to analysis and interpretation of the data: RBW, ML, HS, VP, MA, FB, CA, FF, AB; drafting the article or revising it critically for important intellectual content: RBW, ML, HS, VP, MA, FB, CA, FF, AB; final approval of the version of the article to be published: RBW, ML, HS, VP, MA, FB, CA, FF, AB.

Data availability statement

Qualified researchers whose proposed use of the data has been approved by an independent review panel will be given access to anonymized individual participant data and redacted study documents. Additional information is available at www.clinicalstudydatarequest.com.

References

1 Danielsen K, Olsen AO, Wilsgaard T, Furberg AS. Is the prevalence of psoriasis increasing? A 30-year follow-up of a population-based cohort. *Br J Dermatol* 2013; **168**: 1303–1310.

2 Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. *J Am Acad Dermatol* 2014; **70**: 512–516.

3 Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003–2004. *J Am Acad Dermatol* 2009; **60**: 218–224.

4 Gordon K, Korman N, Frankel E *et al*. Efficacy of etanercept in an integrated multistudy database of patients with psoriasis. *J Am Acad Dermatol* 2006; **54**: S101–S111.

5 Papp KA, Langley RG, Lebwohl M *et al*. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet* 2008; **371**: 1675–1684.

6 Fotiadou C, Lazaridou E, Sotiriou E, Ioannides D. Targeting IL-23 in psoriasis: current perspectives. *Psoriasis (Auckl)* 2018; **8**: 1–5.

7 Blauvelt A, Reich K, Tsai T-F *et al*. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study. *J Am Acad Dermatol* 2017; **76**: 60–69.e9.

8 Puig L, Lebwohl M, Bachelez H, Sobell J, Jacobson AA. Long-term efficacy and safety of brodalumab in the treatment of psoriasis: 120-week results from the randomized, double-blind, placebo- and active comparator–controlled phase 3 AMAGINE-2 trial. *J Am Acad Dermatol* 2020; **82**: 352–359.

9 NICE. NICE Pathways: Psoriasis overview. Available at: https://pathways.nice.org.uk/pathways/psoriasis [Accessed 26 November 2020].

10 Menter A, Strober BE, Kaplan DH *et al*. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol* 2019; **80**: 1029–1072.

11 Smith CH, Jabbar-Lopez ZK, Yiu ZZ *et al*. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol* 2017; **177**: 628–636.

12 Nast A, Spuls PI, van der Kraaij G *et al*. European S3-Guideline on the systemic treatment of psoriasis vulgaris – Update Apremilast and Secukinumab – EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol* 2017; **31**: 1951–1963.

13 Warren RB, Smith CH, Yiu ZZN *et al*. Differential drug survival of biologic therapies for the treatment of psoriasis: a prospective observational cohort study from the british association of dermatologists biologic interventions register (BADBIR). *J Invest Dermatol* 2015; **135**: 2632–2640.

14 Gniadecki R, Bang B, Bryld LE *et al*. Comparison of long-term drug survival and safety of biologic agents in patients with psoriasis vulgaris. *Br J Dermatol* 2015; **172**: 244–252.

15 FDA. Cimzia (Certolizumab Pegol) Prescribing Information. Available at: https://www.accessdata.FDA.gov/drugsatfda_docs/label/2019/125160s237lbl.pdf [Accessed 26 November 2020].

16 Compendium EM. Cimzia. Available at: https://www.medicines.org.uk/emc/medicine/32367 [Accessed 26 November 2020].

17 Weir N, Athwal D, Brown D *et al*. A new generation of high-affinity humanized PEGylated Fab' fragment anti-tumor necrosis factor-[alpha] monoclonal antibodies. *Therapy* 2006; **3**: 535–545.

18 Mariette X, Förger F, Abraham B *et al*. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Ann Rheum Dis* 2018; **77**: 228.

19 Clowse ME, Forger F, Hwang C *et al*. Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. *Ann Rheum Dis* 2017; **76**: 1890–1896.

20 Clowse MEB, Scheuerle AE, Chambers C *et al*. Pregnancy outcomes after exposure to certolizumab pegol: updated results from a pharmacovigilance safety database. *Arthritis Rheumatol* 2018; **70**: 1399–1407.

21 Lebwohl M, Blauvelt A, Paul C *et al*. Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). *J Am Acad Dermatol* 2018; **79**: 266–276.e5.

22 Gottlieb AB, Blauvelt A, Thaçi D *et al*. Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). *J Am Acad Dermatol* 2018; **79**: 302–314.e6.

23 Blauvelt A, Reich K, Lebwohl M *et al*. Certolizumab pegol for the treatment of patients with moderate-to-severe chronic plaque psoriasis: pooled analysis of week 16 data from three randomized controlled trials. *J Eur Acad Dermatol Venereol* 2019; **33**: 546–552.

24 Blauvelt A, Paul C, van de Kerkhof P *et al*. Long-Term Safety of Certolizumab Pegol in Plaque Psoriasis: Pooled Analysis over 3 Years from Three Phase 3, Randomised, Placebo-Controlled Studies. *Br J Dermatol* 2021;**184**: 640–651.

25 Gordon KB, Warren RB, Gottlieb AB *et al*. Long-term efficacy of certolizumab pegol for the treatment of plaque psoriasis: 3-year results from two randomized phase III trials (CIMPASI-1 and CIMPASI-2). *Br J Dermatol* 2021;**184**: 652–662.

26 van der Heijde D, Deodhar A, FitzGerald O *et al*. 4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis. *RMD Open* 2018; **4**: e000582.

27 Levin EC, Gupta R, Brown G, Malakouti M, Koo J. Biologic fatigue in psoriasis. *J Dermatolog Treat* 2014; **25**: 78–82.

28 Keystone E, Landewé R, van Vollenhoven R *et al*. Long-term safety and efficacy of certolizumab pegol in combination with methotrexate in the treatment of rheumatoid arthritis: 5-year results from the RAPID 1 trial and open-label extension. *Ann Rheum Dis* 2014; **73**: 2094–2100.

29 van der Heijde D, Dougados M, Landewé R *et al*. Sustained efficacy, safety and patient-reported outcomes of certolizumab pegol in axial spondyloarthritis: 4-year outcomes from RAPID-axSpA. *Rheumatology (Oxford)* 2017; **56**: 1498–1509.

30 Sandborn WJ, Lee SD, Randall C *et al*. Long-term safety and efficacy of certolizumab pegol in the treatment of Crohn's disease: 7-year results from the PRECiSE 3 study. *Aliment Pharmacol Ther* 2014; **40**: 903–916.

31 Kaushik SB, Lebwohl MG. Psoriasis: Which therapy for which patient: Psoriasis comorbidities and preferred systemic agents. *J Am Acad Dermatol* 2019; **80**: 27–40.

32 Kaushik SB, Lebwohl MG. Psoriasis: Which therapy for which patient: Focus on special populations and chronic infections. *J Am Acad Dermatol* 2019; **80**: 43–53.

33 Gordon K, Papp K, Poulin Y *et al*. Long-term efficacy and safety of adalimumab in patients with moderate to severe psoriasis treated continuously over 3 years: Results from an open-label extension study for patients from REVEAL. *J Am Acad Dermatol* 2012; **66**: 241–251.
34 Reich K, Nestle FO, Papp K *et al*. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. *Lancet* 2005; **366**: 1367–1374.
35 Tyring S, Gordon KB, Poulin Y *et al*. Long-term Safety and Efficacy of 50 mg of Etanercept Twice Weekly in Patients With Psoriasis. *Arch Dermatol* 2007; **143**: 719–726.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Figure S1 Dose adjustment during the open-label period.
Figure S2 PASI 75 responder rates to Week 144 in subgroups of patients who entered the escape arm at Week 16.
Table S1 Summary of efficacy results.