Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo- and Active-Controlled Study Followed by a Placebo-Controlled Maintenance Period and Open-Label Follow-Up to Evaluate the Efficacy and Safety of Certolizumab Pegol in Subjects With Moderate to Severe Chronic Plaque Psoriasis

Summary

EudraCT number	2014-003492-36
Trial protocol	GB DE HU CZ NL PL BG FR
Global end of trial date	17 December 2018

Results information

Result version number	v1
This version publication date	01 January 2020
First version publication date	01 January 2020

Trial information

Trial identification

Sponsor protocol code	PS0003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02346240
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SPRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, B-1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of certolizumab pegol (CZP) administered subcutaneously (sc) at the doses of CZP 400 mg every 2 weeks (Q2W) and CZP 200 mg Q2W after a loading dose of CZP 400 mg Q2W at Weeks 0, 2, and 4 to placebo in the treatment of moderate to severe chronic plaque psoriasis (PSO).

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy/concomitant medication was permitted as defined in the study protocol.

Evidence for comparator:

Etanercept (ETN) is a fusion protein consisting of the fragment crystallizable (Fc) fragment of Immunoglobulin G1 (IgG1) with the Type 2 soluble Tumor Necrosis Factor (TNF) alpha receptor. ETN is specific for TNF alpha and lymphotoxin alpha. ETN was the first TNF alpha inhibitor approved for the treatment of psoriasis and is part of the standard armamentarium. The approved initial dose is 50 milligrams (mg) twice weekly. The safety and efficacy profile of ETN is well established. The first approval worldwide for ETN was in the United States in 1998 for the treatment of rheumatoid arthritis and in 2004 for psoriasis. All of these factors make ETN an ideal active comparator in this study.

Actual start date of recruitment	11 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 25
Country: Number of subjects enrolled	Czech Republic: 80
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 63
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Poland: 233
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	United States: 92
Worldwide total number of subjects	559
EEA total number of subjects	467

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	519
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study started to enroll participants in February 2015, from multiple sites in Europe and United States and concluded in December 2018. 559 participants are included in the Randomized Set (RS) shown in the Participant Flow.

Pre-assignment

Screening details:

The study included a Screening Period, an Initial Treatment Period up to Week 16, a Maintenance Treatment Period up to Week 48, an Open-Label Extension Treatment Period up to Week 144 and a Safety Follow-up Period up to Week 157. The Participants Flow refers to the Randomized Set, the Maintenance Set and the Open Label Set.

Period 1

Period 1 title	Initial Period (Baseline to Week 16)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

CZP and placebo treatments were administered in a double-blind fashion (the sponsor, subject, and blinded site staff remained blinded to treatment assignment during the first 16 weeks of the study). Etanercept treatments were administered in a single-blind fashion (the sponsor and the blinded site staff remained blinded, but the subject and unblinded study staff knew the treatment assignment during the first 16 weeks of the study).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Q2W

Arm description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.
Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Arm title	Etanercept

Arm description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.
•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Arm type	Active comparator

Investigational medicinal product name	Etanercept
Investigational medicinal product code	ETN
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 50 mg twice weekly

Arm title	CZP 200 mg Q2W

Arm description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W

Arm description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Number of subjects in period 1	Placebo Q2W	Etanercept	CZP 200 mg Q2W
Started	57	170	165
Completed Week 16	55	159	159
Finished Wk16 started Maintenance Period	55	159	159

Completed	55	159	159
Not completed	2	11	6
Consent withdrawn by subject	1	2	3
Subject missed 3 visits	-	-	1
Adverse event, non-fatal	-	4	1
Non-compliance	-	1	-
Lost to follow-up	1	2	1
Lack of efficacy	-	1	-
Protocol deviation	-	1	-

Number of subjects in period 1	CZP 400 mg Q2W
Started	167
Completed Week 16	162
Finished Wk16 started Maintenance Period	160
Completed	160
Not completed	7
Consent withdrawn by subject	2
Subject missed 3 visits	-
Adverse event, non-fatal	1
Non-compliance	1
Lost to follow-up	3
Lack of efficacy	-
Protocol deviation	-

Period 2

Period 2 title	Maintenance Period (Week 16 to Week 48)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor, Carer

Blinding implementation details:

Participants who entered the escape arms of the study received open-label CZP 400 mg every 2 weeks. Participants who relapsed were removed from the placebo-controlled Maintenance Period and entered the OLE Period.

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo/Placebo Q2W

Arm description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Arm title	Etanercept/Placebo Q2W

Arm description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Investigational medicinal product name	Etanercept
Investigational medicinal product code	ETN
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 50 mg twice weekly

Arm title	Etanercept/CZP 200 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Investigational medicinal product name	Etanercept
Investigational medicinal product code	ETN
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 50 mg twice weekly

Arm title	CZP 200 mg Q2W/Placebo Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Arm type	Placebo
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Arm title	CZP 200 mg Q2W/CZP 200 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 200 mg Q2W/CZP 400 mg Q4W

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48).

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W/Placebo Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W/CZP 200 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W/CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	Placebo Q2W/Escape CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Arm type	Experimental

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Arm title	Etanercept/Escape CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the Etanercept arm, who did not achieve a PASI75 response at Week 16 escaped from the treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	ETN
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 50 mg twice weekly

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 200 mg Q2W/Escape CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W/Escape CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two

weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Number of subjects in period 2	Placebo/Placebo Q2W	Etanercept/Placebo Q2W	Etanercept/CZP 200 mg Q2W
Started	2	24	50
Completed Maintenance Period	2	23	48
Finished Wk48 entered Open-label Period	2	23	48
Completed	2	23	48
Not completed	0	1	2
Moved out of state	-	-	1
Consent withdrawn by subject	-	1	1
Adverse events and alcohol problem	-	-	-
Withdrawn by Sponsor	-	-	-
Adverse event, non-fatal	-	-	-
Patient’s decisions	-	-	-
Sponsor decision due to non-compliance	-	-	-
Unavailability due to business trip	-	-	-
Lost to follow-up	-	-	-
Patient request due to non-compliance	-	-	-
Lack of efficacy	-	-	-
Did not achieve PASI50	-	-	-

Number of subjects in period 2	CZP 200 mg Q2W/Placebo Q2W	CZP 200 mg Q2W/CZP 200 mg Q2W	CZP 200 mg Q2W/CZP 400 mg Q4W
Started	22	44	44
Completed Maintenance Period	20	40	43
Finished Wk48 entered Open-label Period	20	40	43
Completed	20	40	43
Not completed	2	4	1
Moved out of state	-	-	-
Consent withdrawn by subject	1	1	-
Adverse events and alcohol problem	-	-	1

Withdrawn by Sponsor	-	-	-
Adverse event, non-fatal	1	2	-
Patient's decisions	-	-	-
Sponsor decision due to non-compliance	-	1	-
Unavailability due to business trip	-	-	-
Lost to follow-up	-	-	-
Patient request due to non-compliance	-	-	-
Lack of efficacy	-	-	-
Did not achieve PASI50	-	-	-

Number of subjects in period 2	CZP 400 mg Q2W/Placebo Q2W	CZP 400 mg Q2W/CZP 200 mg Q2W	CZP 400 mg Q2W/CZP 400 mg Q2W
Started	25	50	49
Completed Maintenance Period	23	47	49
Finished Wk48 entered Open-label Period	23	47	49
Completed	23	47	49
Not completed	2	3	0
Moved out of state	-	-	-
Consent withdrawn by subject	1	2	-
Adverse events and alcohol problem	-	-	-
Withdrawn by Sponsor	-	-	-
Adverse event, non-fatal	-	-	-
Patient's decisions	1	-	-
Sponsor decision due to non-compliance	-	1	-
Unavailability due to business trip	-	-	-
Lost to follow-up	-	-	-
Patient request due to non-compliance	-	-	-
Lack of efficacy	-	-	-
Did not achieve PASI50	-	-	-

Number of subjects in period 2	Placebo Q2W/Escape CZP 400 mg Q2W	Etanercept/Escape CZP 400 mg Q2W	CZP 200 mg Q2W/Escape CZP 400 mg Q2W
Started	53	85	49
Completed Maintenance Period	46	71	36
Finished Wk48 entered Open-label Period	45	68	35
Completed	45	68	35
Not completed	8	17	14
Moved out of state	-	-	-
Consent withdrawn by subject	2	5	2
Adverse events and alcohol problem	-	-	-

Withdrawn by Sponsor	-	1	-
Adverse event, non-fatal	1	4	1
Patient’s decisions	-	-	-
Sponsor decision due to non-compliance	1	1	-
Unavailability due to business trip	-	1	-
Lost to follow-up	-	1	-
Patient request due to non-compliance	-	1	-
Lack of efficacy	1	-	3
Did not achieve PASI50	3	3	8

Number of subjects in period 2	CZP 400 mg Q2W/Escape CZP 400 mg Q2W
Started	36
Completed Maintenance Period	30
Finished Wk48 entered Open-label Period	29
Completed	29
Not completed	7
Moved out of state	-
Consent withdrawn by subject	1
Adverse events and alcohol problem	-
Withdrawn by Sponsor	-
Adverse event, non-fatal	2
Patient’s decisions	-
Sponsor decision due to non-compliance	-
Unavailability due to business trip	-
Lost to follow-up	-
Patient request due to non-compliance	-
Lack of efficacy	-
Did not achieve PASI50	4

Period 3

Period 3 title	Open-Label Period (Week 48 to Week 144)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo/CZP 200 mg Q2W OLE

Arm description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who achieved PASI50 response (had no relapse) at Week 48 and entered the 96-Weeks OLE Period receiving CZP 200 mg Q2W.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 200 mg Q2W/CZP 200 mg Q2W OLE

Arm description:

This arm consisted of participants who received CZP 200 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q4W/CZP 200 mg Q2W OLE

Arm description:

This arm consisted of participants who received CZP 400 mg Q4W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	CZP 400 mg Q2W/CZP 200 mg Q2W OLE

Arm description:

This arm consisted of participants who received CZP 400 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

Arm type	Experimental

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	Esc CZP 400 mg Q2W/CZP 400 mg Q2W OLE

Arm description:

This arm consisted of participants who received open-label CZP 400mg Q2W in the Maintenance Period and entered OLE.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	Placebo/CZP 400 mg Q2W OLE

Arm description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who did not achieve PASI50 response (had relapse) and entered the 96-weeks OLE Period receiving CZP 400 mg Q2W.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Arm title	Any CZP/CZP 400 mg Q2W OLE

Arm description:

This arm consisted of participants who relapsed on CZP 200 mg Q2W, CZP 400 mg Q4W and 400 mg Q2W.

Arm type	Experimental
Investigational medicinal product name	Certolizumab pegol
Investigational medicinal product code	CZP
Other name	Cimzia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

Number of subjects in period 3	Placebo/CZP 200 mg Q2W OLE	CZP 200 mg Q2W/CZP 200 mg Q2W OLE	CZP 400 mg Q4W/CZP 200 mg Q2W OLE
Started	34	122	41
Completed	31	105	34
Not completed	3	17	7
Adverse event, serious fatal	-	1	1
Consent withdrawn by subject	-	4	1
Adverse event, non-fatal	1	6	2
Lost to follow-up	2	2	3
No PASI50 response	-	2	-
No efficacy of study medication	-	1	-
Lack of efficacy	-	1	-
Protocol deviation	-	-	-

Number of subjects in period 3	CZP 400 mg Q2W/CZP 200 mg Q2W OLE	Esc CZP 400 mg Q2W/CZP 400 mg Q2W OLE	Placebo/CZP 400 mg Q2W OLE
Started	48	177	34
Completed	45	146	27
Not completed	3	31	7
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	10	1
Adverse event, non-fatal	3	13	3
Lost to follow-up	-	1	1
No PASI50 response	-	4	2
No efficacy of study medication	-	-	-
Lack of efficacy	-	1	-
Protocol deviation	-	1	-

Number of subjects in period 3	Any CZP/CZP 400 mg Q2W OLE
Started	16
Completed	8
Not completed	8
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Adverse event, non-fatal	3
Lost to follow-up	1
No PASI50 response	3
No efficacy of study medication	-
Lack of efficacy	-

Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Q2W

Reporting group description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.
Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

Reporting group title	Etanercept

Reporting group description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.
•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group title	CZP 200 mg Q2W

Reporting group description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group title	CZP 400 mg Q2W

Reporting group description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group values	Placebo Q2W	Etanercept	CZP 200 mg Q2W
Number of subjects	57	170	165
Age categorical Units: Subjects			
<=18 years	0	1	0
Between 18 and 65 years	53	156	153
>=65 years	4	13	12
Age continuous Units: years			
arithmetic mean	46.5	44.6	46.7
standard deviation	± 12.5	± 14.1	± 13.5

Gender categorical Units: Subjects			
Female	23	43	52
Male	34	127	113

Reporting group values	CZP 400 mg Q2W	Total	
Number of subjects	167	559	
Age categorical Units: Subjects			
<=18 years	2	3	
Between 18 and 65 years	154	516	
>=65 years	11	40	
Age continuous Units: years			
arithmetic mean	45.4		
standard deviation	± 12.4	-	
Gender categorical Units: Subjects			
Female	60	178	
Male	107	381	

Subject analysis sets

Subject analysis set title	Placebo Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.
Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	Etanercept (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.
•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	CZP 200 mg Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

Subject analysis set title	CZP 400 mg Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	Placebo/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	Etanercept/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	Etanercept/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W (TCS)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

Subject analysis set title	CZP 400 mg Q2W (TCS)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

Reporting group values	Placebo Q2W (RS)	Etanercept (RS)	CZP 200 mg Q2W (RS)
Number of subjects	57	170	165
Age categorical Units: Subjects			
<=18 years	0	1	0
Between 18 and 65 years	53	156	153
>=65 years	4	13	12
Age continuous Units: years			
arithmetic mean	46.5	44.6	46.7
standard deviation	± 12.5	± 14.1	± 13.5
Gender categorical Units: Subjects			
Female	23	43	52
Male	34	127	113

Reporting group values	CZP 400 mg Q2W (RS)	Placebo/Placebo Q2W (WK16RS)	Etanercept/Placebo Q2W (WK16RS)
Number of subjects	167	2	24
Age categorical Units: Subjects			
<=18 years	2	0	0
Between 18 and 65 years	154	2	24
>=65 years	11	0	0
Age continuous Units: years			
arithmetic mean	45.4	41.5	47.2
standard deviation	± 12.4	± 26.2	± 13.5
Gender categorical Units: Subjects			
Female	60	2	6
Male	107	0	18

Reporting group values	Etanercept/CZP 200	CZP 200 mg	CZP 200 mg

	mg Q2W (WK16RS)	Q2W/Placebo Q2W (WK16RS)	Q2W/CZP 200 mg Q2W (WK16RS)
Number of subjects	50	22	44
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	47	21	43
>=65 years	3	1	1
Age continuous Units: years			
arithmetic mean	43.3	47.3	43.2
standard deviation	± 12.9	± 14.9	± 12.4
Gender categorical Units: Subjects			
Female	13	7	14
Male	37	15	30

Reporting group values	CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS)	CZP 400 mg Q2W/Placebo Q2W (WK16RS)	CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS)
Number of subjects	44	25	50
Age categorical Units: Subjects			
<=18 years	0	1	1
Between 18 and 65 years	38	24	45
>=65 years	6	0	4
Age continuous Units: years			
arithmetic mean	49.4	42.9	43.3
standard deviation	± 15.1	± 9.7	± 11.9
Gender categorical Units: Subjects			
Female	14	11	18
Male	30	14	32

Reporting group values	CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS)	CZP 200 mg Q2W (TCS)	CZP 400 mg Q2W (TCS)
Number of subjects	49	373	412
Age categorical Units: Subjects			
<=18 years	0	2	3
Between 18 and 65 years	45	346	377
>=65 years	4	25	32
Age continuous Units: years			
arithmetic mean	44.6	45.3	45.8
standard deviation	± 13.0	± 13.0	± 13.2
Gender categorical Units: Subjects			
Female	17	115	131
Male	32	258	281

End points

End points reporting groups

Reporting group title	Placebo Q2W

Reporting group description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.
Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

Reporting group title	Etanercept

Reporting group description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.
•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group title	CZP 200 mg Q2W

Reporting group description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group title	CZP 400 mg Q2W

Reporting group description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Reporting group title	Placebo/Placebo Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Reporting group title	Etanercept/Placebo Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Reporting group title	Etanercept/CZP 200 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 200 mg Q2W/Placebo Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 200 mg Q2W/CZP 200 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 200 mg Q2W/CZP 400 mg Q4W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 400 mg Q2W/Placebo Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 400 mg Q2W/CZP 200 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Reporting group title	CZP 400 mg Q2W/CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48).

Reporting group title	Placebo Q2W/Escape CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Reporting group title	Etanercept/Escape CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Etanercept arm, who did not achieve a PASI75 response at Week 16 escaped from the treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Reporting group title	CZP 200 mg Q2W/Escape CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Reporting group title	CZP 400 mg Q2W/Escape CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

Reporting group title	Placebo/CZP 200 mg Q2W OLE

Reporting group description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who achieved PASI50 response (had no relapse) at Week 48 and entered the 96-Weeks OLE Period receiving CZP 200 mg Q2W.

Reporting group title	CZP 200 mg Q2W/CZP 200 mg Q2W OLE

Reporting group description:

This arm consisted of participants who received CZP 200 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE.

Reporting group title	CZP 400 mg Q4W/CZP 200 mg Q2W OLE

Reporting group description:

This arm consisted of participants who received CZP 400 mg Q4W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

Reporting group title	CZP 400 mg Q2W/CZP 200 mg Q2W OLE

Reporting group description:

This arm consisted of participants who received CZP 400 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

Reporting group title	Esc CZP 400 mg Q2W/CZP 400 mg Q2W OLE

Reporting group description:

This arm consisted of participants who received open-label CZP 400mg Q2W in the Maintenance Period and entered OLE.

Reporting group title	Placebo/CZP 400 mg Q2W OLE

Reporting group description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who did not achieve PASI50 response (had relapse) and entered the 96-weeks OLE Period receiving CZP 400 mg Q2W.

Reporting group title	Any CZP/CZP 400 mg Q2W OLE

Reporting group description:

This arm consisted of participants who relapsed on CZP 200 mg Q2W, CZP 400 mg Q4W and 400 mg Q2W.

Subject analysis set title	Placebo Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.
Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	Etanercept (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.
•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	CZP 200 mg Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	CZP 400 mg Q2W (RS)
Subject analysis set type	Full analysis

Subject analysis set description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:
•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.
Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.
Participants formed the Randomized Set (RS).

Subject analysis set title	Placebo/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	Etanercept/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	Etanercept/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/Placebo Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75

response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

Subject analysis set title	CZP 200 mg Q2W (TCS)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

Subject analysis set title	CZP 400 mg Q2W (TCS)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

Primary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 12

End point title	Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 12

End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person’s affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo Q2W (RS)	Etanercept (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	170	165	167
Units: percentage of participants				
number (not applicable)	5.0	53.3	61.3	66.7

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)

Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	61.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	52.1
upper limit	71.2

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	56.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	46.4
upper limit	66

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	37.988
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.312
upper limit	127.576

Notes:

[1] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.	
Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	30.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.971
upper limit	100.481

Notes:

[2] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.	
Comparison groups	Etanercept (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	24.1

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.	
Comparison groups	Etanercept (RS) v CZP 200 mg Q2W (RS)

Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	18.9

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Etanercept (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0152 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.756
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.114
upper limit	2.768

Notes:

[3] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. ETN.

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Etanercept (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1523 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.388
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.886
upper limit	2.175

Notes:

[4] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. ETN

Secondary: Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 12

End point title	Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 12

End point description:

The Investigator assessed the overall severity of Psoriasis (PSO) using the following 5-point scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo Q2W (RS)	Etanercept (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	170	165	167
Units: percentage of participants				
number (not applicable)	1.9	39.2	39.8	50.3

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	48.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	39.33
upper limit	57.63

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables

accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	37.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.88
upper limit	46.96

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	56.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.787
upper limit	404.555

Notes:

[5] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	36.566

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.061
upper limit	264.196

Notes:

[6] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 12

End point title	Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 12

End point description:

The PASI90 response assessments are based on at least 90% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo Q2W (RS)	Etanercept (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	170	165	167
Units: percentage of participants				
number (not applicable)	0.2	27.1	31.2	34.0

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	33.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	20.68
upper limit	46.98

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.18
upper limit	43.8

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	39.949
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.407
upper limit	189.828

Notes:

[7] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	35.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.363
upper limit	167.179

Notes:

[8] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 16

End point title	Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 16

End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person’s affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo Q2W (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	57	165	167	
Units: percentage of participants				
number (not applicable)	3.8	68.2	74.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)

Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	70.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.15
upper limit	79.59

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	64.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	55.12
upper limit	73.63

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	76.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.952
upper limit	324.094

Notes:

[9] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	55.413
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.135
upper limit	233.782

Notes:

[10] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

Secondary: Proportion of subjects who achieve a Physician’s Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 16

End point title	Proportion of subjects who achieve a Physician’s Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 16

End point description:

The Investigator assessed the overall severity of Psoriasis (PSO) using the following 5-point scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo Q2W (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	57	165	167	
Units: percentage of participants				
number (not applicable)	3.4	48.3	58.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	55
Confidence interval	
level	95 %
sides	2-sided
lower limit	45.59
upper limit	64.35

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	44.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.39
upper limit	54.49

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	40.717

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.741
upper limit	170.198

Notes:

[11] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	27.165
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.504
upper limit	113.453

Notes:

[12] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 16

End point title	Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 16

End point description:

The PASI90 response assessments are based on at least 90% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person’s affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo Q2W (RS)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	57	165	167	
Units: percentage of participants				
number (not applicable)	0.3	39.8	49.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	48.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	34.22
upper limit	63.41

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.58
upper limit	53.38

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 400 mg Q2W (RS)
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	72.278
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.65
upper limit	356.602

Notes:

[13] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

Comparison groups	Placebo Q2W (RS) v CZP 200 mg Q2W (RS)
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	49.527
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.002
upper limit	245.256

Notes:

[14] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 48 for those achieving PASI75 at Week 16

End point title	Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 48 for those achieving PASI75 at Week 16

End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person’s affected skin for the respective section. The minimum possible PASI score is

0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo/Placebo Q2W (WK16RS)	Etanercept/Placebo Q2W (WK16RS)	Etanercept/CZP 200 mg Q2W (WK16RS)	CZP 200 mg Q2W/Placebo Q2W (WK16RS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	24	50	22
Units: percentage of participants				
number (not applicable)	100	8.3	82.0	45.5

End point values	CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS)	CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS)	CZP 400 mg Q2W/Placebo Q2W (WK16RS)	CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	44	25	50
Units: percentage of participants				
number (not applicable)	79.5	88.6	36.0	80.0

End point values	CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS)			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: percentage of participants				
number (not applicable)	98.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from Baseline (Week 0) until Week 144.

Adverse event reporting additional description:

At Week 16, most PBO-randomized participants escaped to CZP 400 mg Q2W and all ETN-randomized participants switched to PBO or CZP, leading to a significantly lower exposure in PBO/ETN arms than in CZP arms. Considering the limitations of such comparison, AEs reported while the participants were on PBO or ETN are not included in this summary.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	CZP 200 mg Q2W (TCS)

Reporting group description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

Reporting group title	CZP 400 mg Q2W (TCS)

Reporting group description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

Serious adverse events	CZP 200 mg Q2W (TCS)	CZP 400 mg Q2W (TCS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	37 / 373 (9.92%)	51 / 412 (12.38%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anaplastic oligodendroglioma			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Laryngeal cancer			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy with contraceptive			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodule			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
House dust allergy			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical polyp			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			

subjects affected / exposed	1 / 373 (0.27%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cyst			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 373 (0.54%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Bipolar I disorder			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Mycobacterium tuberculosis complex test negative			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Extradural haematoma			

subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 373 (0.00%)	2 / 412 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			

subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 373 (0.27%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Intracardiac mass			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Angina pectoris			

subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 373 (0.00%)	2 / 412 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Primary progressive multiple sclerosis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tympanic membrane perforation			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			

subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 373 (0.27%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatic failure			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guttate psoriasis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pustular psoriasis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purpura			

subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary bladder haemorrhage			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Sacroiliitis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chondropathy			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility decreased			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 373 (0.80%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreas infection			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 373 (0.27%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 373 (0.27%)	2 / 412 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 373 (0.27%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 373 (0.27%)	0 / 412 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 373 (0.00%)	1 / 412 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	CZP 200 mg Q2W (TCS)	CZP 400 mg Q2W (TCS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	150 / 373 (40.21%)	159 / 412 (38.59%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 373 (5.36%)	24 / 412 (5.83%)	
occurrences (all)	21	24	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 373 (4.56%)	18 / 412 (4.37%)	
occurrences (all)	20	20	
Infections and infestations			
Bronchitis			
subjects affected / exposed	18 / 373 (4.83%)	18 / 412 (4.37%)	
occurrences (all)	21	19	
Nasopharyngitis			
subjects affected / exposed	57 / 373 (15.28%)	66 / 412 (16.02%)	
occurrences (all)	84	83	
Upper respiratory tract infection			
subjects affected / exposed	39 / 373 (10.46%)	45 / 412 (10.92%)	
occurrences (all)	58	64	
Viral upper respiratory tract infection			
subjects affected / exposed	23 / 373 (6.17%)	11 / 412 (2.67%)	
occurrences (all)	38	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2015	Global Protocol Amendment 1 incorporated the country-specific amendments in the UK (Amendments 0.1 and 0.5), the Czech Republic (Amendment 0.2), Germany (Amendment 0.3), and France (Amendment 0.4). In addition, the following changes were made: •Updated study contact information. •The treatment received in Period 3 was based on initial treatment and response to treatment at Week 16. All CZP and Placebo (PBO) treatments were to be administered by dedicated unblinded site personnel at site visits. -Subjects initially randomized to CZP 200 mg Q2W were rerandomized (2:2:1) to receive either CZP 200 mg Q2W or CZP 400 mg Q4W (with PBO administered on alternate dosing weeks to maintain the blind) or PBO •Etanercept (ETN) treatments were allowed to be administered by trained study staff on site or outside of the study center (to allow flexibility around self-administration). If ETN was self-administered, compliance was to be recorded on a drug administration log by the subject and data were to be entered into the electronic Case Report form (eCRF) by study personnel. The percentage of doses missed (2 or more doses changed to 25% or more of the doses) was updated; ETN was administered more frequently than CZP or placebo during the Initial Treatment Period. •The number of planned sites was increased (from 50 to 67) and Australia and Canada were removed. •Exclusion Criterion #6 was clarified to include latex hypersensitivity. •Changes were made to drug accountability to allow for on-site destruction with prior Sponsor approval. •Secukinumab was added as a prohibited concomitant treatment. •Stratification across sites based on prior biologic use was eliminated. •Text describing the modified Nail Psoriasis Severity Index (mNAPSI) was updated. •Elispot testing for tuberculosis was removed. The chest x-ray required at screening was not needed if an x-ray had already been performed within 3 months of screening. •A center-by-treatment interaction analysis was added and described.

23 December 2015	Global Protocol Amendment 2 included the following changes: •CIMPACT (name of the PS0003 protocol) was added. •Updated study contact information. •Having at least a 90% reduction from Baseline in Psoriasis Area and Severity Index (PASI90) at Weeks 12 and 16 were added as secondary efficacy variables and PASI90 at Week 12 was included in the sequential testing procedure for the efficacy analysis. •Added time to onset of PASI90 as an efficacy variable. Deleted time to loss of PASI75 response at Week 16. Added EQ-5D-Visual Analog Scale (VAS) (inadvertently omitted in previous protocol). •Clarified the dosing period during the Initial Treatment Period, assessments performed, and use of unblinded study staff for drug administration. •Clarified study medication administration in Open-label Extension (OLE) Treatment Period. •Added secukinumab 24 weeks prior to the Baseline Visit as an exclusion for prior treatment. •Clarified the withdrawal criteria and addition of a withdrawal criterion to be consistent with the study population. See Exclusion Criterion #6. •Text was added to clarify that the unblinded team at the site was to transition their activities once the Week 48 visits (blinded Maintenance Treatment Period) were completed. •Clarified prohibited concomitant medications and therapies. •Added a window for the Safety Follow-Up (SFU) Visit (10 weeks after final dose); the visit should have occurred no more than 3 days prior to the scheduled visit date and within 14 days after the scheduled visit date (-3 days/+14 days). •Addition of a "Treated with CZP Set" (TCS) to further assess the safety of CZP in subjects with PSO. Addition of a Maintenance Set (MS) to further assess the efficacy and safety of CZP in long-term treatment of PSO.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29660425