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

Summary

EudraCT number	2014-003513-28
Trial protocol	DE CZ HU
Global end of trial date	24 October 2018

Results information

Result version number	v1 (current)
This version publication date	08 November 2019
First version publication date	08 November 2019

Trial information

Trial identification

Sponsor protocol code	PS0005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02326298
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	29 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate 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 at Weeks 0, 2, and 4 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 as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	16 December 2014
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	Czech Republic: 24
Country: Number of subjects enrolled	Canada: 42
Country: Number of subjects enrolled	Germany: 77
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	United States: 78
Worldwide total number of subjects	234
EEA total number of subjects	114

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)	221
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in December 2014 and concluded in October 2018 from multiple sites in Europe and North America. 234 participants were included in the Randomized Set (RS) shown in the Participant Flow.

Pre-assignment

Screening details:

The study included a 5 Week Screening Period, a Double-blind Initial Treatment Period up to Week 16, a Dose-blind Maintenance Treatment Period up to Week 48, an Open-label Treatment Period up to Week 144 and a Post Study Safety Follow-up Period up to Week 152.
Participant Flow refers to the Randomized Set, Open Label Set and Maintenance Set.

Period 1

Period 1 title	Initial Period (Week 0 to Week 16)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Q2W

Arm description:

Placebo sc injection Q2W.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16, who did not achieve a PASI75 response at Week 16 received CZP 400 mg at Weeks 16, 18 and 20 (loading doses) followed by CZP 200 mg Q2W starting at Week 22.
•PASI75 responders at Week 16 continued to receive Placebo.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the Open-label Extension (OLE) Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.

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), administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	CZP 200 mg Q2W

Arm description:

CZP 400 mg at Weeks 0, 2, 4, followed by CZP 200 mg Q2W from Week 6 to Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 200 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W.
Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to

CZP 200 mg Q2W.
Depending on PASI50 or PASI75 responses at Week 60 or a later time point, participants may have switched to CZP 400 mg Q2W or withdrew 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	CZP 400 mg Q2W

Arm description:

CZP 400 mg Q2W through Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 400 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Participants who achieved a PASI75 response during the OLE Period may have switched to CZP 200 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Number of subjects in period 1	Placebo Q2W	CZP 200 mg Q2W	CZP 400 mg Q2W
Started	51	95	88
Completed Week 16	46	92	87
Finished Wk16 started Maintenance Period	46	92	85
Completed	46	92	85
Not completed	5	3	3
Consent withdrawn by subject	3	2	-
Adverse event after completing wk16	-	-	2
Adverse event, non-fatal	-	-	1
Lost to follow-up	1	1	-
Lack of efficacy	1	-	-

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, Carer, Investigator, Assessor

Blinding implementation details:

Participants who entered the escape arms of the study received open-label CZP 400 mg every two weeks.

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 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), administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	Placebo/CZP 200 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI50 response at Week 16 but not a PASI75 response and received CZP 400 mg at Weeks 16, 18, and 20 (loading doses) followed by CZP 200 mg Q2W (starting at Week 22).

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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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), administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	CZP 200 mg Q2W/CZP 200 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg Q2W arm, who achieved a PASI50 response at Week 16 and continued to receive CZP 200 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	CZP 400 mg Q2W/CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg Q2W arm, who achieved a PASI50 response at Week 16 and continued to receive CZP 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	Placebo/Escape CZP 400 mg Q2W

Arm description:

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received unblinded CZP 400 mg Q2W, for 16 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	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), administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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 Q2W arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received CZP unblinded 400 mg Q2W, for 16 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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 Q2W arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received unblinded CZP 400 mg Q2W, for 16 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Number of subjects in period 2	Placebo/Placebo Q2W	Placebo/CZP 200 mg Q2W	CZP 200 mg Q2W/CZP 200 mg Q2W
Started	3	5	74
Completed Week 48	3	5	71
Finished Wk48 entered Open-label Period	3	5	69
Completed	3	5	69
Not completed	0	0	5
Patient did not achieve PASI50 response	-	-	1
Consent withdrawn by subject	-	-	1
No valid reason stated by patient	-	-	-
Adverse event, non-fatal	-	-	-
Pregnancy	-	-	-
Patient cannot attend visits	-	-	1
Did not achieve PASI50 after week 48	-	-	2
Lost to follow-up	-	-	-

Number of subjects in period 2	CZP 400 mg Q2W/CZP 400 mg Q2W	Placebo/Escape CZP 400 mg Q2W	CZP 200 mg Q2W/Escape CZP 400 mg Q2W
Started	77	38	18

Completed Week 48	70	33	13
Finished Wk48 entered Open-label Period	70	33	13
Completed	70	33	13
Not completed	7	5	5
Patient did not achieve PASI50 response	2	-	4
Consent withdrawn by subject	3	1	1
No valid reason stated by patient	-	1	-
Adverse event, non-fatal	-	1	-
Pregnancy	1	-	-
Patient cannot attend visits	-	-	-
Did not achieve PASI50 after week 48	-	-	-
Lost to follow-up	1	2	-

Number of subjects in period 2	CZP 400 mg Q2W/Escape CZP 400 mg Q2W
Started	8
Completed Week 48	7
Finished Wk48 entered Open-label Period	7
Completed	7
Not completed	1
Patient did not achieve PASI50 response	-
Consent withdrawn by subject	1
No valid reason stated by patient	-
Adverse event, non-fatal	-
Pregnancy	-
Patient cannot attend visits	-
Did not achieve PASI50 after week 48	-
Lost to follow-up	-

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 who received dose-blind Placebo during the Maintenance Period, who achieved a PASI50 response at Week 48 and entered the 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), administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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

Arm description:

This arm consisted of participants who received blinded CZP 200mg Q2W in the Maintenance Period, who achieved a PASI50 response 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

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

Arm description:

This arm consisted of participants who received blinded CZP 400mg Q2W in the Maintenance Period, who achieved a PASI50 response 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Arm title	Escape 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 on the CZP 400mg 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, were administered at separate injection sites: lateral abdominal wall and upper outer thigh.

Number of subjects in period 3	Placebo/CZP 200 mg Q2W OLE	CZP 200 mg Q2W/CZP 200 mg Q2W OLE	CZP 400 mg Q2W/CZP 200 mg Q2W OLE
Started	3	74	70
Completed	3	54	51
Not completed	0	20	19
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	7	2
Adverse event, non-fatal	-	3	3
Protocol violation	-	-	-
Lost to follow-up	-	6	6
Lack of efficacy	-	1	1
Did not achieve PASI50	-	2	7
Protocol deviation	-	-	-

Number of subjects in period 3	Escape CZP 400 mg Q2W/CZP 400 mg Q2W OLE
Started	53
Completed	44
Not completed	9
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Protocol violation	1
Lost to follow-up	3
Lack of efficacy	-
Did not achieve PASI50	3
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo Q2W

Reporting group description:

Placebo sc injection Q2W.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16, who did not achieve a PASI75 response at Week 16 received CZP 400 mg at Weeks 16, 18 and 20 (loading doses) followed by CZP 200 mg Q2W starting at Week 22.
•PASI75 responders at Week 16 continued to receive Placebo.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the Open-label Extension (OLE) Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.

Reporting group title	CZP 200 mg Q2W

Reporting group description:

CZP 400 mg at Weeks 0, 2, 4, followed by CZP 200 mg Q2W from Week 6 to Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 200 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W.
Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Depending on PASI50 or PASI75 responses at Week 60 or a later time point, participants may have switched to CZP 400 mg Q2W or withdrew from the study.

Reporting group title	CZP 400 mg Q2W

Reporting group description:

CZP 400 mg Q2W through Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 400 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Participants who achieved a PASI75 response during the OLE Period may have switched to CZP 200 mg Q2W.

Reporting group values	Placebo Q2W	CZP 200 mg Q2W	CZP 400 mg Q2W
Number of subjects	51	95	88
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	45	90	86
>=65 years	6	5	2
Age continuous Units: Years			
arithmetic mean	47.9	44.5	43.6
standard deviation	± 12.8	± 13.1	± 12.1

Gender categorical Units: Subjects			
Female	16	28	28
Male	35	67	60

Reporting group values	Total		
Number of subjects	234		
Age categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	221		
>=65 years	13		
Age continuous Units: Years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	72		
Male	162		

Subject analysis sets

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

Subject analysis set description:

Placebo sc injection Q2W.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16, who did not achieve a PASI75 response at Week 16 received CZP 400 mg at Weeks 16, 18 and 20 (loading doses) followed by CZP 200 mg Q2W starting at Week 22.
•PASI75 responders at Week 16 continued to receive Placebo.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
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 at Weeks 0, 2, 4, followed by CZP 200 mg Q2W from Week 6 to Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 200 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W.
Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Depending on PASI50 or PASI75 responses at Week 60 or a later time point, participants may have switched to CZP 400 mg Q2W or withdrew from the study.
Participants formed the RS.

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

Subject analysis set description:

CZP 400 mg Q2W through Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 400 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Participants who achieved a PASI75 response during the OLE Period may have switched to CZP 200 mg Q2W.
Participants formed the RS.

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)	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)
Number of subjects	51	95	88
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	45	90	86
>=65 years	6	5	2
Age continuous Units: Years			
arithmetic mean	47.9	44.5	43.6
standard deviation	± 12.8	± 13.1	± 12.1
Gender categorical Units: Subjects			
Female	16	28	28
Male	35	67	60

Reporting group values	CZP 200 mg Q2W (TCS)	CZP 400 mg Q2W (TCS)	
Number of subjects	188	167	
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	177	160	
>=65 years	11	7	
Age continuous Units: Years			
arithmetic mean	44.9	44.8	
standard deviation	± 12.9	± 12.1	
Gender categorical Units: Subjects			
Female	55	52	
Male	133	115	

End points

End points reporting groups

Reporting group title	Placebo Q2W

Reporting group description:

Placebo sc injection Q2W.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16, who did not achieve a PASI75 response at Week 16 received CZP 400 mg at Weeks 16, 18 and 20 (loading doses) followed by CZP 200 mg Q2W starting at Week 22.
•PASI75 responders at Week 16 continued to receive Placebo.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the Open-label Extension (OLE) Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.

Reporting group title	CZP 200 mg Q2W

Reporting group description:

CZP 400 mg at Weeks 0, 2, 4, followed by CZP 200 mg Q2W from Week 6 to Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 200 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W.
Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Depending on PASI50 or PASI75 responses at Week 60 or a later time point, participants may have switched to CZP 400 mg Q2W or withdrew from the study.

Reporting group title	CZP 400 mg Q2W

Reporting group description:

CZP 400 mg Q2W through Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 400 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Participants who achieved a PASI75 response during the OLE Period may have switched to CZP 200 mg Q2W.

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 Placebo in the Maintenance Period (Week 16 to Week 48).

Reporting group title	Placebo/CZP 200 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI50 response at Week 16 but not a PASI75 response and received CZP 400 mg at Weeks 16, 18, and 20 (loading doses) followed by CZP 200 mg Q2W (starting at Week 22).

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 Q2W arm, who achieved a PASI50 response at Week 16 and continued to receive CZP 200 mg Q2W.

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 Q2W arm, who achieved a PASI50 response at Week 16 and continued to receive CZP 400 mg Q2W.

Reporting group title	Placebo/Escape CZP 400 mg Q2W

Reporting group description:

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received unblinded CZP 400 mg Q2W, for 16 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 Q2W arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received CZP unblinded 400 mg Q2W, for 16 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 Q2W arm, who did not achieve a PASI50 response at Week 16 escaped from the blinded treatment and received unblinded CZP 400 mg Q2W, for 16 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 who received dose-blind Placebo during the Maintenance Period, who achieved a PASI50 response at Week 48 and entered the 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 blinded CZP 200mg Q2W in the Maintenance Period, who achieved a PASI50 response 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 blinded CZP 400mg Q2W in the Maintenance Period, who achieved a PASI50 response at Week 48, and entered OLE on the CZP 200mg Q2W dose.

Reporting group title	Escape 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 on the CZP 400mg Q2W dose.

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

Subject analysis set description:

Placebo sc injection Q2W.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16, who did not achieve a PASI75 response at Week 16 received CZP 400 mg at Weeks 16, 18 and 20 (loading doses) followed by CZP 200 mg Q2W starting at Week 22.
•PASI75 responders at Week 16 continued to receive Placebo.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
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 at Weeks 0, 2, 4, followed by CZP 200 mg Q2W from Week 6 to Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 200 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to

unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W.
Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Depending on PASI50 or PASI75 responses at Week 60 or a later time point, participants may have switched to CZP 400 mg Q2W or withdrew from the study.
Participants formed the RS.

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

Subject analysis set description:

CZP 400 mg Q2W through Week 14.
Treatment received from Week 16 - 48 was based on initial treatment and response to treatment:
•PASI50 responders at Week 16 continued to receive CZP 400 mg Q2W.
•PASI50 non-responders at Week 16 were removed from blinded study medication and escaped to unblinded 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.
•PASI50 non-responders at Week 32 or a later time point were withdrawn from the study.
Participants who completed the Maintenance Period (with PASI50 response at Week 48) entered the OLE Period on CZP 200 mg Q2W. Week 48 completers in the escape arm continued to receive CZP 400 mg Q2W or may have switched to CZP 200 mg Q2W.
Participants who achieved a PASI75 response during the OLE Period may have switched to CZP 200 mg Q2W.
Participants formed the RS.

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 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	Primary

End point timeframe:

At 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	51	95	88	
Units: percentage of participants				
number (not applicable)	6.5	66.5	75.8	

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	28.962
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	6.968
upper limit	120.371

Notes:

[1] - The p-value for the primary analysis was evaluated at a 2-sided significance level of 0.025 for each CZP dose versus (vs) PBO.

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	45.66
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	10.657
upper limit	195.634

Notes:

[2] - The p-value for the primary analysis was evaluated at a 2-sided significance level of 0.025 for each CZP dose vs PBO.

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	60
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.92
upper limit	72.17

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	69.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	57.65
upper limit	80.99

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

End point title	Proportion of subjects who achieve a Physician’s Global Assessment (PGA) Clear or Almost Clear (with at least 2-category improvement) response 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	Primary
End point timeframe:	
At 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	51	95	88	
Units: percentage of participants				
number (not applicable)	4.2	47.0	57.9	

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	20.116
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	3.699
upper limit	109.399

Notes:

[3] - The p-value for the primary analysis was evaluated at a 2-sided significance level of 0.025 for each CZP dose vs PBO.

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	31.143
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.687
upper limit	170.548

Notes:

[4] - The p-value for the primary analysis was evaluated at a 2-sided significance level of 0.025 for each CZP dose vs PBO.

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	42.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.7
upper limit	54.86

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	53.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	41.33
upper limit	65.94

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:

At 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	51	95	88	
Units: percentage of participants				
number (not applicable)	0.4	35.8	43.6	

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	36.668
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.717
upper limit	235.193

Notes:

[5] - The p-value for this analysis as used in the fixed sequence testing procedure was evaluated at a 2-sided significance level of 0.025 for each CZP dose vs PBO.

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 400 mg Q2W (RS)

Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	50.606
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	7.88
upper limit	324.988

Notes:

[6] - The p-value for this analysis as used in the fixed sequence testing procedure was evaluated at a 2-sided significance level of 0.025 for each CZP dose vs PBO.

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	35.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.85
upper limit	49.87

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Estimated difference in responder rate
Point estimate	43.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.56
upper limit	58.71

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16

End point description:

The DLQI is a subject-reported questionnaire designed for use in adult participants with PSO. The DLQI is a skin disease-specific questionnaire aimed at the evaluation of how symptoms and treatment affect patients' health related quality of life (HRQoL). This instrument asks participants about symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. It has been shown to be valid and reproducible in PSO patients. The DLQI score ranges from 0 to 30 with higher scores indicating lower HRQoL. A higher than of equal to (>=) 4-point change in the DLQI score (DLQI response) has been reported to be meaningful for the patient (within-patient minimal important difference Basra et al, 2015) a DLQI absolute score of lower than or equal to (=<) 1 indicates DLQI remission (i.e., no or small impact of the disease on HRQoL).

End point type	Secondary

End point timeframe:

At 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	51	95	88	
Units: Scores on a scale				
least squares mean (standard error)	-3.3 (± 0.80)	-9.3 (± 0.58)	-10.2 (± 0.60)	

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 200 mg Q2W (RS)
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	ANCOVA
Parameter estimate	Adjusted Mean Treatment Differences
Point estimate	-6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-8.18
upper limit	-3.81

Notes:

[7] - P-value obtained for each treatment group comparison tested at a significance level of 0.025 in the fixed sequence testing procedure.

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 400 mg Q2W (RS)
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	ANCOVA
Parameter estimate	Ajusted Mean Treatment Differences
Point estimate	-6.84
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-9.05
upper limit	-4.62

Notes:

[8] - P-value obtained for each treatment group comparison tested at a significance level of 0.025 in the fixed sequence testing procedure.

Secondary: Proportion of subjects who achieve a Physician’s Global Assessment (PGA) Clear or Almost Clear (with at least 2-category improvement) response at Week 48

End point title	Proportion of subjects who achieve a Physician’s Global Assessment (PGA) Clear or Almost Clear (with at least 2-category improvement) response at Week 48

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:

At Week 48

End point values	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	95	88		
Units: percentage of participants				
number (confidence interval 95%)	52.7 (41.99 to 63.32)	69.5 (59.24 to 79.77)		

Statistical analyses

No statistical analyses for this end point

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

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

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:

At Week 48

End point values	CZP 200 mg Q2W (RS)	CZP 400 mg Q2W (RS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	95	88		
Units: percentage of participants				
number (confidence interval 95%)	67.2 (57.09 to 77.39)	87.1 (79.81 to 94.45)		

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 the Post Study Safety Follow-up Visit (Week 152).

Adverse event reporting additional description:

Participants randomized to PBO switched to CZP 200mg Q2W or CZP 400mg Q2W at Week 16. Participants randomized to CZP were exposed for up to 144 weeks, leading to a significantly lower exposure in the PBO than CZP arm. Considering the imbalance of such comparison, AEs reported while participants were on PBO 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 400 mg Q2W (TCS)

Reporting group description:

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

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.

Serious adverse events	CZP 400 mg Q2W (TCS)	CZP 200 mg Q2W (TCS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 167 (11.38%)	14 / 188 (7.45%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Gastric bypass			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Strangulated hernia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site reaction			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactoid reaction			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

subjects affected / exposed	2 / 167 (1.20%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
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			
Concussion			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
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	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haematoma			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blepharochalasis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal necrosis			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cirrhosis alcoholic			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Psoriasis			

subjects affected / exposed	1 / 167 (0.60%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle atrophy			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (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			

Anal abscess			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Borrelia infection			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 167 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 167 (0.60%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CZP 400 mg Q2W (TCS)	CZP 200 mg Q2W (TCS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 167 (50.90%)	95 / 188 (50.53%)	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 167 (8.38%)	9 / 188 (4.79%)	
occurrences (all)	41	18	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	5 / 167 (2.99%)	9 / 188 (4.79%)	
occurrences (all)	5	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 167 (2.40%)	14 / 188 (7.45%)	
occurrences (all)	5	16	
Back pain			
subjects affected / exposed	11 / 167 (6.59%)	12 / 188 (6.38%)	
occurrences (all)	12	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	51 / 167 (30.54%)	54 / 188 (28.72%)	
occurrences (all)	95	86	
Upper respiratory tract infection			
subjects affected / exposed	26 / 167 (15.57%)	21 / 188 (11.17%)	
occurrences (all)	42	28	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2015	The Global Protocol Amendment 1 included the following changes: -CIMPASI-1 (name of the PS0005 protocol) was added. -Updated study contact information and serious adverse event (SAE) reporting contact information. -Added the secondary efficacy variable: at least 90% reduction from Baseline in PASI (PASI90). -Removed the other efficacy variables: absolute PASI score and absolute body surface area (BSA) affected by PSO. -Corrected: the Subject Questionnaire for Tuberculosis (TB) was removed as a safety variable. -Clarified the responsibilities of the unblinded and blinded study personnel. -Provided additional details regarding breaking the treatment blind in an emergency situation. -Revised Exclusion Criteria number (#) 21 to add secukinumab and require a 24-week washout period. -Allowed flexibility of self-administration of certolizumab pegol (CZP) during the Open-label Treatment Period. -Corrected: subject treatment assignment was stratified by site.

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/29660421