Clinical trial results:
A Double-blind, Randomized, Placebo-controlled Study Evaluating the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of Multiple Doses of UCB4940 Administered as Add-on to Certolizumab Pegol Therapy in Subjects with Moderate-to-Severe Rheumatoid Arthritis

Summary

EudraCT number	2014-003307-30
Trial protocol	HU SK CZ GB
Global end of trial date	19 April 2017

Results information

Result version number	v1 (current)
This version publication date	04 May 2018
First version publication date	04 May 2018

Trial information

Trial identification

Sponsor protocol code	RA0123

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02430909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Celltech, UK Registered Branch of UCB Pharma SA
Sponsor organisation address	208 Bath Road, Slough, Berkshire, United Kingdom, SL1 3WE
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	06 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of bimekizumab (UCB4940) as an add-on therapy to certolizumab pegol (CZP) and background conventional disease-modifying anti-rheumatic drugs (DMARDs) compared to placebo plus CZP treatment and background conventional DMARDs and to evaluate the efficacy of bimekizumab as an add-on therapy to CZP and background conventional DMARDs compared to placebo plus CZP treatment and background conventional DMARDs at Week 20

Protection of trial subjects:

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

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

No

Actual start date of recruitment	05 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Moldova, Republic of: 14
Country: Number of subjects enrolled	Poland: 54
Country: Number of subjects enrolled	Russian Federation: 73
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	159
EEA total number of subjects	72

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	138
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in May 2015 and concluded in April 2017. 288 subjects were included in the Screening Set. 129 subjects dropped screening and were excluded from the Safety Analysis Set.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Analysis Set which included all subjects who took at least 1 dose of study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	CZP / CZP + PBO / CZP

Arm description:

Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + Placebo from Week 8 to Week 18

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

Dosage and administration details:

Certolizumab pegol was supplied in prefilled syringes (PFS) containing a dosage strength of 200 mg/mL and given as a subcutaneous (sc) injection. CZP treatment started with a dosage of 400 mg at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks from Week 6.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was supplied as 0.9 % sodium chloride aqueous solution for intravenous infusion from Week 8 to Week 18 in order to maintain the blinding.

Arm title	CZP / CZP + BKZ / CZP

Arm description:

Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + UCB4940 from Week 8 until Week 18

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	UCB4940
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Active investigational product (infusion solution containing 80 mg/mL UCB4940) administered as intravenous (iv) infusion starting at Week 8 with a 240 mg loading dose followed by 120 mg every 2 weeks.

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

Dosage and administration details:

Certolizumab pegol was supplied in prefilled syringes (PFS) containing a dosage strength of 200 mg/mL and given as a subcutaneous (sc) injection. CZP treatment started with a dosage of 400 mg at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks from Week 6.

Arm title	CZP / CZP / CZP

Arm description:

Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30

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

Dosage and administration details:

Certolizumab pegol was supplied in prefilled syringes (PFS) containing a dosage strength of 200 mg/mL and given as a subcutaneous (sc) injection. CZP treatment started with a dosage of 400 mg at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks from Week 6.

Number of subjects in period 1	CZP / CZP + PBO / CZP	CZP / CZP + BKZ / CZP	CZP / CZP / CZP
Started	27	52	80
Completed	23	43	66
Not completed	4	9	14
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	1	5	2
Adverse event, non-fatal	2	4	8
Pregnancy	-	-	1
Lost to follow-up	-	-	1
Sponsor decision	-	-	2

Baseline characteristics

Reporting groups	
Reporting group title	CZP / CZP + PBO / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + Placebo from Week 8 to Week 18	
Reporting group title	CZP / CZP + BKZ / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + UCB4940 from Week 8 until Week 18	
Reporting group title	CZP / CZP / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30	

Reporting group values	CZP / CZP + PBO / CZP	CZP / CZP + BKZ / CZP	CZP / CZP / CZP
Number of subjects	27	52	80
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	25	47	66
From 65-84 years	2	5	14
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.6	51.7	55.1
standard deviation	± 9.5	± 11.3	± 11.7
Gender categorical Units: Subjects			
Female	23	45	67
Male	4	7	13
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	27	51	79
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	27	52	80

More than one race	0	0	0

Reporting group values	Total		
Number of subjects	159		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	138		
From 65-84 years	21		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	135		
Male	24		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	157		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Black or African American	0		
Native Hawaiian or Other Pacific Islander	0		
White	159		
More than one race	0		

End points

End points reporting groups

Reporting group title	CZP / CZP + PBO / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + Placebo from Week 8 to Week 18	
Reporting group title	CZP / CZP + BKZ / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + UCB4940 from Week 8 until Week 18	
Reporting group title	CZP / CZP / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30	
Subject analysis set title	CZP / CZP + PBO / CZP-SS
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set (SS) consisted of all subjects who received at least 1dose (full or partial) of any study medication. In the case of dosing administration error, analyses on the SS were conducted according to actual treatment received. The SS was used for the safety analyses. The safety analyses of the randomized subjects was conducted on the Safety Subset (SSsub) that was defined as all randomized subjects who received at least 1 dose (full or partial) of bimekizumab or placebo.	
Subject analysis set title	CZP / CZP + BKZ / CZP-SS
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set (SS) consisted of all subjects who received at least 1dose (full or partial) of any study medication. In the case of dosing administration error, analyses on the SS were conducted according to actual treatment received. The SS was used for the safety analyses. The safety analyses of the randomized subjects was conducted on the Safety Subset (SSsub) that was defined as all randomized subjects who received at least 1 dose (full or partial) of bimekizumab or placebo.	
Subject analysis set title	CZP / CZP / CZP-SS
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set (SS) consisted of all subjects who received at least 1dose (full or partial) of any study medication. In the case of dosing administration error, analyses on the SS were conducted according to actual treatment received. The SS was used for the safety analyses. The safety analyses of the randomized subjects was conducted on the Safety Subset (SSsub) that was defined as all randomized subjects who received at least 1 dose (full or partial) of bimekizumab or placebo.	
Subject analysis set title	CZP / CZP + PBO / CZP-FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) consisted of all subjects who received at least 1 dose (full or partial) of any study medication and who had at least 1 available measurement of any efficacy variables post-Baseline 1.	
Subject analysis set title	CZP / CZP + BKZ / CZP-FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) consisted of all subjects who received at least 1 dose (full or partial) of any study medication and who had at least 1 available measurement of any efficacy variables post-Baseline 1.	
Subject analysis set title	CZP / CZP / CZP-FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) consisted of all subjects who received at least 1 dose (full or partial) of any study medication and who had at least 1 available measurement of any efficacy variables post-Baseline 1.	

Primary: Incidence of Adverse Events

End point title	Incidence of Adverse Events[1]

End point description:

All adverse events (AEs) are recorded during the entire study period.

End point type	Primary

End point timeframe:

From Baseline (Week 0) until final study visit (Week 44)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	CZP / CZP + PBO / CZP-SS	CZP / CZP + BKZ / CZP-SS	CZP / CZP / CZP-SS	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	52	80	
Units: percentage of participants				
number (not applicable)	70.4	82.7	67.5	

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline 2 to Week 20 in DAS28(CRP)

End point title	Change from Baseline 2 to Week 20 in DAS28(CRP)[2]

End point description:

DAS28 (Disease Activity Score 28) is a measure of disease activity in Rheumatoid Arthritis (RA) and is a composite score derived from the number of swollen and tender joints (out of 28), the CRP value and the patient global assessment of disease activity.
A negative value in Change from Baseline indicates an improvement from Baseline.

End point type	Primary

End point timeframe:

Week 20

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The Bayesian model uses an informative prior distribution for the PBO+CZP group, vague priors for all other parameters. Fixed effect; treatment. Covariate; DAS28(CRP) at baseline 2.
It is a pre-specified superiority analysis. 70 subjects were included in 2 comparison groups [CZP/CZP + PBO/CZP-FAS; CZP/CZP + BKZ/CZP-FAS]. The posterior probability of a difference from Placebo being greater than 0 was 99.4 %. Point estimate (Mean Difference (SD)): 0.58 (0.23); 95% Credible interval: [0.13, 1.05]

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	46		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.82 (± 0.17)	-1.41 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent improvement in ACR (American College of Rheumatology) criteria (ACRn) based on Baseline 2

End point title	Percent improvement in ACR (American College of Rheumatology) criteria (ACRn) based on Baseline 2

End point description:

ACRn is the percentage improvement from Baseline 2 in the number of tender joints, in the number of swollen joints, and in 3 of the 5 remaining core set measures: Patient's Global Assessment of Disease Activity (PtGADA), Physician's Global Assessment of Disease Activity (PhGADA), Patient's Assessment of Arthritis Pain (PtAAP), physical function as assessed by the Health Assessment Questionnaire - Disability Index (HAQ-DI) and C-Reactive Protein (CRP).

End point type	Secondary

End point timeframe:

Week 20

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	43		
Units: units on a scale				
arithmetic mean (standard deviation)	17.03 (± 40.94)	19.21 (± 60.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20 response based on Baseline 2

End point title	ACR20 response based on Baseline 2

End point description:

The assessments are based on a 20 % or greater improvement from Baseline 2 in the number of tender joints, in the number of swollen joints, and a 20 % or greater improvement in 3 of the 5 remaining core set measures: Patient's Global Assessment of Disease Activity (PtGADA), Physician's Global Assessment of Disease Activity (PhGADA), Patient's Assessment of Arthritis Pain (PtAAP), physical function as assessed by the Health Assessment Questionnaire - Disability Index (HAQ-DI) and C-Reactive Protein (CRP).

End point type	Secondary

End point timeframe:

Week 20

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	43		
Units: percentage of responder				
number (not applicable)	54.2	60.5		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR50 response based on Baseline 2

End point title	ACR50 response based on Baseline 2

End point description:

The assessments are based on a 50 % or greater improvement from Baseline 2 in the number of tender joints, in the number of swollen joints, and a 50 % or greater improvement in 3 of the 5 remaining core set measures: Patient's Global Assessment of Disease Activity (PtGADA), Physician's Global Assessment of Disease Activity (PhGADA), Patient's Assessment of Arthritis Pain (PtAAP), physical function as assessed by the Health Assessment Questionnaire - Disability Index (HAQ-DI) and C-Reactive Protein (CRP).

End point type	Secondary

End point timeframe:

Week 20

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	43		
Units: percentage of responder				
number (not applicable)	8.3	34.9		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR70 response based on Baseline 2

End point title	ACR70 response based on Baseline 2

End point description:

The assessments are based on a 70 % or greater improvement from Baseline 2 in the number of tender joints, in the number of swollen joints, and a 70 % or greater improvement in 3 of the 5 remaining core set measures: Patient's Global Assessment of Disease Activity (PtGADA), Physician's Global Assessment of Disease Activity (PhGADA), Patient's Assessment of Arthritis Pain (PtAAP), physical function as assessed by the Health Assessment Questionnaire - Disability Index (HAQ-DI) and C-Reactive Protein

(CRP).

End point type	Secondary

End point timeframe:

Week 20

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	43		
Units: percentage of responder				
number (not applicable)	0	14.0		

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28(CRP) remission at Week 20

End point title	DAS28(CRP) remission at Week 20

End point description:

DAS28(CRP) remission is defined as DAS28(CRP) < 2.6. DAS28 is a measure of disease activity in Rheumatoid Arthritis (RA) and is a composite score derived from the number of swollen and tender joints (out of 28) , the C-reactive protein value and the patient global assessment of disease activity.

End point type	Secondary

End point timeframe:

Week 20

End point values	CZP / CZP + PBO / CZP-FAS	CZP / CZP + BKZ / CZP-FAS	CZP / CZP / CZP-FAS	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	46	68	
Units: percentage of remitter				
number (not applicable)	8.3	26.1	52.9	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected during the whole study from Study Start (Day 1) until Safety Follow-Up or Withdrawal Visit (up to Week 44)	
Adverse event reporting additional description:	
For the incidence of Treatment-Emergent Adverse Events (TEAEs) by Relationship, related is defined as related to bimekizumab (BKZ)/placebo and/or related to certolizumab pegol (CZP).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	CZP / CZP + PBO / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + Placebo from Week 8 to Week 18	
Reporting group title	CZP / CZP + BKZ / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30 + UCB4940 from Week 8 until Week 18	
Reporting group title	CZP / CZP / CZP
Reporting group description:	
Certolizumab Pegol (400 mg at Weeks 0, 2, and 4 followed by 200 mg every 2 weeks) until Week 30	

Serious adverse events	CZP / CZP + PBO / CZP	CZP / CZP + BKZ / CZP	CZP / CZP / CZP
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	3 / 52 (5.77%)	7 / 80 (8.75%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 27 (0.00%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 27 (3.70%)	0 / 52 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 27 (0.00%)	1 / 52 (1.92%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tension headache			
subjects affected / exposed	1 / 27 (3.70%)	0 / 52 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 52 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 52 (1.92%)	2 / 80 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bursitis infective			
subjects affected / exposed	0 / 27 (0.00%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 52 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 27 (0.00%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 27 (0.00%)	1 / 52 (1.92%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CZP / CZP + PBO / CZP	CZP / CZP + BKZ / CZP	CZP / CZP / CZP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 27 (44.44%)	23 / 52 (44.23%)	26 / 80 (32.50%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)	1 / 52 (1.92%)	6 / 80 (7.50%)
occurrences (all)	1	1	14
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)	2 / 52 (3.85%)	4 / 80 (5.00%)
occurrences (all)	1	2	8
Neutrophil count decreased			
subjects affected / exposed	0 / 27 (0.00%)	3 / 52 (5.77%)	0 / 80 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 27 (11.11%)	0 / 52 (0.00%)	1 / 80 (1.25%)
occurrences (all)	3	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 27 (7.41%)	0 / 52 (0.00%)	0 / 80 (0.00%)
occurrences (all)	2	0	0

Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	0 / 27 (0.00%)	3 / 52 (5.77%)	0 / 80 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 27 (0.00%)	4 / 52 (7.69%)	3 / 80 (3.75%)
occurrences (all)	0	4	4
Rash			
subjects affected / exposed	2 / 27 (7.41%)	1 / 52 (1.92%)	0 / 80 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	4 / 27 (14.81%)	3 / 52 (5.77%)	5 / 80 (6.25%)
occurrences (all)	6	4	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 27 (11.11%)	5 / 52 (9.62%)	8 / 80 (10.00%)
occurrences (all)	4	5	8
Upper respiratory tract infection			
subjects affected / exposed	2 / 27 (7.41%)	4 / 52 (7.69%)	5 / 80 (6.25%)
occurrences (all)	3	5	8
Pharyngitis			
subjects affected / exposed	1 / 27 (3.70%)	3 / 52 (5.77%)	3 / 80 (3.75%)
occurrences (all)	1	5	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported