Clinical trial results:
A MULTICENTER, SUBJECT-BLIND, INVESTIGATOR-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY EVALUATING THE EFFICACY, SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF AN IV LOADING DOSE FOLLOWED BY SC ADMINISTRATION OF BIMEKIZUMAB (UCB4940) IN SUBJECTS WITH MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS

Summary

EudraCT number	2016-000420-26
Trial protocol	CZ ES PL BG
Global end of trial date	30 May 2018

Results information

Result version number	v1 (current)
This version publication date	13 June 2019
First version publication date	13 June 2019

Trial information

Trial identification

Sponsor protocol code	UC0011

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SPRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 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	28 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of bimekizumab in adults with active ulcerative colitis who have not responded to standard therapy.

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:

Not applicable

Actual start date of recruitment	01 November 2016
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: 1
Country: Number of subjects enrolled	Georgia: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Moldova, Republic of: 7
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	23
EEA total number of subjects	5

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)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in November 2016 and concluded in May 2018.

Pre-assignment

Screening details:

The Participant Flow refers to the Randomized Set.

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	Investigator, Subject, Assessor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PBO
Other name	PBO
Pharmaceutical forms	Infusion, Injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Placebo given as an iv infusion at Visit 2 (Day 1) and placebo given as a sc injection at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).

Arm title	BKZ 560/420 mg

Arm description:

Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).

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

Dosage and administration details:

560 mg of bimekizumab (BKZ) given as a loading dose iv infusion at Visit 2 (Day 1) followed by 420 mg BKZ given by sc injection at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).

Number of subjects in period 1	Placebo	BKZ 560/420 mg
Started	8	15
Completed	6	8
Not completed	2	7
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	2
Early study termination	1	3
Lack of efficacy	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).	
Reporting group title	BKZ 560/420 mg
Reporting group description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).	

Reporting group values	Placebo	BKZ 560/420 mg	Total
Number of subjects	8	15	23
Age categorical Units: Subjects			
<=18 years	0	1	1
Between 18 and 65 years	8	14	22
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	36.8	38.9	
standard deviation	± 12.7	± 13.5	-
Gender categorical Units: Subjects			
Male	3	8	11
Female	5	7	12

Subject analysis sets	
Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Full Analysis Set (FAS).	
Subject analysis set title	BKZ 560/420 mg (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the FAS.	
Subject analysis set title	Placebo (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Safety Set (SS).	
Subject analysis set title	BKZ 560/420 mg (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2	

doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the SS.

Subject analysis set title	BKZ 560/420 mg (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Pharmacokinetic-Per Protocol Set (PK-PPS).

Reporting group values	Placebo (FAS)	BKZ 560/420 mg (FAS)	Placebo (SS)
Number of subjects	8	15	8
Age categorical Units: Subjects			
<=18 years	0	1	0
Between 18 and 65 years	8	14	8
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	36.8	38.9	36.8
standard deviation	± 12.7	± 13.5	± 12.7
Gender categorical Units: Subjects			
Male	3	8	3
Female	5	7	5

Reporting group values	BKZ 560/420 mg (SS)	BKZ 560/420 mg (PK-PPS)	
Number of subjects	15	15	
Age categorical Units: Subjects			
<=18 years	1	1	
Between 18 and 65 years	14	14	
>=65 years	0	0	
Age continuous Units: years			
arithmetic mean	38.9	38.9	
standard deviation	± 13.5	± 13.5	
Gender categorical Units: Subjects			
Male	8	8	
Female	7	7	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).	
Reporting group title	BKZ 560/420 mg
Reporting group description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days).	
Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Full Analysis Set (FAS).	
Subject analysis set title	BKZ 560/420 mg (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the FAS.	
Subject analysis set title	Placebo (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Safety Set (SS).	
Subject analysis set title	BKZ 560/420 mg (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the SS.	
Subject analysis set title	BKZ 560/420 mg (PK-PPS)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Pharmacokinetic-Per Protocol Set (PK-PPS).	

Primary: Percentage of Participants with Clinical Response (Per Mayo Score) at Week 8

End point title	Percentage of Participants with Clinical Response (Per Mayo Score) at Week 8[1]
End point description:	
Clinical Response achieved at Week 8 is defined as a decrease from Baseline in Total Mayo Score of at least 3 points and at least 30 percent (%), with an accompanying decrease in the subscore for Rectal Bleeding of at least 1 point or absolute subscore for Rectal Bleeding of 0 (no blood seen) or 1 (streaks of blood with stool less than half the time). The rectal bleeding score ranges from 0 (no blood seen) to 3 (blood alone passes).	
End point type	Primary
End point timeframe:	
At Week 8	

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: Given the lack of Week 8 data, expected at the end of the study (and lack of subjects completing the required dosing regimen), a decision has been made that none of the planned Bayesian analyses would be performed, as they would lack validity, given the data that would be available at the end of the study.

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (confidence interval 95%)	66.7 (30.0 to 90.3)	41.7 (19.3 to 68.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with Adverse Events throughout the study conduct up to Week 20

End point title	Percentage of participants with Adverse Events throughout the study conduct up to Week 20[2]

End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

End point type	Primary

End point timeframe:

Up to 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: Given the lack of Week 8 data, expected at the end of the study (and lack of subjects completing the required dosing regimen), a decision has been made that none of the planned Bayesian analyses would be performed, as they would lack validity, given the data that would be available at the end of the study.

End point values	Placebo (SS)	BKZ 560/420 mg (SS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (not applicable)	25.0	80.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission at Week 8

End point title	Percentage of Participants in Clinical Remission at Week 8

End point description:

Clinical Remission achieved at Week 8 is defined as a Total Mayo Score of lower than or equal to (<=) 2 points, with no individual subscore higher than (>) 1 point. The Mayo score ranges from 0 to 12, with higher scores indicating more severe disease.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	12		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 39.0)	16.7 (4.7 to 44.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Mucosal Healing at Week 8

End point title	Percentage of Participants with Mucosal Healing at Week 8

End point description:

Mucosal Healing achieved at Week 8 is defined as an Endoscopic subscore of <=1 point. The endoscopic scores ranges from 0 (normal or inactive disease) to 3 (severe disease).

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	12		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 39.0)	16.7 (4.7 to 44.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Stool Frequency Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point title	Percentage of Participants With Stool Frequency Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point description:

A score of 0 on the Stool Frequency Subscore indicates normal numbers of stools for the patient per day, while a score of 1 on the Stool Frequency Subscore indicates 1 or 2 stools more than usual.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (confidence interval 95%)	83.3 (43.6 to 97.0)	33.3 (13.8 to 60.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Physician's Global Assessment Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point title	Percentage of Participants With Physician's Global Assessment Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point description:

A score of 0 on the PGA Subscore indicates normal disease, while a score of 1 on the PGA Subscore indicates mild disease.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (confidence interval 95%)	50.0 (18.8 to 81.2)	33.3 (13.8 to 60.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Rectal Bleeding Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point title	Percentage of Participants With Rectal Bleeding Subscore Indicative of Mild Disease (a Score of 0 or 1) at Week 8

End point description:

A score of 0 on the Rectal Bleeding Subscore indicates no blood seen, while a score of 1 on the Rectal Bleeding Subscore indicates streaks of blood with stool less than half the time.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (confidence interval 95%)	100 (61.0 to 100)	83.3 (55.2 to 95.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in C-reactive protein (CRP) plasma level at Week 8

End point title	Change from Baseline in C-reactive protein (CRP) plasma level at Week 8

End point description:

Baseline for CRP was considered Day 1, predose, or if Day 1 measurement was missing, the Screening value was considered Baseline.
CRP, measurements that are below the limit of quantification (BLQ) were imputed with half of the lower limit of quantification (LLOQ) for the purpose of calculating changes from Baseline. Measurements above the upper limit of quantification (ALQ), were imputed to the upper quantification limit.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Placebo (FAS)	BKZ 560/420 mg (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	12		
Units: mg/L				
arithmetic mean (standard deviation)	-5.777 (± 7.725)	20.692 (± 33.249)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, prior to dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, prior to dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.
Note 3: At Day 1, Pre-dose, the BKZ concentrations were not available.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: ng/mL				
geometric mean (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, 1 hour after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, 1 hour after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms

per millilitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
geometric mean (confidence interval 95%)	199600 (180100 to 221200)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, 5 hours after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 1, 5 hours after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per millilitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (confidence interval 95%)	206300 (185700 to 229200)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, Pre-dose

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, Pre-dose

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
geometric mean (confidence interval 95%)	36620 (30090 to 44580)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, 1.5 hours after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, 1.5 hours after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms

per millilitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
geometric mean (confidence interval 95%)	35940 (28650 to 45090)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, 5 hours after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 22, 5 hours after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per millilitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (confidence interval 95%)	36540 (29140 to 45810)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, Pre-dose

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, Pre-dose

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: ng/mL				
geometric mean (confidence interval 95%)	34310 (26380 to 44630)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, 1.5 hours after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, 1.5 hours after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at

the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (confidence interval 95%)	32740 (24140 to 44400)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, 5 hours after dosing

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 43, 5 hours after dosing

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (confidence interval 95%)	36410 (27870 to 47580)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 57

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 57

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (confidence interval 95%)	48460 (37230 to 63060)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 85

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 85

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.
Note 3: Due to low number of subjects (N = 1), Geometric Mean could not be calculated and a placeholder value '999' was used instead, for technical reasons.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 99

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 99

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (confidence interval 95%)	5586 (2481 to 12570)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 141

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 141

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.
Note 3: Due to low number of subjects (N = 1), Geometric Mean could not be calculated and a placeholder value '999' was used instead, for technical reasons.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Bimekizumab (BKZ) over time - at Day 183

End point title	Plasma concentration of Bimekizumab (BKZ) over time - at Day 183

End point description:

BKZ plasma concentration was expressed as geometric mean concentration and measure in nanograms per mililllitre (ng/mL).

Note 1: Values Bellow Limit of Quantification (BLQ) are replaced by value of Lower Limit Of Quantification (LLOQ)/2 (=75ng/mL) in calculations of descriptive statistics.
Note 2: Descriptive statistics were only calculated if at least 2/3 of the concentrations were quantified at the respective timepoint.
Note 3: As more than 1/3 of data was BLQ, or missing, Geometric Mean could not be calculated and a placeholder value '999' was used instead, for technical reasons.

End point type	Secondary

End point timeframe:

Day 1 sampling for PK evaluation was done: predose (1h prior dosing), 1h (post infusion), and 5h (±1h). At Day 22, 43 blood sampling was done prior dosing, at 1.5 and 5 hours after dosing. From Day 57 to Day 183, a single sample was collected.

End point values	BKZ 560/420 mg (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline, at Day 1 and up to Early Withdrawal Visit, post Week 26

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	BKZ 560/420 mg (SS)

Reporting group description:

Subjects were administered 560 mg of bimekizumab (BKZ) iv infusion at Visit 2 (Day 1) and 2 doses of 420 mg sc BKZ injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the SS.

Reporting group title	Placebo (SS)

Reporting group description:

Subjects were administered one dose of intravenous (iv) placebo infusion at Visit 2 (Day 1) and 2 doses of subcutaneous placebo (sc) injections at Visit 3 (Day 22 ± 2 days) and Visit 4 (Day 43 ± 2 days), forming the Safety Set (SS).

Serious adverse events	BKZ 560/420 mg (SS)	Placebo (SS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 3	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	BKZ 560/420 mg (SS)	Placebo (SS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 15 (80.00%)	2 / 8 (25.00%)	
Investigations			
Neutrophil count decreased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Lymphopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Injection site reaction			

subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	3 / 15 (20.00%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Anorectal discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Ileus paralytic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Oropharyngitis fungal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

Metabolism and nutrition disorders Malnutrition subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1	 0 / 8 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2017	Adjusted the timing for the Screening Visits, revised the washout duration for concomitant medications, and introduced wording for a potential interim analysis and a new stopping rule should the interim analysis be carried out.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early study termination, due to an imbalance of adverse events with no clear evidence of benefits, resulted in a number of subjects that was too small to enable any definitive conclusions.

Notes: