EU Clinical Trials Register

Clinical trial results:

A MULTICENTER, PHASE 2B, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, DOSE-RANGING STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN SUBJECTS WITH ACTIVE ANKYLOSING SPONDYLITIS

Summary

EudraCT number	2016-001102-42
Trial protocol	HU ES CZ DE BG GB
Global end of trial date	30 August 2018

Results information

Result version number	v1
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	AS0008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02963506
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	12 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the dose-response based on the efficacy of bimekizumab

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	27 October 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czech Republic: 96
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Poland: 100
Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Ukraine: 21
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	303
EEA total number of subjects	234

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)	291
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in October 2016 and concluded in August 2018.

Pre-assignment

Screening details:

The study included a 28-Day Screening Period, followed by a Double-blind Period from Day 1 to Week 12, prior to treatment re-randomization, a Dose-blind Period, from Week 12 after the treatment re-randomization and up to Week 48 and a Safety Follow-Up (SFU) Period, post Week 48.
The Participant Flow refers to the Randomized Set and Dose-Blind Set.

Period 1

Period 1 title	Double-Blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Assessor, Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo during the 12 weeks Double-Blind Period.

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

Dosage and administration details:

Participants were administered placebo, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 16 mg

Arm description:

Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 64 mg

Arm description:

Participants received Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.

Arm type	Experimental

Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 160 mg

Arm description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 320 mg

Arm description:

Participants received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Number of subjects in period 1	Placebo	BKZ 16 mg	BKZ 64 mg
Started	60	61	61
Completed Double-Blind Period	60	59	59
Completed Week 12 - started Dose-Blind	60	58	59
Completed	60	58	59
Not completed	0	3	2
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	1
Adverse event, non fatal after Wk12	-	1	-
Lost to follow-up	-	1	-

No compliance	-	1	-

Number of subjects in period 1	BKZ 160 mg	BKZ 320 mg
Started	60	61
Completed Double-Blind Period	58	61
Completed Week 12 - started Dose-Blind	58	61
Completed	58	61
Not completed	2	0
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	-
Adverse event, non fatal after Wk12	-	-
Lost to follow-up	-	-
No compliance	-	-

Period 2

Period 2 title	Dose-Blind Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Assessor, Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - BKZ 160 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	Placebo - BKZ 320 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period

Arm type	Experimental

Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 16 mg - BKZ 160 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 16 mg - BKZ 320 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 64 mg - BKZ 160 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 64 mg - BKZ 320 mg

Arm description:

After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.

Arm type	Experimental

Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 160 mg - BKZ 160 mg

Arm description:

Participants randomized to Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 160 mg Q4W in the 36 weeks Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 320 mg - BKZ 320 mg

Arm description:

Participants randomized to Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 320 mg Q4W in the 36 weeks Dose-Blind Period.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	BKZ
Other name	UCB4940
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Number of subjects in period 2	Placebo - BKZ 160 mg	Placebo - BKZ 320 mg	BKZ 16 mg - BKZ 160 mg
Started	24	36	31
Completed	20	31	26
Not completed	4	5	5
Consent withdrawn by subject	1	2	2
Adverse event, non-fatal	1	3	2
Lost to follow-up	1	-	-
Sponsor decision	1	-	-
Meeting exclusion criteria 9	-	-	-
Lack of efficacy	-	-	1

Number of subjects in period 2	BKZ 16 mg - BKZ 320 mg	BKZ 64 mg - BKZ 160 mg	BKZ 64 mg - BKZ 320 mg
Started	27	34	25
Completed	24	30	24
Not completed	3	4	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	2	2	1
Lost to follow-up	1	-	-
Sponsor decision	-	-	-
Meeting exclusion criteria 9	-	-	-
Lack of efficacy	-	1	-

Number of subjects in period 2	BKZ 160 mg - BKZ 160 mg	BKZ 320 mg - BKZ 320 mg
Started	58	61
Completed	56	54
Not completed	2	7
Consent withdrawn by subject	-	-
Adverse event, non-fatal	1	6
Lost to follow-up	1	-
Sponsor decision	-	-
Meeting exclusion criteria 9	-	1
Lack of efficacy	-	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 16 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 64 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 160 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.	
Reporting group title	BKZ 320 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.	

Reporting group values	Placebo	BKZ 16 mg	BKZ 64 mg
Number of subjects	60	61	61
Age categorical			
Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	60	56	59
>=65 years	0	5	2
Age continuous			
Units: years			
arithmetic mean	39.65	43.31	40.41
standard deviation	± 10.30	± 12.59	± 10.93
Gender categorical			
Units: Subjects			
Male	49	53	52
Female	11	8	9

Reporting group values	BKZ 160 mg	BKZ 320 mg	Total
Number of subjects	60	61	303
Age categorical			
Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	56	60	291
>=65 years	4	1	12
Age continuous			
Units: years			
arithmetic mean	42.38	45.02	
standard deviation	± 13.11	± 11.39	-

Gender categorical Units: Subjects			
Male	52	50	256
Female	8	11	47

Subject analysis sets

Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 16 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 64 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 160 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 320 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	All subjects (SS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo, Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) and BKZ 64 mg Q4W during the 12 weeks Double-Blind Period. At Week (Wk) 12, placebo, Bimekizumab (BKZ) 16 mg Q4W and BKZ 64 mg Q4W participants were re-randomized to receive either BKZ 160 mg Q4W or BKZ 320 mg Q4W for 36 weeks Dose-Blind Period. Participants randomized to BKZ 160 mg Q4W and BKZ 320 mg Q4W at Baseline were not re-randomized at Week 12 and remained on their original treatment. Participants formed the Safety Set (SS).

Reporting group values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)
Number of subjects	60	61	61
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	60	56	59
>=65 years	0	5	2
Age continuous Units: years			
arithmetic mean	39.65	43.31	40.41
standard deviation	± 10.30	± 12.59	± 10.93

Gender categorical Units: Subjects			
Male	49	53	52
Female	11	8	9

Reporting group values	BKZ 160 mg (FAS)	BKZ 320 mg (FAS)	All subjects (SS)
Number of subjects	60	61	303
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	56	60	291
>=65 years	4	1	12
Age continuous Units: years			
arithmetic mean	42.38	45.02	42.16
standard deviation	± 13.11	± 11.39	± 11.80
Gender categorical Units: Subjects			
Male	52	50	256
Female	8	11	47

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 16 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 64 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.	
Reporting group title	BKZ 160 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.	
Reporting group title	BKZ 320 mg
Reporting group description:	
Participants received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.	
Reporting group title	Placebo - BKZ 160 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period.	
Reporting group title	Placebo - BKZ 320 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period	
Reporting group title	BKZ 16 mg - BKZ 160 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.	
Reporting group title	BKZ 16 mg - BKZ 320 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.	
Reporting group title	BKZ 64 mg - BKZ 160 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.	
Reporting group title	BKZ 64 mg - BKZ 320 mg
Reporting group description:	
After the 12 weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.	
Reporting group title	BKZ 160 mg - BKZ 160 mg
Reporting group description:	
Participants randomized to Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 160 mg Q4W in the 36 weeks Dose-Blind Period.	
Reporting group title	BKZ 320 mg - BKZ 320 mg
Reporting group description:	
Participants randomized to Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 320 mg Q4W in the 36 weeks Dose-Blind Period.	

Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 16 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 64 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 160 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	BKZ 320 mg (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS).

Subject analysis set title	All subjects (SS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo, Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) and BKZ 64 mg Q4W during the 12 weeks Double-Blind Period. At Week (Wk) 12, placebo, Bimekizumab (BKZ) 16 mg Q4W and BKZ 64 mg Q4W participants were re-randomized to receive either BKZ 160 mg Q4W or BKZ 320 mg Q4W for 36 weeks Dose-Blind Period. Participants randomized to BKZ 160 mg Q4W and BKZ 320 mg Q4W at Baseline were not re-randomized at Week 12 and remained on their original treatment. Participants formed the Safety Set (SS).

Primary: Percentage of participants with Axial Spondyloarthritis International Society 40% response criteria (ASAS40) at Week 12

End point title	Percentage of participants with Axial Spondyloarthritis International Society 40% response criteria (ASAS40) at Week 12

End point description:

The ASAS40 response was defined as relative improvements of at least 40% and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS), where 0 is "not active" and 10 is "very active" in at least 3 of the 4 domains: Patient's Global Assessment of Disease Activity (PGADA), Pain assessment (total spinal pain NRS scores), Function (Bath Ankylosing Spondylitis Functional Index (BASFI)), Inflammation (mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration) and no worsening at all in the remaining domain.

Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: percentage of participants				
number (not applicable)	13.3	29.5	42.6	46.7

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: percentage of participants				
number (not applicable)	45.9			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Statistic and p-value were calculated using a Cochran-Mantel-Haenszel test (test for non-zero correlation statistic) based on modified ridit scores and including geographic region and prior Tumor Necrosis Factor (TNF) inhibitor exposure as stratification factors.

Note: 999 and 0% CI are used as placeholders. Using this methodology no point estimator will be calculated. The respective correlation statistic was 17.9.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS) v BKZ 64 mg (FAS) v BKZ 160 mg (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Correlation statistic
Point estimate	999
Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	999
upper limit	999

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior tumor

necrosis factor (TNF) inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.04 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	6.48

Notes:

[1] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of alpha=0.05, then the pairwise testing continued and the comparison was seen as non-significant.

[2] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.001 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.83
upper limit	10.86

Notes:

[3] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of alpha=0.05, then the pairwise testing continued and the comparison was seen as non-significant.

[4] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.001 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.27
upper limit	13.48

Notes:

[5] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of alpha=0.05, then the pairwise testing continued and the comparison was seen as non-significant.

[6] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	< 0.001 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.19
upper limit	12.92

Notes:

[7] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of alpha=0.05, then the pairwise testing continued and the comparison was seen as non-significant.

[8] - The p-values were displayed as nominal p-values.

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score - C-Reactive Protein (ASDAS [CRP]) at Week 12

End point title	Change from Baseline in Ankylosing Spondylitis Disease Activity Score - C-Reactive Protein (ASDAS [CRP]) at Week 12

End point description:

The ASDAS was calculated as the sum of the following components:
0.121 x Back pain (BASDAI Q2 result)
0.058 x Duration of morning stiffness (BASDAI Q6 result)
0.110 x PGADA
0.073 x Peripheral pain/swelling (BASDAI Q3 result)
$0.579 \times$ (natural logarithm [ln] of the (CRP [mg/L] + 1))

Back pain, PGADA, duration of morning stiffness, peripheral pain/swelling and fatigue were all assessed on a numerical scale (0 to 10 units, where 0 is "not active" and 10 is "very active").
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.

Note: Missing data was imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random.

End point type	Secondary
End point timeframe:	
From Baseline to Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: units on a scale				
least squares mean (standard error)	-0.3 (± 0.17)	-0.8 (± 0.17)	-1.4 (± 0.17)	-1.3 (± 0.17)

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: units on a scale				
least squares mean (standard error)	-1.4 (± 0.17)			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Least squares (LS) Mean, standard error, confidence interval and p-value were derived using the analysis of covariance (ANCOVA) model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.	
Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.24

Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	-0.83
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	-0.72
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	-0.82
Variability estimate	Standard error of the mean
Dispersion value	0.16

Secondary: Percentage of participants with Axial Spondyloarthritis International Society 20% response criteria (ASAS20) at Week 12

End point title	Percentage of participants with Axial Spondyloarthritis International Society 20% response criteria (ASAS20) at Week 12

End point description:

The ASAS20 response was defined as an improvement of at least 20% and absolute improvement of at least 1 unit on a 0 to 10 NRS, where 0 is "not active" and 10 is "very active" in at least 3 of the 4 domains: PGADA, Pain assessment (total spinal pain NRS scores), Function (BASFI), Inflammation (mean of BASDAI questions 5 and 6 concerning morning stiffness intensity and duration) and absence of deterioration in the potential remaining domain [deterioration was defined as a relative worsening of at least 20% and an absolute worsening of at least 1 unit].

Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: percentage of participants				
number (not applicable)	28.3	41.0	62.3	58.3

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: percentage of participants				
number (not applicable)	72.1			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.163 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	3.67

Notes:

[9] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	8.48

Notes:

[10] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	7.61

Notes:

[11] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.92
upper limit	14.28

Notes:

[12] - The p-values were displayed as nominal p-values.

Secondary: Percentage of participants with Axial Spondyloarthritis International Society (ASAS) 5/6 response at Week 12

End point title	Percentage of participants with Axial Spondyloarthritis International Society (ASAS) 5/6 response at Week 12

End point description:

The ASAS 5/6 response was defined as at least 20% improvement in at least 5 of the 6 domains: PGADA, Pain assessment (total spinal pain NRS scores), Function (BASFI), Inflammation (mean of

BASDAI questions 5 and 6 concerning morning stiffness intensity and duration), spinal mobility (lateral spinal flexion) and high sensitivity C-reactive protein (hs-CRP).

Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: percentage of participants				
number (not applicable)	6.7	29.5	49.2	53.3

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: percentage of participants				
number (not applicable)	54.1			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 [13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.74
upper limit	15.96

Notes:

[13] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.03
upper limit	35.38

Notes:

[14] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.81
upper limit	42.46

Notes:

[15] - The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

For differences in relation to Placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	14.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.02
upper limit	44.27

Notes:

[16] - The p-values were displayed as nominal p-values.

Secondary: Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point title	Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

End point description:

The BASDAI is a validated self-reported instrument, which consists of six 10-unit horizontal Numeric Rating Scales (NRS) to measure severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration, respectively) over the last week. The final BASDAI score ranges from 0 to 10, with lower scores indicating lower disease activity.
The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.

Note: Missing data was imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random.

End point type	Secondary

End point timeframe:

From Baseline to Week 12

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: scores on a scale				
least squares mean (standard error)	-1.0 (± 0.38)	-1.6 (± 0.38)	-2.6 (± 0.38)	-2.6 (± 0.38)

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: scores on a scale				
least squares mean (standard error)	-2.9 (± 0.38)			

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.	
Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.094
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.	
Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	-0.91
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.35
upper limit	-0.91
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1.18
Variability estimate	Standard error of the mean
Dispersion value	0.36

Secondary: Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point title	Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

End point description:

The BASFI is a validated disease-specific instrument for assessing physical function. The BASFI comprises 10 items relating to the past week. The BASFI is the mean of the 10 scores such that the total score ranges from 0 (Easy) to 10 (Impossible), with lower scores indicating better physical function. The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.

Note: Missing data was imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random.

End point type	Secondary

End point timeframe:

From Baseline to Week 12

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 64 mg (FAS)	BKZ 160 mg (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	61	61	60
Units: scores on a scale				
least squares mean (standard error)	-0.7 (± 0.39)	-1.4 (± 0.38)	-1.8 (± 0.38)	-1.9 (± 0.38)

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: scores on a scale				
least squares mean (standard error)	-2.2 (± 0.38)			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.074
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 64 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	-0.42

Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference vs Placebo
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.36

Secondary: Percentage of participants with at least one Adverse Event (AE) during the study

End point title	Percentage of participants with at least one Adverse Event (AE) during the study

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation participant 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, 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	Secondary

End point timeframe:

From Screening at Day -28 until Safety Follow-Up Visit (up to Week 72)

End point values	All subjects (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	303			
Units: percentage of participants				
number (not applicable)	78.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with at least one Serious Adverse Event (SAE) during the study

End point title	Percentage of participants with at least one Serious Adverse Event (SAE) during the study

End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose:
- Results in death
- Is life-threatening
- Requires in patient hospitalisation or prolongation of existing hospitalisation
- Is a congenital anomaly or birth defect
- Is an infection that requires treatment parenteral antibiotics
- Other important medical events which based on medical or scientific judgement may jeopardise the patients, or may require medical or surgical intervention to prevent any of the above.

End point type	Secondary

End point timeframe:

From Screening at Day -28 until Safety Follow-Up Visit (up to Week 72)

End point values	All subjects (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	303			
Units: percentage of participants				
number (not applicable)	4.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who withdrew due to an Adverse Event (AE) during the study

End point title	Percentage of participants who withdrew due to an Adverse Event (AE) during the study

End point description:

An AE is any untoward medical occurrence in a participant or trial subject that is administered a drug or biologic (medicinal product) or that is using a medical device.
The event does not necessarily have a causal relationship with that treatment or usage. The results of this Secondary Outcome Measure were summarized from the Adverse Event pages of the Case Report Forms.

End point type	Secondary

End point timeframe:

From Screening at Day -28 until Safety Follow-Up Visit (up to Week 72)

End point values	All subjects (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	303			
Units: percentage of participants				
number (not applicable)	6.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline at Day 1 until the Safety Follow-Up Visit at 20 weeks after the final dose of IMP.

Adverse event reporting additional description:

Participants randomized to placebo (PBO), BKZ 16 mg and BKZ 64 mg at Baseline switched to BKZ 160 mg Q4W or BKZ 320 mg Q4W at Week 12. The exposure imbalance across treatment arms could lead to misinterpretation & questionable conclusions comparing simple counts & percentages of AEs. Therefore, only overall BKZ time is included in this summary.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	All subjects (SS)

Reporting group description:

Participants received placebo, Bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) and BKZ 64 mg Q4W during the 12 weeks Double-Blind Period. At Week (Wk) 12, placebo, Bimekizumab (BKZ) 16 mg Q4W and BKZ 64 mg Q4W participants were re-randomized to receive either BKZ 160 mg Q4W or BKZ 320 mg Q4W for 36 weeks Dose-Blind Period. Participants randomized to BKZ 160 mg Q4W and BKZ 320 mg Q4W at Baseline were not re-randomized at Week 12 and remained on their original treatment. Participants formed the Safety Set (SS).

Serious adverse events	All subjects (SS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 303 (4.29%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laceration			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders

Acute myocardial infarction

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac arrest

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Nervous system disorders

Dizziness

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders

Anaemia

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ear and labyrinth disorders

Inner ear disorder

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders

Pancreatitis acute

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Crohn's disease

subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal haemorrhage				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonia aspiration				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteoarthritis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bursitis infective				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All subjects (SS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 303 (33.66%)		
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	16 / 303 (5.28%)		
occurrences (all)	21		
Oral fungal infection			
subjects affected / exposed	14 / 303 (4.62%)		
occurrences (all)	16		
Bronchitis			
subjects affected / exposed	18 / 303 (5.94%)		
occurrences (all)	18		
Nasopharyngitis			
subjects affected / exposed	34 / 303 (11.22%)		
occurrences (all)	44		
Pharyngitis			
subjects affected / exposed	18 / 303 (5.94%)		
occurrences (all)	18		
Upper respiratory tract infection			

| subjects affected / exposed | 17 / 303 (5.61%) | | |
| occurrences (all) | 19 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2018	The purpose of this substantial protocol amendment was the following: - To update the study contact details for the sponsor study physician and clinical trial biostatistician. - To revise the withdrawal criteria section to provide instructions for the management of participants with newly diagnosed inflammatory bowel disease (IBD) or with IBD flares during the study. - Amend the time window between doses during the Double-Blind Period of the study. - To revise and clarify the SAE criteria for pregnancy for consistency. - Amend the table for identification/exclusion of alternative etiology to include alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported