Clinical trial results:
A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATING THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN SUBJECTS WITH ACTIVE ANKYLOSING SPONDYLITIS

Summary

EudraCT number	2017-003065-95
Trial protocol	DE BE HU GB BG FR ES CZ NL
Global end of trial date	08 August 2022

Results information

Result version number	v1
This version publication date	19 August 2023
First version publication date	19 August 2023

Trial information

Trial identification

Sponsor protocol code	AS0011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03928743
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	UCB BIOSCIENCES GmbH, Clin Trial Reg & Results Disclosure, 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	09 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2021
Global end of trial reached?	Yes
Global end of trial date	08 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the efficacy of bimekizumab administered subcutaneously (sc) compared to placebo in the treatment of subjects with active ankylosing spondylitis (AS)

Protection of trial subjects:

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

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	25 April 2019
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	Belgium: 10
Country: Number of subjects enrolled	Bulgaria: 15
Country: Number of subjects enrolled	China: 44
Country: Number of subjects enrolled	Czechia: 56
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Japan: 12
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 87
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	332
EEA total number of subjects	250

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)	321
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll study participants in April 2019 and concluded in August 2022.

Pre-assignment

Screening details:

The Participant Flow refers to the Randomized Set.

Period 1

Period 1 title	Double-Blind Treatment Period:Weeks 1-16
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (up to Week 16)

Arm description:

Participants received placebo matched to bimekizumab 160 milligrams (mg) every 4 weeks (Q4W) subcutaneously until Week 16.

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

Dosage and administration details:

Participants received placebo Q4W at prespecified time points.

Arm title	Bimekizumab 160 mg Q4W (up to Week 16)

Arm description:

Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	UCB4940
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received bimekizumab 160 mg Q4W at prespecified time points.

Number of subjects in period 1	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)
Started	111	221
Completed	109	213
Not completed	2	8
Due To COVID-19 Pandemic and Site Restrictions	1	1
Consent withdrawn by subject	1	3
Adverse Event, serious non-fatal	-	1
Adverse event	-	2
Lack of efficacy	-	1

Period 2

Period 2 title	Maintenance Period: Weeks 16-52
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Arm title	Bimekizumab 160 mg Q4W (Week 16 up to Week 52)

Arm description:

At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16. Participants received bimekizumab 160 mg Q4W subcutaneously from Week 16 until Week 48.

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	UCB4940
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received bimekizumab 160 mg Q4W at prespecified time points.

Number of subjects in period 2[1]	Bimekizumab 160 mg Q4W (Week 16 up to Week 52)
Started	319
Completed	298
Not completed	21
Consent withdrawn by subject	4
Adverse Event, serious non-fatal	2

Adverse event	9
Lost to follow-up	2
PI Decision Due To Non-Compliance and COVID 19	1
Lack of efficacy	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 3 participants completed the Double blind treatment period but did not enter the Maintenance Period because of the below reason for discontinuation: Adverse event: 1; Withdrawal by study participants: 2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (up to Week 16)
Reporting group description:	
Participants received placebo matched to bimekizumab 160 milligrams (mg) every 4 weeks (Q4W) subcutaneously until Week 16.	
Reporting group title	Bimekizumab 160 mg Q4W (up to Week 16)
Reporting group description:	
Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.	

Reporting group values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)	Total
Number of subjects	111	221	332
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	109	212	321
>=65 years	2	9	11
Age Continuous Units: years			
arithmetic mean	39.2	41.0	
standard deviation	± 12.6	± 12.1	-
Sex: Female, Male Units: participants			
Female	31	61	92
Male	80	160	240

Subject analysis sets	
Subject analysis set title	Double Blind Treatment Period (up to Week 16): Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received placebo matched to bimekizumab 160 mg Q4W subcutaneously until Week 16.	
Subject analysis set title	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.	
Subject analysis set title	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16. All Participants received bimekizumab 160 mg Q4W subcutaneously from Week 16 until Week 48.	
Subject analysis set title	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received bimekizumab 160 mg Q4W subcutaneously from Day 1 and participants who	

switched from placebo arm at Week 16 to receive bimekizumab 160 mg Q4W subcutaneously were included in this group.

Reporting group values	Double Blind Treatment Period (up to Week 16): Placebo	Double Blind Treatment Period(up to Week 16):Bimekizumab16	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg
Number of subjects	111	221	319
Age Categorical Units: participants			
<=18 years Between 18 and 65 years >=65 years			
Age Continuous Units: years arithmetic mean standard deviation	 43.2 ±	 54.3 ±	 68.3 ±
Sex: Female, Male Units: participants			
Female Male			

Reporting group values	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg		
Number of subjects	330		
Age Categorical Units: participants			
<=18 years Between 18 and 65 years >=65 years			
Age Continuous Units: years arithmetic mean standard deviation	 ±	 	
Sex: Female, Male Units: participants			
Female Male			

End points

End points reporting groups

Reporting group title	Placebo (up to Week 16)
Reporting group description:	
Participants received placebo matched to bimekizumab 160 milligrams (mg) every 4 weeks (Q4W) subcutaneously until Week 16.	
Reporting group title	Bimekizumab 160 mg Q4W (up to Week 16)
Reporting group description:	
Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.	
Reporting group title	Bimekizumab 160 mg Q4W (Week 16 up to Week 52)
Reporting group description:	
At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16. Participants received bimekizumab 160 mg Q4W subcutaneously from Week 16 until Week 48.	
Subject analysis set title	Double Blind Treatment Period (up to Week 16): Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received placebo matched to bimekizumab 160 mg Q4W subcutaneously until Week 16.	
Subject analysis set title	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.	
Subject analysis set title	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16. All Participants received bimekizumab 160 mg Q4W subcutaneously from Week 16 until Week 48.	
Subject analysis set title	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received bimekizumab 160 mg Q4W subcutaneously from Day 1 and participants who switched from placebo arm at Week 16 to receive bimekizumab 160 mg Q4W subcutaneously were included in this group.	

Primary: Percentage of Participants With Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response at Week 16

End point title	Percentage of Participants With Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response at Week 16
End point description:	
ASAS40 response: relative improvement of at least 40% and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS), where 0 (not active) and 10 (very active) in at least 3 of 4 domains:Patient's Global Assessment of Disease Activity (PGADA) assessed disease activity on a scale of 0 [not active] to 10 [very active], higher score=more disease activity, Pain assessment on a scale of 0 [no pain] to 10 [most severe pain], higher score=more severity), Function (Bath Ankylosing Spondylitis Functional Index (BASFI)) assessed participant's level of ability on a scale of 0 [easy] to 10 [impossible], Inflammation (morning stiffness intensity and duration, mean of Q5 and Q6 of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) defined as 6 item questionnaire: measured disease activity on a scale of 0 [none] to 10 [severe], higher score=more disease activity) and no worsening at all in remaining domain.Randomized Set consisted of all randomized study participants.	
End point type	Primary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: percentage of participants				
number (not applicable)	22.5	44.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	4.87

Secondary: Percentage of Participants With Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response in TNFα inhibitor-naïve participants at Week 16

End point title	Percentage of Participants With Assessment of SpondyloArthritis International Society 40% response criteria (ASAS40) response in TNFα inhibitor-naïve participants at Week 16

End point description:

ASAS40 response was defined as relative improvement of at least 40% and absolute improvement of at least 2 units on a 0 to 10 NRS, where 0 (not active) and 10 (very active) in at least 3 of the 4 domains: PGADA assessed disease activity on a scale of 0 [not active] to 10 [very active], higher score=more disease activity, Pain assessment on a scale of 0 [no pain] to 10 [most severe pain], higher score=more severity), Function (BASFI) assessed participant's level of ability on a scale of 0 [easy] to 10 [impossible], Inflammation (morning stiffness intensity and duration, mean of Q5 and Q6 of BASDAI defined as 6 item questionnaire: measured disease activity on a scale of 0 [none] to 10 [severe], higher score=more disease activity) and no worsening at all in the remaining domain. The Randomized Set consisted of all randomized study participants. Here, Number of Participants Analyzed signifies those who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	184		
Units: percentage of participants				
number (not applicable)	23.4	45.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.59
upper limit	4.93

Secondary: Percentage of Participants With Assessment of SpondyloArthritis International Society 20% response criteria (ASAS20) response at Week 16

End point title	Percentage of Participants With Assessment of SpondyloArthritis International Society 20% response criteria (ASAS20) response at Week 16

End point description:

ASAS20 response was defined as relative improvements of at least 20% and absolute improvement of at least 1 unit on a 0 to 10 NRS, where 0 (not active) and 10 (very active) in at least 3 of the 4 domains: PGADA assessed disease activity on a scale of 0 [not active] to 10 [very active], higher score=more disease activity, Pain assessment on a scale of 0 [no pain] to 10 [most severe pain], higher score=more severity), Function (BASFI) assessed participant's level of ability on a scale of 0 [easy] to 10 [impossible], Inflammation (morning stiffness intensity and duration, mean of Q5 and Q6 of BASDAI defined as 6 item questionnaire: measured disease activity on a scale of 0 [none] to 10 [severe], higher score=more disease activity) and no worsening at all in the remaining domain. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: percentage of participants				
number (not applicable)	43.2	66.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.65
upper limit	4.28

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) total score at Week 16

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) total score at Week 16

End point description:

BASDAI is a validated self-reported instrument, which consisted of 6 questions to measure the disease activity of ankylosing spondylitis (AS) from the participant's perspective. It measured the severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration). Each question was rated using a numerical rating scale from 0 (none) to 10 (very severe), higher score=high disease activity. The BASDAI score was calculated by computing the mean of questions 5 and 6 and adding it to the sum of questions 1 to 4. This score was then divided by 5. The total BASDAI score was ranged from 0=none to 10= very severe, where higher score indicated high disease activity. A negative value indicated improvement and a positive value indicated worsening. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	-1.70 (± 0.21)	-2.74 (± 0.17)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	-0.59

Secondary: Percentage of Participants With Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR) at Week 16

End point title	Percentage of Participants With Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR) at Week 16

End point description:

The Assessment of SpondyloArthritis International Society partial remission was defined as a score of less than or equal to (<=) 2 units (on a scale of 0-10, where 0=no disease activity and 10=high disease activity) in each of the 4 domains. These 4 domains included: PGADA assessed disease activity on a scale of 0 [not active] to 10 [very active], higher score=more disease activity, Pain assessment on a scale of 0 [no pain] to 10 [most severe pain], higher score=more severity), Function (BASFI) assessed participant's level of ability on a scale of 0 [easy] to 10 [impossible], Inflammation (morning stiffness intensity and duration, mean of Q5 and Q6 of BASDAI defined as 6 item questionnaire: measured disease activity on a scale of 0 [none] to 10 [severe], higher score=more disease activity). The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: percentage of participants				
number (not applicable)	7.2	24.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.93
upper limit	9.39

Secondary: Percentage of Participants With Ankylosing Spondylitis Disease Activity Score major improvement (ASDAS-MI) at Week 16

End point title	Percentage of Participants With Ankylosing Spondylitis Disease Activity Score major improvement (ASDAS-MI) at Week 16

End point description:

ASDAS-MI is achieved when there is a reduction (improvement) of greater than or equal to (>=) 2.0 in the Ankylosing Spondylitis Disease Activity Score (ASDAS) relative to Baseline. ASDAS is calculated as the sum of the following components: 1) 0.121 × Total back pain (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 result), 2) 0.058 × Duration of morning stiffness (BASDAI Q6 result), 3) 0.110 × Patient's Global Assessment of Disease Activity (PGADA), 4) 0.073 × Peripheral pain/swelling (BASDAI Q3 result), 5) 0.579 × (natural logarithm of the C-reactive protein (CRP) [mg/L] + 1). Total back pain, PGADA, duration of morning stiffness, peripheral pain/swelling and fatigue are all assessed on a numerical scale (0 to 10 units). High ASDAS scores mean worse disease. If a participant achieves the ASDAS-MI it indicates a major improvement of their disease. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: percentage of participants				
number (not applicable)	5.4	25.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.67
upper limit	15.65

Secondary: Percentage of Participants With Assessment of SpondyloArthritis International Society (ASAS) 5/6 response at Week 16

End point title	Percentage of Participants With Assessment of SpondyloArthritis International Society (ASAS) 5/6 response at Week 16

End point description:

The Assessment of SpondyloArthritis International Society (ASAS) 5/6 response is defined as achieving at least 20% improvement in 5 of 6 domains: PGADA assessed disease activity on a scale of 0 [not active] to 10 [very active], higher score=more disease activity, Pain assessment on a scale of 0 [no pain] to 10 [most severe pain], higher score=more severity), Function (BASFI) assessed participant's level of ability on a scale of 0 [easy] to 10 [impossible], Inflammation (morning stiffness intensity and duration, mean of Q5 and Q6 of BASDAI defined as 6 item questionnaire: measured disease activity on a scale of 0 [none] to 10 [severe], higher score=more disease activity), spinal mobility (lateral spinal flexion) and high sensitivity C-reactive protein (hs-CRP)]. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: percentage of participants				
number (not applicable)	18.9	49.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.51
upper limit	7.57

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 16

End point title	Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 16

End point description:

The Bath Ankylosing Spondylitis Functional Index (BASFI) assesses physical function in comprising 10 items relating to activities during the past week. Each item ranged from 0 ('Easy') to 10 ('Impossible'). The BASFI is the mean of the 10 scores such that the total score ranges from 0 to 10, with lower scores indicating better physical function. A negative value in BASFI change from Baseline indicates an improvement from Baseline. The higher the negative value the better the improvement. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	-0.95 (± 0.20)	-2.00 (± 0.16)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	-0.63

Secondary: Change from Baseline in nocturnal spinal pain score Numeric Rating Scale (NRS) at Week 16

End point title	Change from Baseline in nocturnal spinal pain score Numeric Rating Scale (NRS) at Week 16

End point description:

Nocturnal spinal pain experienced by ankylosing spondylitis (AS) participants is measured by one question: pain in the spine at night due to AS?. When responding, the participant is to consider the average amount of pain in the preceding week. It is assessed on a numerical scale of 0 to 10 units. A lower score indicates less pain and a negative change represents an improvement. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	-1.68 (± 0.25)	-3.16 (± 0.20)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.96

Secondary: Change from Baseline in the Short Form 36-Item Health Survey (SF-36) physical component summary (PCS) score at Week 16

End point title	Change from Baseline in the Short Form 36-Item Health Survey (SF-36) physical component summary (PCS) score at Week 16

End point description:

The SF-36 is a 36-item health-related quality of life instrument that uses a recall period of 4 weeks. Items are grouped into 8 domains as follows: Physical Functioning (10 items), Role Physical (4 items), Bodily Pain (2 items), General Health (5 items),Vitality (4 items), Social Functioning (2 items), Role Emotional (3 items), Mental Health (5 items), and 1 item for perceived stability or change in health (Health Transition) during the last year. In addition to domain scores, the PCS and Mental Component Summary (MCS) scores are calculated from the 8 domains (excluding the Health Transition item). Each of the SF-36 derived raw scores range from 0 to 100 with a higher score indicating better function. The 2 component summary scores and the 8 domains scores are standardized with a mean of 50 and a standard deviation of 10 in the general US population (Maruish, 2011). A positive change reflects improvement. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	5.17 (± 0.82)	8.54 (± 0.67)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	5.09

Secondary: Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) total score at Week 16

End point title	Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) total score at Week 16

End point description:

The Ankylosing Spondylitis Quality of Life (ASQoL), a validated disease-specific 18-item questionnaire, has been developed specifically for measuring health-related quality of life (HRQoL) in participants with ankylosing spondylitis and has shown to be responsive in axial spondyloarthritis (axSpA). Each statement on the ASQoL is given a score of 1=Yes or 0=No. A score of "1" was given where the item was affirmed, indicating adverse quality of life. All item scores were summed to generate the total score ranging from 0 to 18 with a higher score indicating worse health-related quality of life. A negative change from baseline represents an improvement. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	-3.07 (± 0.41)	-4.59 (± 0.32)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	-0.68

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Metrology Index (BASMI) at Week 16

End point title	Change from Baseline in Bath Ankylosing Spondylitis Disease Metrology Index (BASMI) at Week 16

End point description:

The Bath Ankylosing Spondylitis Disease Metrology Index characterizes the spinal mobility of participants with axial Spondyloarthritis (SpA) and Ankylosing Spondylitis. It is a disease-specific measure consisting of 5 clinical measures to reflect participant axial status: cervical rotation; tragus to wall distance; lateral lumbar flexion; lumbar flexion (modified Schober test); intermalleolar distance. According to the linear definition of the BASMI a score of 0 to 10 was calculated for each item based on the measurement. The mean of the 5 scores provides the total BASMI score (ranging from 0 to 10). The higher the BASMI score, the more severe the participant's limitation of movement due to their axial SpA. A negative value in BASMI change from Baseline indicates an improvement from Baseline. The higher the negative value, the better the improvement. The Randomized Set consisted of all randomized study participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	221		
Units: scores on a scale				
least squares mean (standard error)	-0.17 (± 0.09)	-0.45 (± 0.07)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.08

Secondary: Change from Baseline in the Maastricht Ankylosing Spondylitis Enthesitis (MASES) Index in the subgroup of participants with enthesitis at Baseline at Week 16

End point title	Change from Baseline in the Maastricht Ankylosing Spondylitis Enthesitis (MASES) Index in the subgroup of participants with enthesitis at Baseline at Week 16

End point description:

The Maastricht Ankylosing Spondylitis Enthesitis is an index that measures the severity (ie, intensity and extent) of enthesitis through the assessment of 13 entheses (bilateral costochondral 1, costochondral 7, anterior superior iliac spine, posterior iliac spine, iliac crest and proximal insertion of the Achilles tendon sites, and the fifth lumbar vertebral body spinous process), each scored as 0 or 1 and then summed for a possible score of 0 to 13. A higher score reflects higher severity and a negative change represents an improvement. Subset of study participants in Randomized Set with enthesitis at Baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	132		
Units: scores on a scale				
least squares mean (standard error)	-1.04 (± 0.33)	-2.12 (± 0.26)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Regression, Logistic
Parameter estimate	LS Mean difference
Point estimate	-1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.79
upper limit	-0.38

Secondary: Percentage of Participants With Enthesitis-free state at Week 16 based on the Maastricht Ankylosing Spondylitis Enthesitis Index in the subgroup of participants with enthesitis at Baseline

End point title	Percentage of Participants With Enthesitis-free state at Week 16 based on the Maastricht Ankylosing Spondylitis Enthesitis Index in the subgroup of participants with enthesitis at Baseline

End point description:

The Maastricht Ankylosing Spondylitis Enthesitis is an index that measures the severity (ie, intensity and extent) of enthesitis through the assessment of 13 entheses (bilateral costochondral 1, costochondral 7, anterior superior iliac spine, posterior iliac spine, iliac crest and proximal insertion of the Achilles tendon sites, and the fifth lumbar vertebral body spinous process) each scored as 0 or 1 and then summed for a possible score of 0 to 13. Enthesitis free state is defined as having a MASES score of 0. A higher score reflects higher severity and a negative change represents an improvement. Subset of study participants in Randomized Set with enthesitis at Baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (up to Week 16)	Bimekizumab 160 mg Q4W (up to Week 16)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	132		
Units: percentage of participants				
number (not applicable)	32.8	51.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (up to Week 16) v Bimekizumab 160 mg Q4W (up to Week 16)
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	4.68

Secondary: Percentage of participants with treatment-emergent adverse events (TEAEs) during the study

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs) during the study

End point description:

TEAEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week Safety follow up (SFU) period). TEAEs were analyzed and reported for DBTP (Safety set), MP (Maintenance Set) and Overall Period (Safety set) which includes all participants who received BKZ 60 mg Q4W during the study. The Safety Set consisted of all randomized study participants who received at least one dose of the IMP.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety-Follow-Up (up to Week 68)

End point values	Double Blind Treatment Period (up to Week 16): Placebo	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	111	221	319	330
Units: percentage of participants				
number (not applicable)	43.2	54.3	68.3	75.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment-emergent serious adverse events (SAEs) during the study

End point title	Percentage of participants with treatment-emergent serious adverse events (SAEs) during the study

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that at any dose resulted in 1) Death, 2) Life-threatening (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.), 3) Significant or persistent disability/incapacity, 4) Congenital anomaly/birth defect (including that occurring in a fetus), 5) Important medical event that, based upon appropriate medical judgment, may jeopardize the participant or participant may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious (Important medical events may include, but are not limited to, potential Hy's Law [see allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.) The Safety Set consisted of all randomized study participants who received at least one dose of the IMP.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety-Follow-Up (up to Week 68)

End point values	Double Blind Treatment Period (up to Week 16): Placebo	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	111	221	319	330
Units: percentage of participants				
number (not applicable)	0.9	2.3	4.7	6.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment-emergent adverse events (TEAEs) leading to withdrawal from investigational medicinal product (IMP) during the study

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs) leading to withdrawal from investigational medicinal product (IMP) during the study

End point description:

TEAEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week SFU period). The Safety Set consisted of all randomized study participants who received at least one dose of the IMP.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety-Follow-Up (up to Week 68)

End point values	Double Blind Treatment Period (up to Week 16): Placebo	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	111	221	319	330
Units: percentage of participants				
number (not applicable)	0	3.2	2.8	4.8

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) until Safety-Follow-Up (up to Week 68)

Adverse event reporting additional description:

As pre-specified in SAP, Maintenance Period (MP) included AEs of SFU for participants who did not enter the open label extension or discontinued early in MP. TEAEs were analyzed and reported for DBTP (Safety set), MP (Maintenance Set) and Overall Period (Safety set) which includes all participants who received BKZ 60 mg Q4W during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Double Blind Treatment Period (up to Week 16): Placebo

Reporting group description:

Participants received placebo matched to bimekizumab 160 mg Q4W subcutaneously until Week 16.

Reporting group title	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg

Reporting group description:

Participants who received bimekizumab 160 mg Q4W subcutaneously from Day 1 and participants who switched from placebo arm at Week 16 to receive bimekizumab 160 mg Q4W subcutaneously were included in this group.

Reporting group title	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg

Reporting group description:

At the end of the 16-week Double-Blind Treatment Period, study participants receiving placebo were re-allocated to bimekizumab treatment at Week 16. All Participants received bimekizumab 160 mg Q4W subcutaneously from Week 16 until Week 48.

Reporting group title	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg

Reporting group description:

Participants received bimekizumab 160 mg Q4W subcutaneously until Week 16.

Serious adverse events	Double Blind Treatment Period (up to Week 16): Placebo	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 111 (0.90%)	20 / 330 (6.06%)	15 / 319 (4.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Superficial spreading melanoma stage I			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus node dysfunction			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Rhinoplasty			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 111 (0.00%)	4 / 330 (1.21%)	4 / 319 (1.25%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			

subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 111 (0.90%)	0 / 330 (0.00%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis A			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			

subjects affected / exposed	1 / 111 (0.90%)	0 / 330 (0.00%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 330 (0.30%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 221 (2.26%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			

subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Superficial spreading melanoma stage I			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Sinus node dysfunction			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Rhinoplasty			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 221 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			

subjects affected / exposed	1 / 221 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 221 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 221 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Hepatitis A			

subjects affected / exposed	1 / 221 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 221 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Double Blind Treatment Period (up to Week 16): Placebo	Overall Period (up to Week 48+20 Weeks SFU):Bimekizumab 160 mg	Maintenance Period (Weeks 16 to 52): Bimekizumab 160 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 111 (14.41%)	95 / 330 (28.79%)	64 / 319 (20.06%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 111 (4.50%)	18 / 330 (5.45%)	11 / 319 (3.45%)
occurrences (all)	5	23	13
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 111 (0.90%)	18 / 330 (5.45%)	12 / 319 (3.76%)
occurrences (all)	1	22	15
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 111 (3.60%)	30 / 330 (9.09%)	17 / 319 (5.33%)
occurrences (all)	4	39	18
Upper respiratory tract infection			
subjects affected / exposed	8 / 111 (7.21%)	21 / 330 (6.36%)	16 / 319 (5.02%)
occurrences (all)	11	23	17
Oral candidiasis			
subjects affected / exposed	0 / 111 (0.00%)	20 / 330 (6.06%)	12 / 319 (3.76%)
occurrences (all)	0	25	14

Non-serious adverse events	Double Blind Treatment Period(up to Week 16):Bimekizumab160 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 221 (19.46%)		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 221 (4.07%)		
occurrences (all)	10		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 221 (3.17%)		
occurrences (all)	7		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	17 / 221 (7.69%) 21		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 221 (2.71%) 6		
Oral candidiasis subjects affected / exposed occurrences (all)	10 / 221 (4.52%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 September 2019	Protocol Amendment 1 (11 Sep 2019) implemented changes in response to scientific discussions and feedback provided at meetings with Investigators and advisors or for clarifications. Mainly, imaging assessments were amended with sacroiliac joint and spine MRIs performed at Weeks 16 and 52 for all consenting study participants participating in the MRI substudy regardless of MRI positivity at Baseline. These additional MRIs allowed an exploratory evaluation of any changes in the sacroiliac joints and spine after 16 or 52 weeks in study participants who were MRI-negative at Baseline and on early signals such as the impact on active inflammation at Week 16. Additionally, including MRI-positive and MRI-negative study participants in the substudy was considered a more holistic strategy comparable to the approach used for other compounds. At the same time, the optional participation in the MRI substudy was expanded to all study participants without restriction.
17 October 2019	Protocol Amendment 2 (17 Oct 2019) implemented an update of Inclusion Criterion to reflect the treatment guidelines for axSpA, as presented in the recent European League Against Rheumatism/ASAS and American College of Rheumatology/Spondyloarthritis Research and Treatment Network guidelines. In addition, a minor update for consistency was made.
16 February 2021	Protocol Amendment 4 (16 Feb 2021) updated the handling of missing data for the statistical analysis of the primary endpoint in response to an agency request. The COVID-19 Free Set (CFS) was added in response to industry recommendations for evaluating the impact of the pandemic. In addition, other previously planned supportive analyses defined in the Statistical Analysis Plan (SAP) were added for completeness.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported