



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 ACTIVE PSORIATIC ARTHRITIS

Summary

EudraCT number	2016-001103-23
Trial protocol	HU CZ DE GB
Global end of trial date	16 July 2018

Results information

Result version number	v1
This version publication date	08 September 2019
First version publication date	08 September 2019

Trial information

Trial identification

Sponsor protocol code	PA0008
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02969525
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	06 December 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 July 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 this study all study participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol. No medication increases or decreases were permitted for medications taken for psoriatic arthritis (PsA) until after the Week 16 protocol assessments. However, a decrease in dosing or dosing frequency of any agent was permitted for reasons of intolerance/Adverse Events (AEs)/side effects at any time.

Evidence for comparator:

Not applicable

Actual start date of recruitment	27 October 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 26
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Poland: 108
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	United States: 40
Worldwide total number of subjects	206
EEA total number of subjects	153

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)	185
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in October 2016 and concluded in July 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	Subject, Investigator, Carer, Assessor

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:

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

Arm title	BKZ 16 mg
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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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 160 mg
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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
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Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 160 mg LD
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Arm description:

Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-Blind Period.

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

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 320 mg
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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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Number of subjects in period 1	Placebo	BKZ 16 mg	BKZ 160 mg
Started	42	41	41
Completed Double-Blind Period	42	41	40
Completed Wk12 and started Dose-Blind	40	41	40
Completed	40	41	40
Not completed	2	0	1
Adverse event, non-fatal	-	-	1
Study medication discontinued before Wk12	2	-	-
LOW EGFR	-	-	-

Number of subjects in period 1	BKZ 160 mg LD	BKZ 320 mg
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Started	41	41
Completed Double-Blind Period	39	41
Completed Wk12 and started Dose-Blind	37	41
Completed	37	41
Not completed	4	0
Adverse event, non-fatal	1	-
Study medication discontinued before Wk12	2	-
LOW EGFR	1	-

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, Carer, 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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	Placebo - BZK 320 mg
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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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 16 mg - BKZ 160 mg
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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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BZK 16 mg - BZK 320 mg
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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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BZK 160 mg LD - BZK 160 mg
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Arm description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg at Baseline followed by 160 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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BZK 160 mg - BKZ dose 160 mg
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Arm description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 160 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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Arm title	BKZ 320 mg - BKZ 320 mg
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Arm description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 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	UCB4940
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered different BKZ doses, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

Number of subjects in period 2	Placebo - BKZ 160 mg	Placebo - BZK 320 mg	BKZ 16 mg - BKZ 160 mg
Started	20	20	22
Completed	20	18	22
Not completed	0	2	0
Consent withdrawn by subject	-	2	-
Non-cooperating patient	-	-	-
Adverse event, non-fatal	-	-	-
Withdrew before Safety Follow-up visit	-	-	-

Number of subjects in period 2	BZK 16 mg - BZK 320 mg	BZK 160 mg LD - BZK 160 mg	BZK 160 mg - BKZ dose 160 mg
Started	19	37	40
Completed	18	34	38
Not completed	1	3	2
Consent withdrawn by subject	1	2	-
Non-cooperating patient	-	-	-
Adverse event, non-fatal	-	1	1
Withdrew before Safety Follow-up visit	-	-	1

Number of subjects in period 2	BKZ 320 mg - BKZ 320 mg
Started	41
Completed	39
Not completed	2
Consent withdrawn by subject	-
Non-cooperating patient	1
Adverse event, non-fatal	1
Withdrew before Safety Follow-up visit	-

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 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 160 mg LD
Reporting group description: Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-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 160 mg
Number of subjects	42	41	41
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	38	35	40
>=65 years	4	6	1
Age continuous Units: years			
arithmetic mean	49.02	49.98	48.00
standard deviation	± 12.07	± 13.56	± 11.65
Gender categorical Units: Subjects			
Male	24	24	20
Female	18	17	21

Reporting group values	BKZ 160 mg LD	BKZ 320 mg	Total
Number of subjects	41	41	206
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	36	36	185
>=65 years	5	5	21
Age continuous Units: years			
arithmetic mean	49.05	50.39	-
standard deviation	± 12.99	± 12.08	-

Gender categorical			
Units: Subjects			
Male	14	23	105
Female	27	18	101

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 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 160 mg LD (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-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	BKZ 160 mg + BKZ 160 mg LD (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) and Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg Q4W during the 12 Weeks Double-Blind Period followed by Bimekizumab (BKZ) 160 mg Q4W during the 36 Weeks Dose-Blind Period, forming the Safety Set (SS).

Subject analysis set title	BKZ 320 mg (SS)
Subject analysis set type	Safety 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 Safety Set (SS).

Subject analysis set title	Placebo (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Placebo during the 12 Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 16 mg (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12

Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 160 mg (PK-PPS)
Subject analysis set type	Per protocol

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 Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 160 mg LD (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 320 mg (PK-PPS)
Subject analysis set type	Per protocol

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 Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	Placebo - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	Placebo - BZK 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BKZ 16 mg - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 16 mg - BZK 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 160 mg LD - BZK 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 160 mg - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

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

Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BKZ 320 mg - BKZ 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Reporting group values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)
Number of subjects	42	41	41
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	38	35	40
>=65 years	4	6	1
Age continuous Units: years			
arithmetic mean	49.02	49.98	48.00
standard deviation	± 12.07	± 13.56	± 11.65
Gender categorical Units: Subjects			
Male	24	24	20
Female	18	17	21

Reporting group values	BKZ 160 mg LD (FAS)	BKZ 320 mg (FAS)	BKZ 160 mg + BKZ 160 mg LD (SS)
Number of subjects	41	41	126
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	36	36	
>=65 years	5	5	
Age continuous Units: years			
arithmetic mean	49.05	50.39	
standard deviation	± 12.99	± 12.08	±
Gender categorical Units: Subjects			
Male	14	23	
Female	27	18	

Reporting group values	BKZ 320 mg (SS)	Placebo (PK-PPS)	BKZ 16 mg (PK-PPS)
Number of subjects	80	42	41
Age categorical Units: Subjects			
<=18 years		0	0
Between 18 and 65 years		38	35
>=65 years		4	6
Age continuous Units: years			
arithmetic mean		49.02	49.98

standard deviation	±	± 12.07	± 13.56
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Gender categorical Units: Subjects			
Male		24	24
Female		18	17

Reporting group values	BKZ 160 mg (PK-PPS)	BKZ 160 mg LD (PK-PPS)	BKZ 320 mg (PK-PPS)
Number of subjects	41	41	41
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	40	36	36
>=65 years	1	5	5
Age continuous Units: years			
arithmetic mean	48.00	49.05	50.39
standard deviation	± 11.65	± 12.99	± 12.08
Gender categorical Units: Subjects			
Male	20	14	23
Female	21	27	18

Reporting group values	Placebo - BKZ 160 mg (DBS)	Placebo - BZK 320 mg (DBS)	BKZ 16 mg - BKZ 160 mg (DBS)
Number of subjects	20	20	22
Age categorical Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			
Age continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender categorical Units: Subjects			
Male			
Female			

Reporting group values	BZK 16 mg - BZK 320 mg (DBS)	BZK 160 mg LD - BZK 160 mg (DBS)	BZK 160 mg - BKZ 160 mg (DBS)
Number of subjects	19	37	40
Age categorical Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			

Age continuous Units: years arithmetic mean standard deviation	\pm	\pm	\pm
Gender categorical Units: Subjects			
Male Female			

Reporting group values	BKZ 320 mg - BKZ 320 mg (DBS)		
Number of subjects	41		
Age categorical Units: Subjects			
<=18 years Between 18 and 65 years >=65 years			
Age continuous Units: years arithmetic mean standard deviation	\pm		
Gender categorical Units: Subjects			
Male Female			

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 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 160 mg LD
Reporting group description: Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-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 - BZK 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	BZK 16 mg - BZK 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	BZK 160 mg LD - BZK 160 mg
Reporting group description: After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg at Baseline followed by 160 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	BZK 160 mg - BKZ dose 160 mg
Reporting group description: After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 160 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 320 mg - BKZ 320 mg
Reporting group description: After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the 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 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 160 mg LD (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-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	BKZ 160 mg + BKZ 160 mg LD (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) and Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg Q4W during the 12 Weeks Double-Blind Period followed by Bimekizumab (BKZ) 160 mg Q4W during the 36 Weeks Dose-Blind Period, forming the Safety Set (SS).

Subject analysis set title	BKZ 320 mg (SS)
Subject analysis set type	Safety 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 Safety Set (SS).

Subject analysis set title	Placebo (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Placebo during the 12 Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 16 mg (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 160 mg (PK-PPS)
Subject analysis set type	Per protocol

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 Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 160 mg LD (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) during the 12 Weeks Double-Blind Period, forming the Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	BKZ 320 mg (PK-PPS)
Subject analysis set type	Per protocol

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 Pharmacokinetic Per-Protocol Set (PK-PPS).

Subject analysis set title	Placebo - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	Placebo - BZK 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BKZ 16 mg - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 16 mg - BZK 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set 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. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 160 mg LD - BZK 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BZK 160 mg - BKZ 160 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Subject analysis set title	BKZ 320 mg - BKZ 320 mg (DBS)
Subject analysis set type	Per protocol

Subject analysis set description:

After the 12 Weeks Double-Blind Period participants randomized to Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period. Participants are a subgroup from the Dose-Blind Set (DBS). The subgroup contained participants who were part of the PK-PPS and DBS.

Primary: ACR50 (American College of Rheumatology 50% Improvement) Response at Week 12

End point title	ACR50 (American College of Rheumatology 50% Improvement) Response at Week 12
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End point description:

The ACR50 response rate was based on 50% improvement relative to Baseline in the following measures:

- Tender Joint Count (TJC) based on 78 joints
- Swollen Joint Count (SJC) based on 76 joints
- 3 of the 5 remaining core set measures:
 - Disease activity as assessed by Patient's Global Assessment of Disease Activity (PGADA)
 - Disease activity as assessed by Physician's Global Assessment of Disease Activity (PhGADA)
 - Pain as assessed by Patient's Assessment of Arthritis Pain (PtAAP)
 - Physical function as assessed by Health Assessment Questionnaire – Disability Index (HAQ-DI)
 - Acute phase response as assessed by high sensitivity C-reactive protein (hs CRP).

End point type	Primary
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End point timeframe:

Week 12

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)	BKZ 160 mg LD (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	41	41
Units: percentage of subjects				
number (not applicable)	7.1	26.8	41.5	46.3

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	24.4			

Statistical analyses

Statistical analysis title	Statistical analysis 1
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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.

The 160 loading dose arm was not considered in the dose-response because this is a mixed dose and the test is examining linear dose response.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS) v BKZ 160 mg (FAS) v BKZ 160 mg LD (FAS) v BKZ 320 mg (FAS)
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Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.031
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

Notes:

[1] - 999 and 0% CI are used as placeholders. Using this methodology no point estimator was calculated. The respective correlation statistic was 4.6.

Statistical analysis title	Statistical analysis 2
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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 Factor Necrosis (TNF) inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	= 0.032 ^[3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	15.23

Notes:

[2] - 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.

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

Statistical analysis title	Statistical analysis 3
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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 Factor Necrosis (TNF) inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other ^[4]
P-value	= 0.001 ^[5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.28
upper limit	28.74

Notes:

[4] - 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.

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

Statistical analysis title	Statistical analysis 4
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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 Factor Necrosis (TNF) inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 160 mg LD (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other ^[6]
P-value	< 0.001 ^[7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.73
upper limit	34.26

Notes:

[6] - 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.

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

Statistical analysis title	Statistical analysis 5
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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 Factor Necrosis (TNF) inhibitor exposure.

Comparison groups	Placebo (FAS) v BKZ 320 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other ^[8]
P-value	= 0.051 ^[9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	13.68

Notes:

[8] - 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.

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

Secondary: ACR20 (American College of Rheumatology 20% Improvement) Response at Week 12

End point title	ACR20 (American College of Rheumatology 20% Improvement) Response at Week 12
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End point description:

The ACR20 response rate was based on 20% improvement relative to Baseline in the following measures:

- TJC based on 78 joints
- SJC based on 76 joints
- 3 of the 5 remaining core set measures:
 - Disease activity as assessed by PGADA
 - Disease activity as assessed by PhGADA
 - Pain as assessed by PtAAP
 - Physical function as assessed by HAQ-DI
 - Acute phase response as assessed by hs CRP

Note: Nonresponder imputation was used to account for missing data in the primary analysis, the study participants with a missing ACR score at Week 12 or who discontinued IMP prior to the Week 12 Visit were considered nonresponders for the primary analysis.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)	BKZ 160 mg LD (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	41	41
Units: percentage of subjects				
number (not applicable)	19.0	53.7	73.2	61.0

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	51.2			

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 Tumor Necrosis Factor (TNF) inhibitor exposure.	
Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002 ^[10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	12.39

Notes:

[10] - No sequential testing procedure was used for the secondary efficacy variables. 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 Tumor Necrosis Factor (TNF) inhibitor exposure.	
Comparison groups	Placebo (FAS) v BKZ 160 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.91
upper limit	30.95

Notes:

[11] - No sequential testing procedure was used for the secondary efficacy variables. 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 Tumor Necrosis Factor (TNF) inhibitor exposure.	
Comparison groups	Placebo (FAS) v BKZ 160 mg LD (FAS)

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.31
upper limit	16.84

Notes:

[12] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 4
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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 320 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004 ^[13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.59
upper limit	11.35

Notes:

[13] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Secondary: ACR70 (American College of Rheumatology 70% Improvement) Response at Week 12

End point title	ACR70 (American College of Rheumatology 70% Improvement) Response at Week 12
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End point description:

The ACR70 response rate was based on 70% improvement relative to Baseline in the following measures:

- TJC based on 78 joints
- SJC based on 76 joints
- 3 of the 5 remaining core set measures:
 - Disease activity as assessed by PGADA
 - Disease activity as assessed by PhGADA
 - Pain as assessed by PtAAP
 - Physical function as assessed by HAQ-DI
 - Acute phase response as assessed by hs CRP

Note: Nonresponder imputation was used to account for missing data in the primary analysis, the study participants with a missing ACR score at Week 12 or who discontinued IMP prior to the Week 12 Visit were considered nonresponders for the primary analysis.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)	BKZ 160 mg LD (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	41	41
Units: percentage of subjects				
number (not applicable)	4.8	12.2	19.5	31.7

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	14.6			

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 Tumor Necrosis Factor (TNF) inhibitor exposure.	
Comparison groups	Placebo (FAS) v BKZ 16 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.279 ^[14]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	11.31

Notes:

[14] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 2
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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 160 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.065 ^[15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	17.88

Notes:

[15] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 3
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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 160 mg LD (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.006 ^[16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	31.28

Notes:

[16] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Statistical analysis title	Statistical analysis 4
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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 320 mg (FAS)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.172 ^[17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	13.39

Notes:

[17] - No sequential testing procedure was used for the secondary efficacy variables. The p-values were displayed as nominal p-values.

Secondary: PASI90 (Psoriasis Area Severity Index) Response at Week 12 in the Subgroup of Subjects With Psoriasis Involving at Least 3 % Body Surface Area (BSA) at Baseline/Day 1

End point title	PASI90 (Psoriasis Area Severity Index) Response at Week 12 in the Subgroup of Subjects With Psoriasis Involving at Least 3 % Body Surface Area (BSA) at Baseline/Day 1
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End point description:

The PASI90 response assessments are based on at least 90% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)	BKZ 160 mg LD (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	14	16	17
Units: percentage of subjects				
number (not applicable)	10.0	35.7	62.5	52.9

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percentage of subjects				
number (not applicable)	45.5			

Statistical analyses

No statistical analyses for this end point

Secondary: PASI75 (Psoriasis Area Severity Index) Response at Week 12 in the Subgroup of Subjects With Psoriasis Involving at Least 3 % Body Surface Area (BSA) at Baseline/Day 1

End point title	PASI75 (Psoriasis Area Severity Index) Response at Week 12 in the Subgroup of Subjects With Psoriasis Involving at Least 3 % Body Surface Area (BSA) at Baseline/Day 1
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End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	BKZ 16 mg (FAS)	BKZ 160 mg (FAS)	BKZ 160 mg LD (FAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	14	16	17
Units: percentage of subjects				
number (not applicable)	10.0	57.1	68.8	70.6

End point values	BKZ 320 mg (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percentage of subjects				
number (not applicable)	72.7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 1 and up to the end of safety follow-up visit, 20 weeks after the final dose

Adverse event reporting additional description:

At Week 12, Placebo and BKZ 16 mg subjects were re-randomized to either BKZ 160 mg or BKZ 320 mg. Subjects randomized to BKZ 160 mg with 160 mg loading dose at Baseline remained on BKZ 160 mg treatment. Subjects randomized to BKZ 160 mg and BKZ 320 mg at Baseline were not re-randomized at Week 12 and remained on their original treatment.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	BKZ 320 mg (SS)
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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, forming the Safety Set (SS).

Reporting group title	BKZ 160 mg + BKZ 160 mg LD (SS)
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Reporting group description:

Participants received Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) and Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg Q4W during the 12 Weeks Double-Blind Period followed by Bimekizumab (BKZ) 160 mg Q4W during the 36 Weeks Dose-Blind Period, forming the Safety Set (SS).

Serious adverse events	BKZ 320 mg (SS)	BKZ 160 mg + BKZ 160 mg LD (SS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 80 (0.00%)	8 / 126 (6.35%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Drug-induced liver injury subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	0 / 80 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BKZ 320 mg (SS)	BKZ 160 mg + BKZ 160 mg LD (SS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 80 (31.25%)	39 / 126 (30.95%)	
Infections and infestations			

Respiratory tract infection subjects affected / exposed occurrences (all)	2 / 80 (2.50%) 3	8 / 126 (6.35%) 8	
Bronchitis subjects affected / exposed occurrences (all)	3 / 80 (3.75%) 3	7 / 126 (5.56%) 8	
Nasopharyngitis subjects affected / exposed occurrences (all)	11 / 80 (13.75%) 11	12 / 126 (9.52%) 15	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 80 (10.00%) 10	12 / 126 (9.52%) 12	
Pharyngitis subjects affected / exposed occurrences (all)	7 / 80 (8.75%) 7	4 / 126 (3.17%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2018	<p>Protocol Amendment 2 was a substantial amendment dated 09 Mar 2018. The purpose of this protocol amendment was the following:</p> <ul style="list-style-type: none">•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 study participants with newly diagnosed inflammatory bowel disease (IBD) or with IBD flares during the study.•To amend the time window between doses during the Double-blind Period of the study.•To add new details for the IMP packaging.•To revise and clarify the SAE criteria for pregnancy for consistency.•To amend the table for identification/exclusion of alternative etiology to include aspartate aminotransferase (AST) and alanine aminotransferase (ALT). <p>A total of 308 study participants were screened and 206 study participants were randomized at the time of this amendment.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported