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	v2 (current)
This version publication date	13 December 2020
First version publication date	08 September 2019
Version creation reason	• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.

Trial information

Trial identification

Sponsor protocol code	PA0008

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	Czechia: 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	Carer, Investigator, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received Placebo during the 12 Weeks Double-Blind Period.

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

Dosage and administration details:

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

Arm title	BKZ 16 mg

Arm description:

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

Arm type	Experimental
Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	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

Arm description:

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

Arm type	Experimental

Investigational medicinal product name	Bimekizumab
Investigational medicinal product code	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

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

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
Study medication discontinued prior Wk12	2	-	-
Adverse event, non-fatal	-	-	1
LOW EGFR	-	-	-

Number of subjects in period 1	BKZ 160 mg LD	BKZ 320 mg

Started	41	41
Completed Double-Blind Period	39	41
Completed Wk12 and started Dose-Blind	37	41
Completed	37	41
Not completed	4	0
Study medication discontinued prior Wk12	2	-
Adverse event, non-fatal	1	-
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

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

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

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

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

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

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

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	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.

Subject analysis set title	Placebo (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received Placebo during the 12 Weeks Double-Blind Period, forming the Safety Set (SS).

Subject analysis set title	BKZ 16 mg (SS)
Subject analysis set type	Safety 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 SS.

Subject analysis set title	BKZ 160 mg (SS)
Subject analysis set type	Safety 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 SS.

Subject analysis set title	BKZ 160 mg LD (SS)
Subject analysis set type	Safety 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 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 SS.

Subject analysis set title	Placebo (SS) - up to Wk 12
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received Placebo at any time in the study (up to Week 12). Participants formed the Safety Set (SS).

Subject analysis set title	BKZ 16 mg (SS) - up to Wk 12
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS.

Subject analysis set title	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) and Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) at any time in the study (up to Week 68). Participants formed the SS.

Subject analysis set title	BKZ 320 mg (SS) - up to Wk 68
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of all participants who received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) at any time in the study (up to Week 68). Participants formed the SS.

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

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).
The Full Analysis Set (FAS) consisted of all randomized study participants who received at least 1 dose of investigational medicinal product (IMP) and had a valid measurement of the primary efficacy variable at Baseline.

End point type	Primary

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

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)
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

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

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

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

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

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.
The FAS consisted of all randomized study participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

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

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

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.
The FAS consisted of all randomized study participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

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

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

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

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

End point description:

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/scaliness of the psoriatic lesions (0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head/arms/trunk to groin/legs to top of buttocks. Assignment of an average score for the redness/thickness/scaling for each of the 4 body areas with a score of 0 (clear)-4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0-6 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. Minimum possible PASI score is 0=no disease, maximum score is 72=maximal disease.
Subset of study participants in the FAS with ≥3% PSO BSA at Baseline (NRI).

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

End point description:

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/scaliness of the psoriatic lesions (0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head/arms/trunk to groin/legs to top of buttocks. Assignment of an average score for the redness/thickness/scaling for each of the 4 body areas with a score of 0 (clear)-4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0-6 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. Minimum possible PASI score is 0=no disease, maximum score is 72=maximal disease.
Subset of study participants in the FAS with ≥3% PSO BSA at Baseline (NRI).

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

Secondary: Percentage of participants with at least one adverse event (AE) during the study

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of investigational medicinal product (IMP), whether or not considered related to the IMP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP.
The Safety Set (SS) consisted of all randomized study participants who received at least 1 dose of IMP. The 160mg LD group and 160mg groups are combined into one column to see the effect of the 160mg dose overall.

End point type	Secondary

End point timeframe:

From Screening Period until the Safety Follow-Up Visit (up to Week 72)

End point values	Placebo (SS) - up to Wk 12	BKZ 16 mg (SS) - up to Wk 12	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68	BKZ 320 mg (SS) - up to Wk 68
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	39	126	80
Units: percentage of participants				
number (not applicable)	57.1	33.33	74.6	72.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with at least one serious adverse event (SAE) during the study

End point title	Percentage of participants with at least one serious adverse event (SAE) during the study

End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose:
- Results in death
- Is life-threatening
- Requires in patient hospitalization or prolongation of existing hospitalization
- Is a congenital anomaly or birth defect
- Is an infection that requires treatment parenteral antibiotics

• Other important medical events which based on medical or scientific judgement may jeopardize the patients, or may require medical or surgical intervention to prevent any of the above.
The Safety Set (SS) consisted of all randomized study participants who received at least 1 dose of IMP. The 160mg LD group and 160mg groups are combined into one column to see the effect of the 160mg dose overall.

End point type	Secondary

End point timeframe:

From Screening Period until the Safety Follow-Up Visit (up to Week 72)

End point values	Placebo (SS) - up to Wk 12	BKZ 16 mg (SS) - up to Wk 12	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68	BKZ 320 mg (SS) - up to Wk 68
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	39	126	80
Units: percentage of participants				
number (not applicable)	2.4	0	6.3	0

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of investigational medicinal product (IMP), whether or not considered related to the IMP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP.
The Safety Set (SS) consisted of all randomized study participants who received at least 1 dose of IMP. The 160mg LD group and 160mg groups are combined into one column to see the effect of the 160mg dose overall.

End point type	Secondary

End point timeframe:

From Screening Period until the Safety Follow-Up Visit (up to Week 72)

End point values	Placebo (SS) - up to Wk 12	BKZ 16 mg (SS) - up to Wk 12	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68	BKZ 320 mg (SS) - up to Wk 68
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	39	126	80
Units: percentage of participants				
number (not applicable)	4.8	0	4.8	2.5

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in vital signs during the study (diastolic blood pressure, systolic blood pressure)

End point title	Changes from Baseline in vital signs during the study (diastolic blood pressure, systolic blood pressure)

End point description:

Diastolic and systolic blood pressure (BP) were measured in millimeters of mercury (mmHg).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, 30 min and 1 hour post dose, Week 1, Week 2, pre- and post dose for the following Weeks: 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 and 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	39	43	41
Units: mmHg				
arithmetic mean (standard deviation)				
Diastolic BP 30 min post dose (42, 39, 43, 41, 41)	1.3 (± 8.9)	-1.2 (± 4.9)	-1.2 (± 5.4)	0.6 (± 6.1)
Diastolic BP 1 h post dose (42, 39, 43, 41, 41)	1.1 (± 8.8)	-2.0 (± 6.3)	-0.7 (± 8.1)	1.2 (± 6.7)
Diastolic BP Wk 1 (41, 39, 43, 41, 41)	0.1 (± 9.6)	-0.3 (± 6.5)	0.6 (± 11.4)	-0.9 (± 6.6)
Diastolic BP Wk 2 (42, 39, 43, 41, 41)	0.7 (± 10.4)	-0.7 (± 6.5)	-1.0 (± 8.9)	-2.7 (± 8.3)
Diastolic BP Wk 4 pre-dose (41, 39, 42, 41, 41)	0.0 (± 8.2)	-1.7 (± 8.4)	-1.4 (± 10.7)	-0.8 (± 7.8)
Diastolic BP Wk 4 post dose (41, 39, 41, 40, 40)	-2.0 (± 8.7)	-1.0 (± 7.3)	-1.2 (± 8.9)	-0.9 (± 8.3)
Diastolic BP Wk 8 pre-dose (41, 39, 43, 39, 41)	1.0 (± 8.2)	-1.3 (± 8.7)	0.3 (± 8.7)	-0.5 (± 7.0)
Diastolic BP Wk 8 post dose (41, 39, 42, 39, 41)	-0.9 (± 9.1)	-1.1 (± 8.4)	0.6 (± 8.7)	-0.7 (± 7.3)
Diastolic BP Wk 12 pre-dose (42, 39, 42, 39, 41)	0.2 (± 9.1)	-1.1 (± 10.4)	0.2 (± 8.5)	-1.5 (± 7.9)
Diastolic BP Wk 12 post dose (40, 39, 42, 37, 41)	-0.3 (± 9.6)	-2.0 (± 10.0)	0.3 (± 8.3)	-1.8 (± 7.9)
Diastolic BP Wk 16 pre-dose (42, 39, 42, 38, 41)	-2.7 (± 9.6)	-3.5 (± 8.9)	-0.8 (± 8.6)	-1.2 (± 8.7)
Diastolic BP Wk 16 post dose (40, 39, 39, 36, 39)	-3.0 (± 9.1)	-1.9 (± 8.3)	-1.7 (± 9.2)	-1.1 (± 7.9)

Diastolic BP Wk 20 pre-dose (40, 39, 42, 37, 40)	0.5 (± 10.3)	-1.8 (± 9.0)	-0.6 (± 8.3)	-1.4 (± 8.3)
Diastolic BP Wk 20 post dose (39, 39, 38, 36, 40)	0.1 (± 9.5)	-3.1 (± 8.3)	-0.4 (± 9.2)	-3.0 (± 9.3)
Diastolic BP Wk 24 pre-dose (39, 39, 41, 36, 40)	-0.4 (± 7.6)	-1.6 (± 7.2)	-0.7 (± 9.3)	1.0 (± 6.9)
Diastolic BP Wk 24 post dose (39, 38, 38, 35, 39)	-0.6 (± 7.5)	-1.7 (± 7.9)	-0.3 (± 8.2)	-0.3 (± 7.6)
Diastolic BP Wk 28 pre-dose (39, 39, 41, 35, 40)	1.4 (± 7.9)	-0.6 (± 9.7)	0.9 (± 9.5)	-0.6 (± 6.9)
Diastolic BP Wk 28 post dose (38, 39, 39, 34, 39)	1.2 (± 8.7)	-2.0 (± 9.4)	1.2 (± 9.0)	-0.2 (± 7.1)
Diastolic BP Wk 32 pre-dose (39, 39, 40, 35, 39)	0.2 (± 8.5)	-1.7 (± 8.6)	1.6 (± 9.2)	-0.3 (± 9.3)
Diastolic BP Wk 32 post dose (36, 39, 37, 34, 39)	0.7 (± 10.0)	-3.0 (± 8.6)	0.1 (± 9.6)	-0.6 (± 8.5)
Diastolic BP Wk 36 pre-dose (38, 38, 41, 34, 39)	0.0 (± 8.6)	-0.6 (± 9.2)	1.4 (± 8.9)	-0.9 (± 7.2)
Diastolic BP Wk 36 post dose (37, 38, 38, 31, 38)	1.6 (± 7.7)	-1.6 (± 9.2)	1.3 (± 9.3)	-1.7 (± 6.8)
Diastolic BP Wk 40 pre-dose (37, 38, 41, 34, 40)	0.8 (± 7.6)	-2.5 (± 9.7)	1.0 (± 9.5)	-1.0 (± 7.2)
Diastolic BP Wk 40 post dose (37, 38, 40, 33, 37)	0.9 (± 7.7)	-1.8 (± 9.1)	0.2 (± 8.3)	-0.8 (± 6.6)
Diastolic BP Wk 44 pre-dose (38, 38, 41, 34, 40)	1.4 (± 9.3)	-2.1 (± 7.7)	1.3 (± 9.2)	-0.4 (± 6.7)
Diastolic BP Wk 44 post dose (36, 38, 40, 33, 39)	2.3 (± 9.2)	-1.3 (± 7.6)	-0.7 (± 8.7)	-1.4 (± 8.1)
Diastolic BP Wk 48 (38, 38, 41, 34, 40)	1.8 (± 9.2)	0.4 (± 9.7)	1.1 (± 9.1)	0.6 (± 8.7)
Systolic BP 30 min post dose (42, 39, 43, 41, 41)	0.8 (± 8.1)	0.5 (± 9.7)	-0.8 (± 8.2)	1.5 (± 8.8)
Systolic BP 1 hour post dose (42, 39, 43, 41, 41)	-0.6 (± 9.4)	-2.0 (± 10.5)	0.2 (± 8.7)	1.0 (± 8.4)
Systolic BP Wk 1 (41, 39, 43, 41, 41)	-1.7 (± 10.8)	-1.3 (± 10.0)	1.7 (± 12.9)	-2.4 (± 8.3)
Systolic BP Wk 2 (42, 39, 43, 41, 41)	-0.7 (± 12.9)	-0.2 (± 9.8)	-0.1 (± 13.2)	-2.7 (± 8.2)
Systolic BP Wk 4 pre-dose (41, 39, 42, 41, 41)	-2.6 (± 11.4)	-1.5 (± 10.6)	-1.0 (± 13.0)	-2.3 (± 10.5)
Systolic BP Wk 4 post dose (41, 39, 41, 40, 40)	-3.5 (± 12.1)	-0.6 (± 10.4)	-2.2 (± 11.8)	-0.6 (± 9.1)
Systolic BP Wk 8 pre-dose (41, 39, 43, 39, 41)	-2.1 (± 13.1)	-0.8 (± 10.7)	-1.1 (± 11.3)	-3.6 (± 11.7)
Systolic BP Wk 8 post dose (41, 39, 42, 39, 41)	-3.2 (± 12.6)	-1.9 (± 11.6)	-0.3 (± 11.1)	-2.8 (± 10.2)
Systolic BP Wk 12 pre-dose (42, 39, 42, 39, 41)	-3.3 (± 12.4)	1.6 (± 13.7)	-3.1 (± 11.7)	-4.4 (± 10.8)
Systolic BP Wk 12 post dose (40, 39, 42, 37, 41)	-3.9 (± 14.1)	2.1 (± 11.1)	-1.9 (± 12.0)	-3.6 (± 10.1)
Systolic BP Wk 16 pre-dose (42, 39, 42, 38, 41)	-3.6 (± 15.1)	-2.3 (± 12.3)	-4.3 (± 11.3)	-4.3 (± 12.5)
Systolic BP Wk 16 post dose (40, 39, 39, 36, 39)	-3.7 (± 17.1)	-2.6 (± 11.7)	-3.4 (± 12.7)	-2.7 (± 11.0)
Systolic BP Wk 20 pre-dose (40, 39, 42, 37, 40)	-2.0 (± 13.1)	-3.2 (± 12.5)	-2.6 (± 11.9)	-5.4 (± 9.7)
Systolic BP Wk 20 post dose (39, 39, 38, 36, 40)	-1.9 (± 14.5)	-3.2 (± 13.0)	-3.7 (± 12.2)	-7.9 (± 11.9)
Systolic BP Wk 24 pre-dose (39, 39, 41, 36, 40)	-3.1 (± 10.5)	-1.1 (± 9.5)	-2.7 (± 12.3)	-3.6 (± 10.1)
Systolic BP Wk 24 post dose (39, 38, 38, 35, 39)	-2.6 (± 10.9)	-2.8 (± 10.5)	-2.2 (± 11.7)	-3.0 (± 9.7)
Systolic BP Wk 28 pre-dose (39, 39, 41, 35, 40)	-0.1 (± 11.4)	-2.5 (± 12.8)	-2.5 (± 13.1)	0.4 (± 11.6)

Systolic BP Wk 28 post dose (38, 39, 39, 34, 39)	-1.1 (± 12.1)	-2.9 (± 11.1)	-2.6 (± 12.4)	-0.7 (± 11.9)
Systolic BP Wk 32 pre-dose (39, 39, 40, 35, 39)	-0.9 (± 13.1)	-1.5 (± 13.3)	-0.6 (± 12.4)	0.6 (± 11.0)
Systolic BP Wk 32 post dose (36, 39, 37, 34, 39)	-1.7 (± 12.6)	-2.2 (± 11.6)	0.3 (± 12.5)	-0.4 (± 11.1)
Systolic BP Wk 36 pre-dose (38, 38, 41, 34, 39)	-3.1 (± 11.9)	1.1 (± 13.9)	-0.2 (± 13.6)	-1.8 (± 11.2)
Systolic BP Wk 36 post dose (37, 38, 38, 31, 38)	-0.6 (± 11.1)	1.3 (± 12.6)	-0.5 (± 12.4)	-3.8 (± 10.8)
Systolic BP Wk 40 pre-dose (37, 38, 41, 34, 40)	-3.3 (± 12.1)	-3.1 (± 11.4)	-1.6 (± 12.9)	-4.0 (± 9.5)
Systolic BP Wk 40 post dose (37, 38, 40, 33, 37)	-2.3 (± 11.7)	-0.4 (± 12.7)	-1.2 (± 13.8)	-3.2 (± 11.6)
Systolic BP Wk 44 pre-dose (38, 38, 41, 34, 40)	-2.8 (± 12.3)	-2.8 (± 9.9)	0.0 (± 13.1)	-5.1 (± 9.9)
Systolic BP Wk 44 post dose (36, 38, 40, 33, 39)	-1.8 (± 14.5)	-1.2 (± 9.5)	-0.6 (± 10.4)	-4.6 (± 10.3)
Systolic BP Wk 48 (38, 38, 41, 34, 40)	-1.1 (± 14.0)	-0.1 (± 12.5)	-0.1 (± 12.6)	-2.8 (± 11.5)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: mmHg				
arithmetic mean (standard deviation)				
Diastolic BP 30 min post dose (42, 39, 43, 41, 41)	-0.6 (± 5.3)			
Diastolic BP 1 h post dose (42, 39, 43, 41, 41)	-1.0 (± 5.5)			
Diastolic BP Wk 1 (41, 39, 43, 41, 41)	-0.4 (± 6.5)			
Diastolic BP Wk 2 (42, 39, 43, 41, 41)	-0.1 (± 9.0)			
Diastolic BP Wk 4 pre-dose (41, 39, 42, 41, 41)	-1.3 (± 7.4)			
Diastolic BP Wk 4 post dose (41, 39, 41, 40, 40)	-1.6 (± 7.6)			
Diastolic BP Wk 8 pre-dose (41, 39, 43, 39, 41)	0.2 (± 6.9)			
Diastolic BP Wk 8 post dose (41, 39, 42, 39, 41)	-2.2 (± 7.4)			
Diastolic BP Wk 12 pre-dose (42, 39, 42, 39, 41)	-0.6 (± 8.2)			
Diastolic BP Wk 12 post dose (40, 39, 42, 37, 41)	-2.6 (± 8.0)			
Diastolic BP Wk 16 pre-dose (42, 39, 42, 38, 41)	-0.4 (± 7.9)			
Diastolic BP Wk 16 post dose (40, 39, 39, 36, 39)	-2.4 (± 8.7)			
Diastolic BP Wk 20 pre-dose (40, 39, 42, 37, 40)	-1.8 (± 7.3)			
Diastolic BP Wk 20 post dose (39, 39, 38, 36, 40)	-2.6 (± 7.1)			
Diastolic BP Wk 24 pre-dose (39, 39, 41, 36, 40)	-1.0 (± 6.6)			
Diastolic BP Wk 24 post dose (39, 38, 38, 35, 39)	-1.4 (± 7.9)			

Diastolic BP Wk 28 pre-dose (39, 39, 41, 35, 40)	-0.5 (± 7.5)			
Diastolic BP Wk 28 post dose (38, 39, 39, 34, 39)	-1.8 (± 7.1)			
Diastolic BP Wk 32 pre-dose (39, 39, 40, 35, 39)	-1.2 (± 8.6)			
Diastolic BP Wk 32 post dose (36, 39, 37, 34, 39)	-2.1 (± 8.5)			
Diastolic BP Wk 36 pre-dose (38, 38, 41, 34, 39)	0.8 (± 7.5)			
Diastolic BP Wk 36 post dose (37, 38, 38, 31, 38)	-0.1 (± 7.1)			
Diastolic BP Wk 40 pre-dose (37, 38, 41, 34, 40)	-1.9 (± 6.8)			
Diastolic BP Wk 40 post dose (37, 38, 40, 33, 37)	-0.1 (± 7.3)			
Diastolic BP Wk 44 pre-dose (38, 38, 41, 34, 40)	-2.4 (± 10.9)			
Diastolic BP Wk 44 post dose (36, 38, 40, 33, 39)	-1.5 (± 6.5)			
Diastolic BP Wk 48 (38, 38, 41, 34, 40)	-0.8 (± 6.4)			
Systolic BP 30 min post dose (42, 39, 43, 41, 41)	-2.5 (± 9.7)			
Systolic BP 1 hour post dose (42, 39, 43, 41, 41)	-1.8 (± 7.1)			
Systolic BP Wk 1 (41, 39, 43, 41, 41)	-1.6 (± 11.0)			
Systolic BP Wk 2 (42, 39, 43, 41, 41)	-0.4 (± 11.9)			
Systolic BP Wk 4 pre-dose (41, 39, 42, 41, 41)	-2.7 (± 11.2)			
Systolic BP Wk 4 post dose (41, 39, 41, 40, 40)	-3.7 (± 11.3)			
Systolic BP Wk 8 pre-dose (41, 39, 43, 39, 41)	-1.3 (± 10.4)			
Systolic BP Wk 8 post dose (41, 39, 42, 39, 41)	-1.9 (± 12.0)			
Systolic BP Wk 12 pre-dose (42, 39, 42, 39, 41)	-2.6 (± 9.7)			
Systolic BP Wk 12 post dose (40, 39, 42, 37, 41)	-2.4 (± 10.1)			
Systolic BP Wk 16 pre-dose (42, 39, 42, 38, 41)	-2.3 (± 11.4)			
Systolic BP Wk 16 post dose (40, 39, 39, 36, 39)	-5.7 (± 8.5)			
Systolic BP Wk 20 pre-dose (40, 39, 42, 37, 40)	-4.5 (± 10.5)			
Systolic BP Wk 20 post dose (39, 39, 38, 36, 40)	-4.4 (± 9.9)			
Systolic BP Wk 24 pre-dose (39, 39, 41, 36, 40)	-0.3 (± 10.5)			
Systolic BP Wk 24 post dose (39, 38, 38, 35, 39)	-1.1 (± 10.5)			
Systolic BP Wk 28 pre-dose (39, 39, 41, 35, 40)	-2.9 (± 11.3)			
Systolic BP Wk 28 post dose (38, 39, 39, 34, 39)	-4.6 (± 11.2)			
Systolic BP Wk 32 pre-dose (39, 39, 40, 35, 39)	-3.7 (± 12.4)			
Systolic BP Wk 32 post dose (36, 39, 37, 34, 39)	-4.8 (± 10.6)			
Systolic BP Wk 36 pre-dose (38, 38, 41, 34, 39)	-3.2 (± 11.1)			

Systolic BP Wk 36 post dose (37, 38, 38, 31, 38)	-3.8 (± 11.4)			
Systolic BP Wk 40 pre-dose (37, 38, 41, 34, 40)	-1.2 (± 11.0)			
Systolic BP Wk 40 post dose (37, 38, 40, 33, 37)	-2.2 (± 9.6)			
Systolic BP Wk 44 pre-dose (38, 38, 41, 34, 40)	-3.9 (± 10.3)			
Systolic BP Wk 44 post dose (36, 38, 40, 33, 39)	-3.8 (± 10.5)			
Systolic BP Wk 48 (38, 38, 41, 34, 40)	-5.2 (± 9.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in vital signs during the study (pulse rate)

End point title	Changes from Baseline in vital signs during the study (pulse rate)

End point description:

Pulse rate was measured in beats per minute (beats/min).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, 30 min and 1 hour post dose, Week 1, Week 2, pre- and post dose for the following Weeks: 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 and 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	39	43	41
Units: beats/min				
arithmetic mean (standard deviation)				
30 min post dose (42, 39, 43, 41, 41)	0.4 (± 5.4)	-0.8 (± 5.6)	-1.5 (± 7.2)	-2.3 (± 7.5)
1 hour post dose (42, 39, 43, 41, 41)	0.3 (± 6.7)	1.0 (± 11.3)	-0.8 (± 7.6)	-0.8 (± 8.1)
Week 1 (41, 39, 43, 41, 41)	2.9 (± 8.3)	-1.5 (± 7.5)	-0.7 (± 7.1)	0.6 (± 8.9)
Week 2 (42, 39, 43, 41, 41)	1.2 (± 6.4)	-1.7 (± 5.7)	-0.7 (± 7.9)	-1.0 (± 9.1)
Week 4 pre-dose (41, 39, 42, 41, 41)	-0.2 (± 5.3)	-2.1 (± 6.9)	-1.9 (± 8.1)	0.1 (± 9.8)
Week 4 post dose (41, 39, 41, 40, 40)	0.4 (± 8.6)	-2.6 (± 6.6)	-2.7 (± 9.5)	-0.5 (± 9.4)
Week 8 pre-dose (41, 39, 43, 39, 41)	0.9 (± 6.5)	-0.6 (± 8.0)	-1.6 (± 8.6)	0.8 (± 6.9)
Week 8 post dose (41, 39, 42, 39, 41)	-0.1 (± 6.9)	-1.3 (± 8.6)	-1.9 (± 8.6)	0.0 (± 8.5)
Week 12 pre-dose (42, 39, 42, 39, 41)	1.1 (± 10.2)	-2.2 (± 8.5)	-2.9 (± 10.5)	-1.7 (± 9.5)
Week 12 post dose (40, 39, 42, 37, 41)	-0.6 (± 8.8)	-3.3 (± 8.8)	-3.6 (± 9.4)	-2.1 (± 9.7)
Week 16 pre-dose (42, 39, 42, 38, 41)	-0.2 (± 8.5)	-2.1 (± 5.8)	-2.9 (± 8.0)	-1.9 (± 10.1)
Week 16 post dose (40, 39, 39, 36, 39)	-0.1 (± 9.9)	-3.5 (± 5.5)	-3.7 (± 9.7)	-2.1 (± 9.8)
Week 20 pre-dose (40, 39, 42, 37, 40)	-0.1 (± 10.3)	-2.4 (± 7.0)	-1.7 (± 10.3)	0.0 (± 9.0)
Week 20 post dose (39, 39, 38, 36, 40)	-0.7 (± 6.8)	-2.3 (± 7.8)	-2.1 (± 9.7)	-0.1 (± 8.5)

Week 24 pre-dose (39, 39, 41, 36, 40)	-0.5 (± 7.9)	-2.0 (± 8.1)	-2.8 (± 10.4)	-0.7 (± 7.3)
Week 24 post dose (39, 38, 38, 35, 39)	-0.9 (± 7.8)	-2.9 (± 8.5)	-3.0 (± 9.6)	-1.3 (± 6.9)
Week 28 pre-dose (39, 39, 41, 35, 40)	1.9 (± 9.7)	-2.1 (± 10.0)	0.0 (± 9.3)	-0.5 (± 11.2)
Week 28 post dose (38, 39, 39, 34, 39)	1.8 (± 7.5)	-3.0 (± 9.4)	-0.5 (± 8.5)	-0.8 (± 10.0)
Week 32 pre-dose (39, 39, 40, 35, 39)	3.3 (± 10.0)	-0.9 (± 7.9)	-2.0 (± 9.2)	-1.2 (± 10.6)
Week 32 post dose (36, 39, 37, 34, 39)	3.3 (± 8.4)	-0.8 (± 7.8)	-3.0 (± 9.5)	-1.9 (± 9.6)
Week 36 pre-dose (38, 38, 41, 34, 39)	0.7 (± 8.5)	0.2 (± 7.5)	-2.6 (± 8.6)	-2.6 (± 10.2)
Week 36 post dose (37, 38, 38, 31, 38)	1.1 (± 7.6)	-0.8 (± 8.2)	-3.0 (± 9.8)	-2.5 (± 8.2)
Week 40 pre-dose (37, 38, 41, 34, 40)	2.7 (± 10.3)	-0.5 (± 8.8)	1.0 (± 10.1)	-1.7 (± 7.6)
Week 40 post dose (37, 38, 40, 33, 37)	0.9 (± 8.3)	-1.7 (± 8.3)	0.0 (± 8.9)	-2.0 (± 8.4)
Week 44 pre-dose (38, 38, 41, 34, 40)	2.2 (± 8.9)	-1.6 (± 6.9)	-0.4 (± 10.1)	-1.4 (± 8.2)
Week 44 post dose (36, 38, 40, 33, 38)	2.9 (± 6.9)	-1.7 (± 8.0)	-0.5 (± 11.0)	-2.8 (± 7.7)
Week 48 (38, 38, 41, 34, 40)	2.0 (± 8.9)	-3.7 (± 7.8)	-2.5 (± 10.4)	-4.2 (± 9.5)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: beats/min				
arithmetic mean (standard deviation)				
30 min post dose (42, 39, 43, 41, 41)	-1.1 (± 7.2)			
1 hour post dose (42, 39, 43, 41, 41)	-0.4 (± 7.0)			
Week 1 (41, 39, 43, 41, 41)	-0.8 (± 9.0)			
Week 2 (42, 39, 43, 41, 41)	-0.4 (± 6.9)			
Week 4 pre-dose (41, 39, 42, 41, 41)	-1.0 (± 6.6)			
Week 4 post dose (41, 39, 41, 40, 40)	-1.1 (± 6.2)			
Week 8 pre-dose (41, 39, 43, 39, 41)	-1.3 (± 8.2)			
Week 8 post dose (41, 39, 42, 39, 41)	-2.3 (± 8.3)			
Week 12 pre-dose (42, 39, 42, 39, 41)	-1.1 (± 8.4)			
Week 12 post dose (40, 39, 42, 37, 41)	-2.0 (± 7.8)			
Week 16 pre-dose (42, 39, 42, 38, 41)	-1.3 (± 7.2)			
Week 16 post dose (40, 39, 39, 36, 39)	-2.2 (± 7.3)			
Week 20 pre-dose (40, 39, 42, 37, 40)	-1.2 (± 9.0)			
Week 20 post dose (39, 39, 38, 36, 40)	-1.3 (± 8.9)			
Week 24 pre-dose (39, 39, 41, 36, 40)	-1.2 (± 7.8)			
Week 24 post dose (39, 38, 38, 35, 39)	-2.5 (± 7.1)			
Week 28 pre-dose (39, 39, 41, 35, 40)	0.2 (± 8.3)			
Week 28 post dose (38, 39, 39, 34, 39)	0.0 (± 7.5)			
Week 32 pre-dose (39, 39, 40, 35, 39)	-0.3 (± 7.8)			
Week 32 post dose (36, 39, 37, 34, 39)	-2.0 (± 8.8)			
Week 36 pre-dose (38, 38, 41, 34, 39)	-0.5 (± 9.7)			
Week 36 post dose (37, 38, 38, 31, 38)	-1.4 (± 9.6)			
Week 40 pre-dose (37, 38, 41, 34, 40)	2.0 (± 9.4)			
Week 40 post dose (37, 38, 40, 33, 37)	0.5 (± 9.1)			
Week 44 pre-dose (38, 38, 41, 34, 40)	0.7 (± 9.7)			
Week 44 post dose (36, 38, 40, 33, 38)	-0.2 (± 10.3)			
Week 48 (38, 38, 41, 34, 40)	-3.1 (± 9.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in body weight during the study

End point title	Changes from Baseline in body weight during the study

End point description:

Body weight was measured in kilograms.
The SS consisted of all randomized study participants who received at least 1 dose of IMP.
Overall number of participants analyzed include only those for whom body weight was measured and analyzed during the study.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 24, Week 36 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	39	43	38
Units: kilograms				
arithmetic mean (standard deviation)				
Week 12 (41, 39, 43, 38, 41)	0.14 (± 3.38)	-0.87 (± 3.12)	0.21 (± 1.78)	-0.38 (± 1.80)
Week 24 (39, 38, 41, 36, 40)	0.33 (± 4.10)	-0.03 (± 3.48)	-0.07 (± 2.63)	-0.13 (± 2.37)
Week 36 (38, 38, 41, 34, 39)	0.32 (± 5.15)	-0.14 (± 2.90)	0.27 (± 3.42)	0.15 (± 2.36)
Week 48 (38, 38, 41, 34, 40)	0.21 (± 4.42)	0.45 (± 3.41)	0.80 (± 3.84)	-0.14 (± 3.32)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: kilograms				
arithmetic mean (standard deviation)				
Week 12 (41, 39, 43, 38, 41)	-0.04 (± 2.39)			
Week 24 (39, 38, 41, 36, 40)	-0.39 (± 3.73)			
Week 36 (38, 38, 41, 34, 39)	-0.04 (± 4.19)			
Week 48 (38, 38, 41, 34, 40)	0.11 (± 4.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in electrocardiogram (ECG) intervals during the study (QTcB, QTcF, PR, QRS, QT, RR)

End point title	Changes from Baseline in electrocardiogram (ECG) intervals during the study (QTcB, QTcF, PR, QRS, QT, RR)

End point description:

Electrocardiogram (ECG) intervals (QTcB= QT interval corrected for heart rate (Bazett's formula); QTcF= QT interval corrected for heart rate (Fridericia's formula)) were measured in milliseconds.
The SS consisted of all randomized study participants who received at least 1 dose of IMP.
Overall number of participants analyzed include only those for whom electrocardiogram data was measured and analyzed during the study.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 12 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	36	42	34
Units: msec				
arithmetic mean (standard deviation)				
QTcB Week 12 (38, 36, 42, 34, 40)	3.4 (± 32.7)	-2.8 (± 29.9)	-5.6 (± 41.8)	1.5 (± 18.2)
QTcB Week 48 (35, 37, 40, 31, 39)	-2.5 (± 34.8)	-5.8 (± 36.5)	-5.9 (± 22.2)	-4.7 (± 21.0)
QTcF Week 12 (37, 32, 35, 32, 39)	4.5 (± 27.5)	-2.5 (± 22.4)	-2.2 (± 14.2)	-0.5 (± 17.0)
QTcF Week 48 (35, 32, 34, 29, 38)	-0.1 (± 30.7)	-6.1 (± 31.4)	-0.2 (± 15.6)	-2.2 (± 20.0)
PR Week 12 (39, 37, 42, 36, 41)	-1.7 (± 23.3)	-1.0 (± 23.7)	-19.6 (± 102.1)	3.2 (± 18.2)
PR Week 48 (37, 38, 40, 33, 40)	2.6 (± 33.7)	17.5 (± 128.8)	4.0 (± 163.0)	0.8 (± 18.9)
QRS Week 12 (40, 38, 42, 36, 41)	2.6 (± 22.3)	-2.9 (± 10.8)	-1.8 (± 7.6)	-0.2 (± 5.4)
QRS Week 48 (38, 38, 40, 33, 40)	5.6 (± 21.4)	-1.5 (± 16.1)	-4.0 (± 13.0)	0.6 (± 16.2)
QT Week 12 (40, 38, 42, 36, 41)	-2.0 (± 46.6)	1.7 (± 34.0)	9.5 (± 21.4)	3.8 (± 25.6)
QT Week 48 (38, 38, 40, 33, 40)	-0.7 (± 33.4)	3.1 (± 29.9)	3.9 (± 22.8)	5.4 (± 26.7)
RR Week 12 (39, 36, 42, 34, 41)	3.3 (± 99.3)	-22.5 (± 212.6)	75.8 (± 179.3)	11.0 (± 125.1)
RR Week 48 (37, 36, 40, 31, 40)	-0.6 (± 116.1)	11.9 (± 187.1)	65.2 (± 139.0)	44.3 (± 124.0)

End point values	BKZ 320 mg			

	(SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: msec				
arithmetic mean (standard deviation)				
QTcB Week 12 (38, 36, 42, 34, 40)	-1.9 (± 31.4)			
QTcB Week 48 (35, 37, 40, 31, 39)	-5.7 (± 27.7)			
QTcF Week 12 (37, 32, 35, 32, 39)	-3.0 (± 18.8)			
QTcF Week 48 (35, 32, 34, 29, 38)	4.6 (± 44.6)			
PR Week 12 (39, 37, 42, 36, 41)	-9.5 (± 32.3)			
PR Week 48 (37, 38, 40, 33, 40)	-2.8 (± 26.5)			
QRS Week 12 (40, 38, 42, 36, 41)	6.1 (± 42.8)			
QRS Week 48 (38, 38, 40, 33, 40)	0.1 (± 18.7)			
QT Week 12 (40, 38, 42, 36, 41)	11.5 (± 80.8)			
QT Week 48 (38, 38, 40, 33, 40)	0.7 (± 31.6)			
RR Week 12 (39, 36, 42, 34, 41)	-17.0 (± 182.1)			
RR Week 48 (37, 36, 40, 31, 40)	25.1 (± 148.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (basophils, eosinophils, leukocytes, lymphocytes, monocytes, neutrophils)

End point title	Changes from Baseline in hematology parameters during the study (basophils, eosinophils, leukocytes, lymphocytes, monocytes, neutrophils)

End point description:

Basophils, eosinophils, leukocytes, lymphocytes, monocytes, neutrophils were measured in number of white blood cells per liter (10^9/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: 10^9 white blood cells per liter				
arithmetic mean (standard deviation)				
Basophils Week 1 (41, 38, 43, 41, 40)	0.000 (± 0.0387)	0.000 (± 0.0329)	-0.002 (± 0.0408)	0.007 (± 0.0264)
Basophils Week 2 (42, 38, 43, 41, 41)	0.002 (± 0.0269)	0.003 (± 0.0283)	0.000 (± 0.0488)	0.000 (± 0.0316)

Basophils Week 4 (41, 38, 42, 41, 41)	0.002 (± 0.0474)	0.005 (± 0.0324)	-0.007 (± 0.0463)	0.005 (± 0.0312)
Basophils Week 8 (41, 39, 41, 38, 41)	-0.002 (± 0.0353)	0.000 (± 0.0229)	-0.005 (± 0.0384)	0.003 (± 0.0367)
Basophils Week 12 (41, 39, 43, 38, 41)	0.002 (± 0.0353)	0.003 (± 0.0280)	-0.002 (± 0.0462)	0.000 (± 0.0329)
Basophils Week 16 (42, 38, 42, 38, 40)	0.010 (± 0.0431)	0.005 (± 0.0324)	-0.007 (± 0.0463)	0.000 (± 0.0329)
Basophils Week 20 (39, 39, 41, 37, 39)	-0.003 (± 0.0362)	0.003 (± 0.0362)	0.000 (± 0.0500)	0.005 (± 0.0329)
Basophils Week 24 (39, 38, 40, 36, 40)	0.000 (± 0.0397)	0.005 (± 0.0324)	-0.003 (± 0.0530)	0.008 (± 0.0368)
Basophils Week 28 (39, 38, 40, 35, 40)	0.005 (± 0.0394)	0.000 (± 0.0329)	0.008 (± 0.0526)	0.011 (± 0.0323)
Basophils Week 32 (39, 39, 40, 34, 39)	0.000 (± 0.0324)	0.005 (± 0.0320)	-0.010 (± 0.0441)	0.009 (± 0.0379)
Basophils Week 36 (37, 38, 41, 33, 39)	0.000 (± 0.0408)	0.003 (± 0.0283)	-0.002 (± 0.0474)	0.012 (± 0.0415)
Basophils Week 40 (36, 38, 40, 34, 38)	0.003 (± 0.0506)	0.005 (± 0.0399)	-0.010 (± 0.0379)	0.006 (± 0.0343)
Basophils Week 44 (36, 37, 41, 34, 36)	0.006 (± 0.0410)	0.003 (± 0.0372)	0.000 (± 0.0387)	0.006 (± 0.0422)
Basophils Week 48 (38, 36, 40, 32, 39)	-0.005 (± 0.0462)	0.003 (± 0.291)	-0.010 (± 0.0441)	0.006 (± 0.0354)
Eosinophils Week 1 (41, 38, 43, 41, 40)	0.010 (± 0.0860)	0.016 (± 0.0718)	-0.002 (± 0.0801)	-0.005 (± 0.0999)
Eosinophils Week 2 (42, 38, 43, 41, 41)	0.005 (± 0.0731)	0.013 (± 0.0777)	0.002 (± 0.0913)	0.002 (± 0.0880)
Eosinophils Week 4 (41, 38, 42, 41, 41)	0.002 (± 0.0987)	0.016 (± 0.0594)	0.002 (± 0.0780)	0.005 (± 0.0999)
Eosinophils Week 8 (41, 39, 41, 38, 41)	0.024 (± 0.0969)	-0.003 (± 0.0707)	0.000 (± 0.1000)	0.008 (± 0.0941)
Eosinophils Week 12 (41, 39, 43, 38, 41)	0.020 (± 0.0954)	0.010 (± 0.0882)	0.002 (± 0.0831)	-0.026 (± 0.1155)
Eosinophils Week 16 (42, 38, 42, 38, 40)	0.045 (± 0.1253)	0.021 (± 0.0935)	0.010 (± 0.0759)	-0.005 (± 0.1559)
Eosinophils Week 20 (39, 39, 41, 37, 39)	0.036 (± 0.1038)	0.026 (± 0.1186)	0.024 (± 0.1157)	-0.014 (± 0.1228)
Eosinophils Week 24 (39, 38, 40, 36, 40)	0.031 (± 0.1301)	0.013 (± 0.0844)	0.058 (± 0.2111)	-0.019 (± 0.1238)
Eosinophils Week 28 (39, 38, 40, 35, 40)	0.036 (± 0.0986)	0.018 (± 0.0926)	0.053 (± 0.1826)	-0.000 (± 0.1213)
Eosinophils Week 32 (39, 39, 40, 34, 39)	0.049 (± 0.1502)	0.033 (± 0.0838)	0.020 (± 0.1418)	0.024 (± 0.1577)
Eosinophils Week 36 (37, 38, 41, 33, 39)	0.054 (± 0.1726)	0.018 (± 0.0955)	0.022 (± 0.0909)	0.027 (± 0.1526)
Eosinophils Week 40 (36, 38, 40, 34, 38)	0.050 (± 0.1444)	0.018 (± 0.0865)	0.018 (± 0.0958)	0.015 (± 0.1971)
Eosinophils Week 44 (36, 37, 41, 34, 36)	0.072 (± 0.1523)	0.019 (± 0.0908)	0.024 (± 0.0994)	-0.009 (± 0.1798)
Eosinophils Week 48 (38, 36, 40, 32, 39)	0.045 (± 0.1811)	0.006 (± 0.0754)	0.023 (± 0.0891)	0.009 (± 0.2833)
Leukocytes Week 1 (41, 38, 43, 41, 40)	-0.271 (± 1.1885)	-0.597 (± 1.1490)	-0.656 (± 1.2593)	-1.029 (± 1.6496)
Leukocytes Week 2 (42, 39, 43, 41, 41)	0.157 (± 1.3195)	-0.131 (± 2.1769)	-0.309 (± 1.3735)	-0.954 (± 2.0441)
Leukocytes Week 4 (41, 38, 42, 41, 41)	-0.049 (± 1.1938)	-0.411 (± 1.1988)	-0.336 (± 1.5088)	-1.017 (± 1.9397)
Leukocytes Week 8 (41, 39, 41, 38, 41)	0.429 (± 1.7036)	-0.333 (± 1.4014)	-0.185 (± 1.2889)	-1.071 (± 1.9639)
Leukocytes Week 12 (41, 39, 43, 38, 41)	0.190 (± 1.6223)	-0.438 (± 1.3854)	-0.495 (± 1.6904)	-0.997 (± 2.1806)

Leukocytes Week 16 (42, 38, 42, 38, 40)	-0.400 (± 1.5616)	-0.839 (± 1.8179)	-0.590 (± 1.4668)	-1.318 (± 2.3324)
Leukocytes Week 20 (39, 39, 41, 37, 40)	-0.936 (± 1.2756)	-1.100 (± 1.5599)	-0.432 (± 1.3032)	-0.932 (± 2.2832)
Leukocytes Week 24 (39, 38, 40, 36, 40)	-1.251 (± 1.3888)	-0.884 (± 1.7768)	-0.495 (± 1.4216)	-1.119 (± 2.2807)
Leukocytes Week 28 (39, 38, 41, 35, 40)	-0.700 (± 1.8180)	-0.316 (± 2.3086)	-0.100 (± 1.4942)	-0.894 (± 1.7119)
Leukocytes Week 32 (39, 39, 40, 34, 39)	-0.762 (± 1.4273)	-0.862 (± 2.0091)	-0.330 (± 1.5750)	-0.918 (± 2.6184)
Leukocytes Week 36 (37, 38, 41, 33, 39)	-0.541 (± 1.5971)	-0.974 (± 1.7389)	-0.366 (± 1.4549)	-1.082 (± 2.3389)
Leukocytes Week 40 (36, 38, 41, 34, 38)	-0.783 (± 1.7693)	-0.826 (± 1.5942)	-0.437 (± 1.7878)	-1.226 (± 2.3856)
Leukocytes Week 44 (37, 37, 41, 34, 36)	-1.065 (± 1.6070)	-0.978 (± 1.8151)	-0.537 (± 1.5641)	-1.032 (± 2.1585)
Leukocytes Week 48 (38, 36, 40, 32, 39)	-0.739 (± 1.7774)	-0.869 (± 1.7109)	-0.473 (± 1.7104)	-1.225 (± 2.5952)
Lymphocytes Week 1 (41, 38, 43, 41, 40)	-0.083 (± 0.5074)	-0.024 (± 0.4142)	0.044 (± 0.5039)	-0.017 (± 0.4189)
Lymphocytes Week 2 (42, 38, 43, 41, 41)	0.105 (± 0.3246)	0.026 (± 0.4137)	0.021 (± 0.6006)	0.007 (± 0.3643)
Lymphocytes Week 4 (41, 38, 42, 41, 41)	0.037 (± 0.4386)	0.024 (± 0.3259)	0.010 (± 0.6003)	-0.032 (± 0.3996)
Lymphocytes Week 8 (41, 39, 41, 38, 41)	0.120 (± 0.3776)	0.054 (± 0.3783)	0.063 (± 0.5928)	0.053 (± 0.4980)
Lymphocytes Week 12 (41, 39, 43, 38, 41)	0.041 (± 0.3647)	0.051 (± 0.4167)	0.000 (± 0.5640)	-0.047 (± 0.3703)
Lymphocytes Week 16 (42, 38, 42, 38, 40)	0.052 (± 0.5567)	0.071 (± 0.3571)	0.026 (± 0.5539)	-0.029 (± 0.4991)
Lymphocytes Week 20 (39, 39, 41, 37, 39)	0.003 (± 0.4934)	0.008 (± 0.3970)	0.149 (± 0.4675)	-0.035 (± 0.4566)
Lymphocytes Week 24 (39, 38, 40, 36, 40)	-0.041 (± 0.3905)	0.050 (± 0.3630)	0.048 (± 0.4455)	-0.036 (± 0.3788)
Lymphocytes Week 28 (39, 38, 40, 35, 40)	0.036 (± 0.5869)	0.105 (± 0.3594)	0.210 (± 0.5999)	0.103 (± 0.5544)
Lymphocytes Week 32 (39, 39, 40, 34, 39)	-0.000 (± 0.5109)	0.103 (± 0.4233)	0.083 (± 0.6524)	0.112 (± 0.5056)
Lymphocytes Week 36 (37, 38, 41, 33, 39)	0.078 (± 0.4894)	0.039 (± 0.4227)	0.134 (± 0.5673)	0.103 (± 0.5491)
Lymphocytes Week 40 (36, 38, 40, 34, 38)	0.139 (± 0.4871)	0.168 (± 0.4281)	0.120 (± 0.6018)	0.038 (± 0.4335)
Lymphocytes Week 44 (36, 37, 41, 34, 36)	-0.008 (± 0.5390)	0.105 (± 0.4136)	0.124 (± 0.5366)	0.115 (± 0.4881)
Lymphocytes Week 48 (38, 36, 40, 32, 39)	0.066 (± 0.5313)	0.103 (± 0.3645)	0.078 (± 0.5041)	0.019 (± 0.3763)
Monocytes Week 1 (41, 38, 43, 41, 40)	0.007 (± 0.2184)	-0.008 (± 0.1477)	-0.012 (± 0.1679)	-0.088 (± 0.2315)
Monocytes Week 2 (42, 38, 43, 41, 41)	0.076 (± 0.1358)	-0.011 (± 0.1673)	0.014 (± 0.1897)	-0.095 (± 0.2701)
Monocytes Week 4 (41, 38, 42, 41, 41)	0.032 (± 0.1588)	-0.021 (± 0.1473)	-0.040 (± 0.1862)	-0.066 (± 0.2404)
Monocytes Week 8 (41, 39, 41, 38, 41)	0.059 (± 0.1910)	-0.041 (± 0.1743)	0.005 (± 0.1580)	-0.103 (± 0.2520)
Monocytes Week 12 (41, 39, 43, 38, 41)	0.020 (± 0.1913)	-0.031 (± 0.1608)	-0.033 (± 0.1686)	-0.105 (± 0.2630)
Monocytes Week 16 (42, 38, 42, 38, 40)	-0.007 (± 0.1629)	-0.050 (± 0.1673)	-0.024 (± 0.1265)	-0.079 (± 0.2384)
Monocytes Week 20 (39, 39, 41, 37, 39)	-0.008 (± 0.1783)	-0.041 (± 0.1534)	-0.015 (± 0.1509)	-0.081 (± 0.2448)
Monocytes Week 24 (39, 38, 40, 36, 40)	-0.026 (± 0.1292)	-0.034 (± 0.1361)	0.003 (± 0.1476)	-0.056 (± 0.2602)

Monocytes Week 28 (39, 38, 40, 35, 40)	0.026 (± 0.2087)	0.042 (± 0.1981)	0.055 (± 0.1724)	-0.029 (± 0.2729)
Monocytes Week 32 (39, 39, 40, 34, 39)	0.064 (± 0.2356)	-0.005 (± 0.1731)	-0.003 (± 0.1271)	-0.035 (± 0.2684)
Monocytes Week 36 (37, 38, 41, 33, 39)	0.054 (± 0.1626)	-0.024 (± 0.1792)	0.032 (± 0.1404)	-0.036 (± 0.2644)
Monocytes Week 40 (36, 38, 40, 34, 38)	0.053 (± 0.1647)	0.008 (± 0.1323)	0.020 (± 0.1636)	-0.059 (± 0.2830)
Monocytes Week 44 (36, 37, 41, 34, 36)	0.019 (± 0.1939)	-0.008 (± 0.1588)	0.044 (± 0.1644)	-0.032 (± 0.2446)
Monocytes Week 48 (38, 36, 40, 32, 39)	0.021 (± 0.2145)	0.000 (± 0.1707)	-0.013 (± 0.1399)	-0.078 (± 0.2511)
Neutrophils Week 1 (41, 38, 43, 41, 40)	-0.200 (± 1.0959)	-0.558 (± 0.9627)	-0.693 (± 1.2971)	-0.934 (± 1.4768)
Neutrophils Week 2 (42, 38, 43, 41, 41)	-0.026 (± 1.1945)	-0.418 (± 1.1627)	-0.337 (± 1.3109)	-0.880 (± 1.8457)
Neutrophils Week 4 (41, 38, 42, 41, 41)	-0.102 (± 1.0044)	-0.405 (± 1.1246)	-0.290 (± 1.3463)	-0.924 (± 1.9975)
Neutrophils Week 8 (41, 39, 41, 38, 41)	0.249 (± 1.5358)	-0.346 (± 1.2640)	-0.256 (± 1.3898)	-1.021 (± 1.7129)
Neutrophils Week 12 (41, 39, 43, 38, 41)	0.117 (± 1.5103)	-0.456 (± 1.1227)	-0.458 (± 1.6879)	-0.832 (± 2.2192)
Neutrophils Week 16 (42, 38, 42, 38, 40)	-0.490 (± 1.6866)	-0.879 (± 1.5752)	-0.617 (± 1.6027)	-1.203 (± 2.2840)
Neutrophils Week 20 (39, 39, 41, 37, 39)	-0.972 (± 1.2085)	-1.069 (± 1.4219)	-0.595 (± 1.4319)	-0.827 (± 2.2663)
Neutrophils Week 24 (39, 38, 40, 36, 40)	-1.210 (± 1.4067)	-0.895 (± 1.6288)	-0.593 (± 1.5309)	-1.011 (± 2.2968)
Neutrophils Week 28 (39, 38, 40, 35, 40)	-0.774 (± 1.8189)	-0.484 (± 2.2620)	-0.555 (± 1.2608)	-0.949 (± 1.7676)
Neutrophils Week 32 (39, 39, 40, 34, 39)	-0.869 (± 1.2796)	-0.969 (± 1.8241)	-0.433 (± 1.7889)	-1.038 (± 2.4800)
Neutrophils Week 36 (37, 38, 41, 33, 39)	-0.722 (± 1.6422)	-0.992 (± 1.6583)	-0.541 (± 1.5519)	-1.185 (± 2.1881)
Neutrophils Week 40 (36, 38, 40, 34, 38)	-1.006 (± 1.7393)	-0.992 (± 1.4740)	-0.575 (± 1.9567)	-1.229 (± 2.4065)
Neutrophils Week 44 (36, 37, 41, 34, 36)	-0.978 (± 1.2444)	-1.086 (± 1.6049)	-0.717 (± 1.6966)	-1.109 (± 2.2673)
Neutrophils Week 48 (38, 36, 40, 32, 39)	-0.861 (± 1.6858)	-0.939 (± 1.5670)	-0.558 (± 1.7944)	-1.178 (± 2.6503)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: 10^9 white blood cells per liter				
arithmetic mean (standard deviation)				
Basophils Week 1 (41, 38, 43, 41, 40)	0.008 (± 0.0350)			
Basophils Week 2 (42, 38, 43, 41, 41)	0.005 (± 0.0384)			
Basophils Week 4 (41, 38, 42, 41, 41)	0.005 (± 0.0312)			
Basophils Week 8 (41, 39, 41, 38, 41)	0.002 (± 0.0418)			
Basophils Week 12 (41, 39, 43, 38, 41)	0.010 (± 0.0374)			

Basophils Week 16 (42, 38, 42, 38, 40)	0.008 (± 0.0417)			
Basophils Week 20 (39, 39, 41, 37, 39)	0.000 (± 0.0397)			
Basophils Week 24 (39, 38, 40, 36, 40)	0.005 (± 0.0389)			
Basophils Week 28 (39, 38, 40, 35, 40)	0.005 (± 0.0450)			
Basophils Week 32 (39, 39, 40, 34, 39)	0.010 (± 0.0384)			
Basophils Week 36 (37, 38, 41, 33, 39)	0.013 (± 0.0409)			
Basophils Week 40 (36, 38, 40, 34, 38)	0.000 (± 0.0403)			
Basophils Week 44 (36, 37, 41, 34, 36)	0.000 (± 0.0338)			
Basophils Week 48 (38, 36, 40, 32, 39)	0.000 (± 0.0324)			
Eosinophils Week 1 (41, 38, 43, 41, 40)	0.017 (± 0.0636)			
Eosinophils Week 2 (42, 38, 43, 41, 41)	0.029 (± 0.0929)			
Eosinophils Week 4 (41, 38, 42, 41, 41)	0.027 (± 0.0895)			
Eosinophils Week 8 (41, 39, 41, 38, 41)	0.005 (± 0.0669)			
Eosinophils Week 12 (41, 39, 43, 38, 41)	0.017 (± 0.0704)			
Eosinophils Week 16 (42, 38, 42, 38, 40)	0.033 (± 0.0829)			
Eosinophils Week 20 (39, 39, 41, 37, 39)	0.038 (± 0.0935)			
Eosinophils Week 24 (39, 38, 40, 36, 40)	0.037 (± 0.1192)			
Eosinophils Week 28 (39, 38, 40, 35, 40)	0.025 (± 0.0870)			
Eosinophils Week 32 (39, 39, 40, 34, 39)	0.041 (± 0.1141)			
Eosinophils Week 36 (37, 38, 41, 33, 39)	0.015 (± 0.0961)			
Eosinophils Week 40 (36, 38, 40, 34, 38)	0.039 (± 0.1128)			
Eosinophils Week 44 (36, 37, 41, 34, 36)	0.006 (± 0.0893)			
Eosinophils Week 48 (38, 36, 40, 32, 39)	-0.005 (± 0.0857)			
Leukocytes Week 1 (41, 38, 43, 41, 40)	-0.285 (± 1.6896)			
Leukocytes Week 2 (42, 39, 43, 41, 41)	-0.322 (± 1.5501)			
Leukocytes Week 4 (41, 38, 42, 41, 41)	-0.656 (± 1.4264)			
Leukocytes Week 8 (41, 39, 41, 38, 41)	-0.629 (± 1.5489)			
Leukocytes Week 12 (41, 39, 43, 38, 41)	-0.634 (± 1.6084)			
Leukocytes Week 16 (42, 38, 42, 38, 40)	-0.293 (± 1.8427)			
Leukocytes Week 20 (39, 39, 41, 37, 40)	-0.455 (± 1.7116)			
Leukocytes Week 24 (39, 38, 40, 36, 40)	-0.765 (± 1.8691)			

Leukocytes Week 28 (39, 38, 41, 35, 40)	-0.342 (± 1.5683)			
Leukocytes Week 32 (39, 39, 40, 34, 39)	-0.505 (± 1.4800)			
Leukocytes Week 36 (37, 38, 41, 33, 39)	-0.126 (± 2.2565)			
Leukocytes Week 40 (36, 38, 41, 34, 38)	-0.266 (± 1.7976)			
Leukocytes Week 44 (37, 37, 41, 34, 36)	-0.825 (± 1.8917)			
Leukocytes Week 48 (38, 36, 40, 32, 39)	-0.777 (± 1.8593)			
Lymphocytes Week 1 (41, 38, 43, 41, 40)	0.020 (± 0.3006)			
Lymphocytes Week 2 (42, 38, 43, 41, 41)	0.161 (± 0.4277)			
Lymphocytes Week 4 (41, 38, 42, 41, 41)	0.095 (± 0.3263)			
Lymphocytes Week 8 (41, 39, 41, 38, 41)	0.129 (± 0.3939)			
Lymphocytes Week 12 (41, 39, 43, 38, 41)	0.061 (± 0.3301)			
Lymphocytes Week 16 (42, 38, 42, 38, 40)	0.135 (± 0.4197)			
Lymphocytes Week 20 (39, 39, 41, 37, 39)	0.126 (± 0.4216)			
Lymphocytes Week 24 (39, 38, 40, 36, 40)	0.053 (± 0.3974)			
Lymphocytes Week 28 (39, 38, 40, 35, 40)	0.172 (± 0.3776)			
Lymphocytes Week 32 (39, 39, 40, 34, 39)	0.146 (± 0.3966)			
Lymphocytes Week 36 (37, 38, 41, 33, 39)	0.118 (± 0.3810)			
Lymphocytes Week 40 (36, 38, 40, 34, 38)	0.176 (± 0.3709)			
Lymphocytes Week 44 (36, 37, 41, 34, 36)	0.153 (± 0.4462)			
Lymphocytes Week 48 (38, 36, 40, 32, 39)	0.072 (± 0.3755)			
Monocytes Week 1 (41, 38, 43, 41, 40)	-0.027 (± 0.1724)			
Monocytes Week 2 (42, 38, 43, 41, 41)	-0.010 (± 0.1882)			
Monocytes Week 4 (41, 38, 42, 41, 41)	-0.085 (± 0.1459)			
Monocytes Week 8 (41, 39, 41, 38, 41)	-0.071 (± 0.1834)			
Monocytes Week 12 (41, 39, 43, 38, 41)	-0.059 (± 0.1414)			
Monocytes Week 16 (42, 38, 42, 38, 40)	-0.043 (± 0.1752)			
Monocytes Week 20 (39, 39, 41, 37, 39)	-0.003 (± 0.1899)			
Monocytes Week 24 (39, 38, 40, 36, 40)	-0.027 (± 0.1921)			
Monocytes Week 28 (39, 38, 40, 35, 40)	-0.012 (± 0.1911)			
Monocytes Week 32 (39, 39, 40, 34, 39)	0.010 (± 0.1744)			
Monocytes Week 36 (37, 38, 41, 33, 39)	0.049 (± 0.2327)			

Monocytes Week 40 (36, 38, 40, 34, 38)	-0.018 (± 0.1504)			
Monocytes Week 44 (36, 37, 41, 34, 36)	-0.019 (± 0.2202)			
Monocytes Week 48 (38, 36, 40, 32, 39)	-0.077 (± 0.1709)			
Neutrophils Week 1 (41, 38, 43, 41, 40)	-0.325 (± 1.5720)			
Neutrophils Week 2 (42, 38, 43, 41, 41)	-0.537 (± 1.3989)			
Neutrophils Week 4 (41, 38, 42, 41, 41)	-0.732 (± 1.4028)			
Neutrophils Week 8 (41, 39, 41, 38, 41)	-0.717 (± 1.4589)			
Neutrophils Week 12 (41, 39, 43, 38, 41)	-0.673 (± 1.3887)			
Neutrophils Week 16 (42, 38, 42, 38, 40)	-0.448 (± 1.6816)			
Neutrophils Week 20 (39, 39, 41, 37, 39)	-0.618 (± 1.5716)			
Neutrophils Week 24 (39, 38, 40, 36, 40)	-0.850 (± 1.6461)			
Neutrophils Week 28 (39, 38, 40, 35, 40)	-0.568 (± 1.3889)			
Neutrophils Week 32 (39, 39, 40, 34, 39)	-0.718 (± 1.4299)			
Neutrophils Week 36 (37, 38, 41, 33, 39)	-0.354 (± 2.1441)			
Neutrophils Week 40 (36, 38, 40, 34, 38)	-0.495 (± 1.5857)			
Neutrophils Week 44 (36, 37, 41, 34, 36)	-0.983 (± 1.6556)			
Neutrophils Week 48 (38, 36, 40, 32, 39)	-0.805 (± 1.6631)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular hemoglobin (HGB) concentration, hemoglobin)

End point title	Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular hemoglobin (HGB) concentration, hemoglobin)

End point description:

Erythrocytes mean corpuscular hemoglobin concentration (MCHC) and hemoglobin were measured in grams per liter (g/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: g/L				
arithmetic mean (standard deviation)				
MCHC Week 1 (41, 38, 43, 41, 40)	-2.293 (± 8.4594)	0.789 (± 8.9719)	-1.860 (± 8.0551)	0.927 (± 9.1088)
MCHC Week 2 (42, 39, 43, 41, 41)	-2.310 (± 7.9923)	2.564 (± 9.8216)	0.465 (± 8.4778)	0.707 (± 8.6263)
MCHC Week 4 (41, 38, 42, 41, 41)	-3.927 (± 10.0633)	1.474 (± 10.5849)	-2.500 (± 11.5045)	-0.878 (± 9.4026)
MCHC Week 8 (41, 39, 41, 38, 41)	-5.195 (± 11.7158)	-1.897 (± 11.3249)	-3.780 (± 10.7576)	-3.079 (± 10.7033)
MCHC Week 12 (41, 39, 43, 38, 41)	-7.927 (± 14.6704)	-3.179 (± 13.4122)	-3.907 (± 11.5404)	-2.684 (± 9.4099)
MCHC Week 16 (42, 38, 42, 38, 40)	-6.286 (± 12.3393)	-3.000 (± 14.5751)	-5.262 (± 12.1917)	-1.026 (± 11.6816)
MCHC Week 20 (40, 39, 41, 37, 40)	-5.050 (± 12.8102)	0.923 (± 11.8108)	-1.902 (± 12.8078)	0.919 (± 8.7349)
MCHC Week 24 (39, 38, 40, 36, 40)	1.000 (± 10.9232)	4.132 (± 10.3849)	-0.625 (± 14.6685)	4.583 (± 11.3121)
MCHC Week 28 (39, 38, 41, 35, 40)	2.179 (± 10.3285)	4.658 (± 9.6906)	1.707 (± 9.9505)	4.400 (± 13.7524)
MCHC Week 32 (39, 39, 40, 34, 39)	6.308 (± 9.7796)	10.231 (± 9.5957)	4.850 (± 11.3692)	7.971 (± 12.3497)
MCHC Week 36 (38, 38, 41, 33, 39)	5.500 (± 9.7779)	10.921 (± 10.2229)	2.732 (± 12.4097)	6.788 (± 12.2034)
MCHC Week 40 (37, 38, 41, 34, 38)	3.108 (± 9.8736)	8.237 (± 12.0706)	4.976 (± 11.5639)	9.088 (± 11.5480)
MCHC Week 44 (37, 38, 41, 34, 36)	6.297 (± 10.6975)	7.289 (± 12.6254)	3.415 (± 12.6293)	6.353 (± 14.3038)
MCHC Week 48 (38, 37, 41, 33, 40)	5.079 (± 10.4916)	7.216 (± 9.3812)	2.122 (± 11.8769)	5.394 (± 12.9300)
Hemoglobin Week 1 (41, 38, 43, 41, 40)	-4.854 (± 5.6726)	0.000 (± 5.6569)	1.302 (± 5.1480)	0.512 (± 6.0462)
Hemoglobin Week 2 (42, 39, 43, 41, 41)	-4.810 (± 6.5154)	-0.359 (± 5.2339)	0.070 (± 6.5915)	-1.561 (± 6.7047)
Hemoglobin Week 4 (41, 38, 42, 41, 41)	-4.390 (± 7.5162)	0.895 (± 7.6434)	0.881 (± 6.4551)	0.512 (± 5.7189)
Hemoglobin Week 8 (41, 39, 41, 38, 41)	-4.561 (± 7.0995)	0.308 (± 7.0865)	2.195 (± 7.7628)	0.553 (± 6.8010)
Hemoglobin Week 12 (41, 39, 43, 38, 41)	-5.220 (± 6.7879)	0.692 (± 7.7601)	2.488 (± 7.6512)	0.868 (± 7.3344)
Hemoglobin Week 16 (42, 38, 42, 38, 40)	-1.619 (± 6.4768)	2.579 (± 8.3880)	1.524 (± 8.7853)	1.737 (± 7.3547)
Hemoglobin Week 20 (40, 39, 41, 37, 40)	-0.400 (± 7.3233)	2.667 (± 8.6764)	2.268 (± 6.9822)	1.892 (± 7.6186)
Hemoglobin Week 24 (39, 38, 40, 36, 40)	0.564 (± 8.1879)	3.658 (± 9.0622)	4.075 (± 8.0714)	2.000 (± 6.6462)
Hemoglobin Week 28 (39, 38, 41, 35, 40)	-1.513 (± 8.0259)	3.342 (± 8.9511)	3.122 (± 8.6261)	0.857 (± 7.2645)
Hemoglobin Week 32 (39, 39, 40, 34, 39)	-0.282 (± 8.2684)	4.487 (± 8.3094)	4.300 (± 9.4032)	2.118 (± 7.4254)
Hemoglobin Week 36 (38, 38, 41, 33, 39)	0.947 (± 9.1738)	6.053 (± 8.1405)	4.293 (± 9.5766)	3.818 (± 7.3334)

Hemoglobin Week 40 (37, 38, 41, 34, 38)	1.432 (± 9.1090)	5.868 (± 8.7863)	4.317 (± 9.6552)	3.618 (± 7.8277)
Hemoglobin Week 44 (37, 38, 41, 34, 36)	1.486 (± 10.1040)	5.000 (± 9.2998)	3.659 (± 9.1750)	4.912 (± 8.5895)
Hemoglobin Week 48 (38, 37, 41, 33, 40)	2.474 (± 9.7002)	5.270 (± 9.1974)	3.780 (± 9.9210)	4.030 (± 9.2550)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: g/L				
arithmetic mean (standard deviation)				
MCHC Week 1 (41, 38, 43, 41, 40)	1.200 (± 12.2395)			
MCHC Week 2 (42, 39, 43, 41, 41)	2.854 (± 10.1822)			
MCHC Week 4 (41, 38, 42, 41, 41)	1.756 (± 11.8697)			
MCHC Week 8 (41, 39, 41, 38, 41)	0.610 (± 12.7493)			
MCHC Week 12 (41, 39, 43, 38, 41)	1.732 (± 13.3959)			
MCHC Week 16 (42, 38, 42, 38, 40)	-0.700 (± 16.1026)			
MCHC Week 20 (40, 39, 41, 37, 40)	0.200 (± 16.1725)			
MCHC Week 24 (39, 38, 40, 36, 40)	4.250 (± 13.4064)			
MCHC Week 28 (39, 38, 41, 35, 40)	6.150 (± 12.5382)			
MCHC Week 32 (39, 39, 40, 34, 39)	10.462 (± 12.9855)			
MCHC Week 36 (38, 38, 41, 33, 39)	9.462 (± 12.7998)			
MCHC Week 40 (37, 38, 41, 34, 38)	9.079 (± 11.5393)			
MCHC Week 44 (37, 38, 41, 34, 36)	9.278 (± 12.8076)			
MCHC Week 48 (38, 37, 41, 33, 40)	8.250 (± 11.3448)			
Hemoglobin Week 1 (41, 38, 43, 41, 40)	-0.875 (± 4.8368)			
Hemoglobin Week 2 (42, 39, 43, 41, 41)	0.317 (± 5.3499)			
Hemoglobin Week 4 (41, 38, 42, 41, 41)	1.195 (± 5.8916)			
Hemoglobin Week 8 (41, 39, 41, 38, 41)	1.195 (± 7.4439)			
Hemoglobin Week 12 (41, 39, 43, 38, 41)	2.488 (± 8.2344)			
Hemoglobin Week 16 (42, 38, 42, 38, 40)	3.125 (± 7.7400)			
Hemoglobin Week 20 (40, 39, 41, 37, 40)	2.925 (± 7.7207)			
Hemoglobin Week 24 (39, 38, 40, 36, 40)	3.425 (± 6.2834)			

Hemoglobin Week 28 (39, 38, 41, 35, 40)	3.400 (± 8.6730)			
Hemoglobin Week 32 (39, 39, 40, 34, 39)	5.615 (± 8.6378)			
Hemoglobin Week 36 (38, 38, 41, 33, 39)	4.949 (± 8.4851)			
Hemoglobin Week 40 (37, 38, 41, 34, 38)	4.132 (± 7.7987)			
Hemoglobin Week 44 (37, 38, 41, 34, 36)	4.722 (± 8.5511)			
Hemoglobin Week 48 (38, 37, 41, 33, 40)	4.725 (± 7.3554)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular hemoglobin (HGB))

End point title	Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular hemoglobin (HGB))

End point description:

Erythrocytes mean corpuscular hemoglobin (HGB) was measured in picograms (pg).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: picograms (pg)				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.073 (± 0.4980)	0.058 (± 0.4624)	-0.049 (± 0.4050)	0.073 (± 0.3975)
Week 2 (42, 39, 43, 41, 41)	-0.050 (± 0.3890)	0.126 (± 0.5149)	0.023 (± 0.4225)	0.066 (± 0.4357)
Week 4 (41, 38, 42, 41, 41)	-0.112 (± 0.5501)	0.089 (± 0.5584)	0.060 (± 0.5910)	0.012 (± 0.4691)
Week 8 (41, 39, 41, 38, 41)	-0.110 (± 0.6778)	0.141 (± 0.6801)	0.007 (± 0.5926)	0.034 (± 0.6851)
Week 12 (41, 39, 43, 38, 41)	-0.285 (± 0.6770)	0.023 (± 0.7253)	0.091 (± 0.8358)	-0.132 (± 0.8335)
Week 16 (42, 38, 42, 38, 40)	-0.233 (± 0.7281)	0.097 (± 0.8824)	0.014 (± 0.9236)	-0.118 (± 0.8440)
Week 20 (40, 39, 41, 37, 40)	-0.290 (± 0.8145)	-0.033 (± 0.9172)	0.029 (± 0.9819)	-0.035 (± 0.7013)

Week 24 (39, 38, 40, 36, 40)	-0.249 (± 1.0443)	0.108 (± 0.9947)	-0.057 (± 1.1804)	-0.097 (± 0.7284)
Week 28 (39, 38, 41, 35, 40)	-0.103 (± 1.0101)	0.029 (± 0.7241)	-0.122 (± 1.1130)	-0.211 (± 0.8277)
Week 32 (39, 39, 40, 34, 39)	0.003 (± 1.2619)	0.297 (± 0.8561)	0.058 (± 1.1522)	0.026 (± 0.7684)
Week 36 (38, 38, 41, 33, 39)	-0.082 (± 1.3242)	0.237 (± 0.8722)	-0.093 (± 1.0792)	-0.248 (± 0.8581)
Week 40 (37, 38, 41, 34, 38)	-0.170 (± 1.3453)	0.134 (± 0.8960)	-0.134 (± 1.2095)	-0.147 (± 0.8645)
Week 44 (37, 38, 41, 34, 36)	0.097 (± 1.3103)	0.129 (± 0.8742)	-0.080 (± 1.1771)	-0.159 (± 0.7480)
Week 48 (38, 37, 41, 33, 40)	0.137 (± 1.4139)	0.178 (± 0.9369)	-0.120 (± 1.1279)	-0.030 (± 0.7888)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: picograms (pg)				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.055 (± 0.4455)			
Week 2 (42, 39, 43, 41, 41)	0.085 (± 0.4287)			
Week 4 (41, 38, 42, 41, 41)	0.066 (± 0.6085)			
Week 8 (41, 39, 41, 38, 41)	0.095 (± 0.7994)			
Week 12 (41, 39, 43, 38, 41)	0.039 (± 1.0454)			
Week 16 (42, 38, 42, 38, 40)	-0.067 (± 1.1713)			
Week 20 (40, 39, 41, 37, 40)	0.075 (± 1.0824)			
Week 24 (39, 38, 40, 36, 40)	-0.007 (± 1.2338)			
Week 28 (39, 38, 41, 35, 40)	0.020 (± 1.2950)			
Week 32 (39, 39, 40, 34, 39)	0.167 (± 1.2472)			
Week 36 (38, 38, 41, 33, 39)	0.118 (± 1.1473)			
Week 40 (37, 38, 41, 34, 38)	0.034 (± 1.0839)			
Week 44 (37, 38, 41, 34, 36)	0.108 (± 1.2532)			
Week 48 (38, 37, 41, 33, 40)	0.140 (± 1.2161)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular volume)

End point title	Changes from Baseline in hematology parameters during the study (erythrocytes mean corpuscular volume)

End point description:

Erythrocytes mean corpuscular volume was measured in femtolitres (fL).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: femtolitres (fL)				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	0.422 (± 1.8855)	-0.087 (± 1.9540)	0.386 (± 2.2542)	-0.017 (± 2.1066)
Week 2 (42, 39, 43, 41, 41)	0.450 (± 1.8867)	-0.362 (± 2.1689)	-0.021 (± 1.8767)	-0.039 (± 2.3876)
Week 4 (41, 38, 42, 41, 41)	0.829 (± 2.3409)	-0.163 (± 2.4631)	0.945 (± 3.2325)	0.354 (± 2.8851)
Week 8 (41, 39, 41, 38, 41)	1.163 (± 3.6524)	0.938 (± 2.9445)	1.110 (± 3.0283)	0.916 (± 3.0058)
Week 12 (41, 39, 43, 38, 41)	1.478 (± 3.9560)	0.951 (± 3.4617)	1.367 (± 3.8471)	0.342 (± 3.1129)
Week 16 (42, 38, 42, 38, 40)	1.107 (± 3.4022)	1.168 (± 3.7760)	1.571 (± 4.3326)	-0.016 (± 3.6944)
Week 20 (40, 39, 41, 37, 40)	0.497 (± 3.5197)	-0.349 (± 2.8975)	0.649 (± 3.7758)	-0.338 (± 2.5959)
Week 24 (39, 38, 40, 36, 40)	-1.033 (± 2.9007)	-0.858 (± 2.1793)	0.143 (± 4.9985)	-1.522 (± 3.1692)
Week 28 (39, 38, 41, 35, 40)	-0.910 (± 2.6477)	-1.184 (± 2.3264)	-0.754 (± 3.3662)	-1.854 (± 3.6605)
Week 32 (39, 39, 40, 34, 39)	-1.654 (± 2.7565)	-1.851 (± 2.4024)	-1.075 (± 3.5390)	-2.071 (± 3.7652)
Week 36 (38, 38, 41, 33, 39)	-1.724 (± 3.1037)	-2.266 (± 2.3516)	-0.912 (± 3.9627)	-2.558 (± 3.8468)
Week 40 (37, 38, 41, 34, 38)	-1.386 (± 2.8575)	-1.882 (± 3.1285)	-1.698 (± 3.0263)	-2.885 (± 3.1443)
Week 44 (37, 38, 41, 34, 36)	-1.405 (± 3.4627)	-1.632 (± 3.4207)	-1.117 (± 3.4616)	-2.171 (± 4.4367)
Week 48 (38, 37, 41, 33, 40)	-0.942 (± 3.5913)	-1.492 (± 2.5065)	-0.846 (± 3.1243)	-1.527 (± 3.6540)

End point values	BKZ 320 mg (SS)			

Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: femtolitres (fL)				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.510 (± 2.7686)			
Week 2 (42, 39, 43, 41, 41)	-0.549 (± 2.5751)			
Week 4 (41, 38, 42, 41, 41)	-0.259 (± 2.5328)			
Week 8 (41, 39, 41, 38, 41)	0.090 (± 3.5125)			
Week 12 (41, 39, 43, 38, 41)	-0.390 (± 3.3907)			
Week 16 (42, 38, 42, 38, 40)	0.048 (± 4.4345)			
Week 20 (40, 39, 41, 37, 40)	0.202 (± 4.2993)			
Week 24 (39, 38, 40, 36, 40)	-1.195 (± 3.5759)			
Week 28 (39, 38, 41, 35, 40)	-1.638 (± 3.3447)			
Week 32 (39, 39, 40, 34, 39)	-2.351 (± 3.1052)			
Week 36 (38, 38, 41, 33, 39)	-2.236 (± 3.2869)			
Week 40 (37, 38, 41, 34, 38)	-2.421 (± 2.9445)			
Week 44 (37, 38, 41, 34, 36)	-2.186 (± 3.4915)			
Week 48 (38, 37, 41, 33, 40)	-1.788 (± 3.5554)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (erythrocytes)

End point title	Changes from Baseline in hematology parameters during the study (erythrocytes)

End point description:

Erythrocytes was measured in number of red blood cells per liter (10^12/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: 10^12 red blood cells per liter				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.148 (± 0.2071)	-0.008 (± 0.1927)	0.050 (± 0.1773)	0.008 (± 0.2109)
Week 2 (42, 39, 43, 41, 41)	-0.149 (± 0.2244)	-0.029 (± 0.1788)	-0.004 (± 0.2280)	-0.063 (± 0.2236)
Week 4 (41, 38, 42, 41, 41)	-0.132 (± 0.2780)	0.018 (± 0.2535)	0.023 (± 0.2135)	0.013 (± 0.1955)
Week 8 (41, 39, 41, 38, 41)	-0.135 (± 0.2546)	-0.011 (± 0.2206)	0.074 (± 0.2466)	0.014 (± 0.2190)
Week 12 (41, 39, 43, 38, 41)	-0.131 (± 0.2678)	0.021 (± 0.2561)	0.069 (± 0.2419)	0.051 (± 0.2243)
Week 16 (42, 38, 42, 38, 40)	-0.020 (± 0.2375)	0.075 (± 0.2898)	0.047 (± 0.2810)	0.074 (± 0.2255)
Week 20 (40, 39, 41, 37, 40)	0.036 (± 0.2618)	0.096 (± 0.2855)	0.068 (± 0.2089)	0.064 (± 0.2273)
Week 24 (39, 38, 40, 36, 40)	0.059 (± 0.2639)	0.110 (± 0.2974)	0.142 (± 0.2573)	0.074 (± 0.2250)
Week 28 (39, 38, 41, 35, 40)	-0.034 (± 0.2453)	0.108 (± 0.2681)	0.122 (± 0.2445)	0.058 (± 0.2359)
Week 32 (39, 39, 40, 34, 39)	-0.010 (± 0.2461)	0.104 (± 0.2660)	0.133 (± 0.2716)	0.061 (± 0.2555)
Week 36 (38, 38, 41, 33, 39)	0.044 (± 0.2524)	0.166 (± 0.2542)	0.156 (± 0.2849)	0.161 (± 0.2399)
Week 40 (37, 38, 41, 34, 38)	0.079 (± 0.2682)	0.177 (± 0.2733)	0.163 (± 0.2736)	0.141 (± 0.2535)
Week 44 (37, 38, 41, 34, 36)	0.035 (± 0.2645)	0.146 (± 0.2846)	0.133 (± 0.2622)	0.188 (± 0.2933)
Week 48 (38, 37, 41, 33, 40)	0.061 (± 0.2693)	0.146 (± 0.2994)	0.141 (± 0.2747)	0.135 (± 0.2934)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: 10^12 red blood cells per liter				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.017 (± 0.1609)			
Week 2 (42, 39, 43, 41, 41)	0.000 (± 0.1809)			
Week 4 (41, 38, 42, 41, 41)	0.031 (± 0.2065)			
Week 8 (41, 39, 41, 38, 41)	0.026 (± 0.2264)			
Week 12 (41, 39, 43, 38, 41)	0.075 (± 0.2393)			
Week 16 (42, 38, 42, 38, 40)	0.110 (± 0.2533)			
Week 20 (40, 39, 41, 37, 40)	0.081 (± 0.2191)			
Week 24 (39, 38, 40, 36, 40)	0.110 (± 0.1931)			

Week 28 (39, 38, 41, 35, 40)	0.106 (± 0.2567)			
Week 32 (39, 39, 40, 34, 39)	0.156 (± 0.2714)			
Week 36 (38, 38, 41, 33, 39)	0.145 (± 0.2377)			
Week 40 (37, 38, 41, 34, 38)	0.129 (± 0.2403)			
Week 44 (37, 38, 41, 34, 36)	0.135 (± 0.2128)			
Week 48 (38, 37, 41, 33, 40)	0.129 (± 0.2354)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (hematocrit)

End point title	Changes from Baseline in hematology parameters during the study (hematocrit)

End point description:

Hematocrit was measured in volume percentage (%) of red blood cells in blood.
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: volume % of red blood cells				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.011 (± 0.0189)	-0.001 (± 0.0211)	0.007 (± 0.0181)	0.000 (± 0.0206)
Week 2 (42, 39, 43, 41, 41)	-0.011 (± 0.0230)	-0.004 (± 0.0204)	-0.000 (± 0.0205)	-0.006 (± 0.0220)
Week 4 (41, 38, 42, 41, 41)	-0.008 (± 0.0254)	0.001 (± 0.0211)	0.006 (± 0.0220)	0.003 (± 0.0190)
Week 8 (41, 39, 41, 38, 41)	-0.007 (± 0.0239)	0.003 (± 0.0244)	0.012 (± 0.0237)	0.005 (± 0.0208)
Week 12 (41, 39, 43, 38, 41)	-0.005 (± 0.0287)	0.007 (± 0.0281)	0.013 (± 0.0276)	0.006 (± 0.0219)
Week 16 (42, 38, 42, 38, 40)	0.004 (± 0.0202)	0.012 (± 0.0259)	0.011 (± 0.0254)	0.006 (± 0.0240)
Week 20 (40, 39, 41, 37, 40)	0.006 (± 0.0217)	0.007 (± 0.0270)	0.010 (± 0.0211)	0.004 (± 0.0241)

Week 24 (39, 38, 40, 36, 40)	0.001 (± 0.0192)	0.006 (± 0.0253)	0.014 (± 0.0256)	-0.000 (± 0.0222)
Week 28 (39, 38, 41, 35, 40)	-0.007 (± 0.0210)	0.004 (± 0.0248)	0.008 (± 0.0241)	-0.003 (± 0.0229)
Week 32 (39, 39, 40, 34, 39)	-0.009 (± 0.0207)	0.000 (± 0.0249)	0.007 (± 0.0225)	-0.004 (± 0.0196)
Week 36 (38, 38, 41, 33, 39)	-0.004 (± 0.0222)	0.004 (± 0.0228)	0.009 (± 0.0258)	0.003 (± 0.0221)
Week 40 (37, 38, 41, 34, 38)	0.000 (± 0.0231)	0.007 (± 0.0278)	0.007 (± 0.0246)	-0.001 (± 0.0221)
Week 44 (37, 38, 41, 34, 36)	-0.003 (± 0.0272)	0.006 (± 0.0297)	0.007 (± 0.0239)	0.007 (± 0.0246)
Week 48 (38, 37, 41, 33, 40)	0.001 (± 0.0243)	0.007 (± 0.0257)	0.009 (± 0.0260)	0.005 (± 0.0252)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: volume % of red blood cells				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.004 (± 0.0206)			
Week 2 (42, 39, 43, 41, 41)	-0.003 (± 0.0174)			
Week 4 (41, 38, 42, 41, 41)	0.001 (± 0.0209)			
Week 8 (41, 39, 41, 38, 41)	0.003 (± 0.0232)			
Week 12 (41, 39, 43, 38, 41)	0.005 (± 0.0231)			
Week 16 (42, 38, 42, 38, 40)	0.010 (± 0.0252)			
Week 20 (40, 39, 41, 37, 40)	0.008 (± 0.0246)			
Week 24 (39, 38, 40, 36, 40)	0.005 (± 0.0219)			
Week 28 (39, 38, 41, 35, 40)	0.002 (± 0.0238)			
Week 32 (39, 39, 40, 34, 39)	0.003 (± 0.0248)			
Week 36 (38, 38, 41, 33, 39)	0.003 (± 0.0234)			
Week 40 (37, 38, 41, 34, 38)	0.000 (± 0.0206)			
Week 44 (37, 38, 41, 34, 36)	0.002 (± 0.0194)			
Week 48 (38, 37, 41, 33, 40)	0.004 (± 0.0212)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in hematology parameters during the study (platelets)

End point title	Changes from Baseline in hematology parameters during the study (platelets)

End point description:

Platelets was measured in number of platelets per liter (10^9/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: 10^9 platelets per liter				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-5.073 (± 30.2609)	-3.368 (± 25.9515)	3.209 (± 30.5883)	-2.098 (± 24.6412)
Week 2 (42, 39, 42, 41, 41)	4.000 (± 27.3112)	-5.179 (± 38.2800)	-3.810 (± 41.8250)	-15.122 (± 32.8414)
Week 4 (41, 38, 41, 41, 41)	-3.927 (± 29.6643)	-6.868 (± 29.7487)	-13.878 (± 43.7568)	-19.415 (± 32.6450)
Week 8 (41, 39, 40, 38, 41)	1.561 (± 29.1042)	-12.077 (± 28.9876)	-5.475 (± 44.7718)	-17.605 (± 29.8442)
Week 12 (41, 39, 42, 38, 41)	-2.171 (± 32.0795)	-17.359 (± 35.4308)	-11.286 (± 40.7451)	-10.079 (± 44.8977)
Week 16 (42, 38, 42, 38, 40)	-18.833 (± 50.4844)	-18.263 (± 37.3259)	-13.952 (± 50.7173)	-9.895 (± 35.3246)
Week 20 (40, 39, 41, 37, 40)	-18.625 (± 50.3988)	-23.077 (± 39.6534)	-10.512 (± 48.0755)	-15.324 (± 28.8329)
Week 24 (39, 38, 40, 36, 40)	-19.974 (± 49.0196)	-14.000 (± 37.7760)	-4.600 (± 49.4025)	-10.972 (± 36.8375)
Week 28 (39, 38, 41, 35, 40)	-24.256 (± 51.8001)	-16.868 (± 40.6635)	-7.683 (± 47.8155)	-12.800 (± 30.7904)
Week 32 (39, 39, 40, 34, 39)	-22.410 (± 51.9553)	-18.590 (± 41.7226)	-13.575 (± 51.9304)	-20.618 (± 38.8969)
Week 36 (38, 38, 41, 33, 39)	-25.000 (± 52.6990)	-16.474 (± 46.8844)	-14.561 (± 50.2106)	-18.848 (± 40.0563)
Week 40 (37, 38, 41, 34, 38)	-23.432 (± 53.2747)	-20.895 (± 41.4845)	-14.927 (± 51.2652)	-24.088 (± 33.4133)
Week 44 (37, 38, 39, 34, 36)	-22.703 (± 57.8383)	-22.474 (± 41.0627)	-18.051 (± 49.1646)	-24.735 (± 38.4710)
Week 48 (38, 37, 41, 33, 39)	-27.395 (± 56.2963)	-23.811 (± 47.1150)	-24.220 (± 46.2458)	-22.273 (± 37.4243)

End point values	BKZ 320 mg (SS)			

Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: 10^9 platelets per liter				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-9.325 (± 23.4109)			
Week 2 (42, 39, 42, 41, 41)	-15.415 (± 31.7025)			
Week 4 (41, 38, 41, 41, 41)	-27.073 (± 41.9299)			
Week 8 (41, 39, 40, 38, 41)	-26.195 (± 44.1719)			
Week 12 (41, 39, 42, 38, 41)	-23.171 (± 47.2995)			
Week 16 (42, 38, 42, 38, 40)	-25.425 (± 37.6556)			
Week 20 (40, 39, 41, 37, 40)	-22.725 (± 42.2502)			
Week 24 (39, 38, 40, 36, 40)	-22.900 (± 47.4092)			
Week 28 (39, 38, 41, 35, 40)	-19.600 (± 42.3052)			
Week 32 (39, 39, 40, 34, 39)	-23.179 (± 42.2018)			
Week 36 (38, 38, 41, 33, 39)	-23.846 (± 45.1340)			
Week 40 (37, 38, 41, 34, 38)	-21.789 (± 46.1467)			
Week 44 (37, 38, 39, 34, 36)	-31.389 (± 48.5306)			
Week 48 (38, 37, 41, 33, 39)	-28.974 (± 42.9960)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in biochemistry parameters during the study (alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, gamma glutamyl transferase, lactate dehydrogenase)

End point title	Changes from Baseline in biochemistry parameters during the study (alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, gamma glutamyl transferase, lactate dehydrogenase)

End point description:

Alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), lactate dehydrogenase (LDH) were measured in units per liter (U/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: U/L				
arithmetic mean (standard deviation)				
ALT Week 1 (41, 38, 43, 41, 40)	-1.366 (± 12.7451)	2.526 (± 15.5211)	2.628 (± 42.1234)	3.122 (± 10.2791)
ALT Week 2 (42, 39, 43, 41, 41)	-1.714 (± 15.4624)	2.026 (± 8.9428)	-1.047 (± 41.1223)	4.927 (± 20.9623)
ALT Week 4 (41, 38, 42, 41, 41)	-3.854 (± 15.1897)	1.553 (± 16.2758)	-3.952 (± 38.9546)	22.756 (± 139.8531)
ALT Week 8 (41, 39, 43, 39, 41)	-4.707 (± 13.6478)	-1.385 (± 9.4580)	5.465 (± 68.0764)	0.795 (± 11.4321)
ALT Week 12 (41, 39, 42, 38, 41)	-4.220 (± 15.1765)	0.359 (± 12.2356)	-4.429 (± 38.1756)	1.184 (± 13.0692)
ALT Week 16 (42, 38, 42, 38, 41)	-2.048 (± 18.0026)	2.684 (± 16.3229)	-4.857 (± 38.6211)	0.579 (± 12.9273)
ALT Week 20 (40, 39, 42, 37, 40)	0.300 (± 39.9482)	3.821 (± 13.0139)	-4.881 (± 39.1808)	-0.838 (± 11.1118)
ALT Week 24 (39, 38, 41, 36, 40)	-1.564 (± 19.4974)	2.789 (± 14.5475)	-5.659 (± 39.6652)	1.528 (± 11.0259)
ALT Week 28 (39, 38, 41, 35, 40)	-3.385 (± 17.7373)	2.658 (± 12.8174)	-3.244 (± 43.4688)	-0.171 (± 8.7228)
ALT Week 32 (39, 39, 40, 34, 39)	-4.487 (± 16.5400)	2.385 (± 12.8956)	-4.150 (± 44.0126)	-2.176 (± 12.7742)
ALT Week 36 (38, 38, 41, 34, 39)	0.579 (± 10.5411)	0.184 (± 11.8660)	-2.976 (± 42.9275)	-0.471 (± 11.2848)
ALT Week 40 (37, 38, 41, 34, 38)	-0.622 (± 10.2506)	0.816 (± 12.6680)	-2.780 (± 44.9719)	-3.853 (± 11.1059)
ALT Week 44 (37, 38, 41, 34, 36)	2.649 (± 19.7993)	1.474 (± 13.1514)	-3.415 (± 43.2966)	-3.882 (± 12.8741)
ALT Week 48 (38, 37, 41, 34, 40)	2.605 (± 14.0646)	2.216 (± 12.8542)	-4.561 (± 43.1926)	-3.794 (± 13.1628)
ALP Week 1 (41, 38, 43, 41, 40)	-1.098 (± 6.0034)	-1.342 (± 8.0983)	-2.721 (± 7.2056)	-3.244 (± 4.9989)
ALP Week 2 (42, 39, 43, 41, 41)	-1.905 (± 6.7960)	-3.282 (± 7.8370)	-4.349 (± 9.5963)	-4.805 (± 7.8237)
ALP Week 4 (41, 39, 42, 41, 41)	-1.634 (± 9.0630)	-1.077 (± 10.4236)	-3.262 (± 9.9144)	-1.439 (± 18.3508)
ALP Week 8 (41, 39, 43, 39, 41)	-2.220 (± 8.3711)	0.308 (± 12.6515)	1.233 (± 37.8014)	-5.026 (± 10.2019)
ALP Week 12 (41, 39, 42, 38, 41)	-2.463 (± 8.8122)	-0.462 (± 12.1066)	-5.952 (± 11.0695)	-4.947 (± 12.0538)
ALP Week 16 (42, 38, 42, 38, 41)	-8.357 (± 12.7276)	-0.895 (± 13.1515)	-7.238 (± 10.7722)	-4.605 (± 11.6539)
ALP Week 20 (40, 39, 42, 37, 40)	-10.425 (± 14.0510)	-5.410 (± 15.1895)	-10.143 (± 13.0264)	-7.027 (± 11.8544)
ALP Week 24 (39, 39, 41, 36, 40)	-12.795 (± 15.4752)	-4.769 (± 13.8097)	-9.463 (± 11.3448)	-6.361 (± 12.7843)
ALP Week 28 (39, 38, 41, 35, 40)	-12.795 (± 16.9351)	-5.684 (± 15.7259)	-11.244 (± 12.6249)	-8.314 (± 10.9054)
ALP Week 32 (39, 39, 41, 35, 40)	-13.667 (± 16.1870)	-4.769 (± 16.1530)	-10.900 (± 13.0026)	-9.118 (± 12.5765)
ALP Week 36 (38, 38, 41, 34, 39)	-11.816 (± 19.2436)	-6.368 (± 15.4735)	-11.122 (± 12.3495)	-8.059 (± 9.5217)

ALP Week 40 (37, 38, 41, 34, 38)	-11.000 (± 16.9706)	-5.658 (± 15.7485)	-11.024 (± 12.9180)	-10.559 (± 11.6987)
ALP Week 44 (37, 38, 41, 34, 40)	-12.622 (± 17.6373)	-6.421 (± 14.9099)	-10.537 (± 13.5759)	-8.647 (± 10.5483)
ALP Week 48 (38, 38, 41, 34, 40)	-12.211 (± 19.0379)	-6.500 (± 16.5313)	-11.049 (± 14.4827)	-7.765 (± 12.3290)
AST Week 1 (41, 38, 43, 41, 40)	-2.854 (± 10.3212)	1.447 (± 6.2155)	-0.023 (± 27.5409)	2.244 (± 6.7889)
AST Week 2 (42, 39, 43, 41, 41)	-1.762 (± 10.5294)	0.487 (± 4.0967)	-2.233 (± 26.3266)	3.805 (± 14.7635)
AST Week 4 (41, 38, 42, 41, 41)	-3.976 (± 10.6642)	1.289 (± 7.5584)	-3.262 (± 25.1047)	8.927 (± 52.0660)
AST Week 8 (41, 39, 43, 39, 41)	-3.537 (± 10.5477)	-0.077 (± 5.8687)	2.279 (± 34.7805)	1.410 (± 5.5900)
AST Week 12 (41, 39, 42, 38, 41)	-3.049 (± 12.2106)	0.436 (± 5.3054)	-2.595 (± 22.5324)	1.053 (± 6.9006)
AST Week 16 (42, 38, 42, 38, 41)	-1.048 (± 12.1313)	2.974 (± 8.3649)	-2.595 (± 24.3852)	1.526 (± 6.6688)
AST Week 20 (40, 39, 42, 37, 40)	6.375 (± 60.1309)	2.821 (± 6.6367)	-1.095 (± 25.1317)	1.324 (± 7.1065)
AST Week 24 (39, 38, 41, 36, 40)	1.718 (± 23.7940)	2.237 (± 6.9182)	-1.902 (± 26.1054)	2.889 (± 6.2554)
AST Week 28 (39, 38, 41, 35, 40)	-1.179 (± 13.4905)	2.289 (± 6.9512)	-1.805 (± 27.4583)	2.229 (± 6.3063)
AST Week 32 (39, 39, 40, 34, 39)	-1.385 (± 12.2895)	1.949 (± 6.2826)	-0.575 (± 28.3177)	0.324 (± 6.2654)
AST Week 36 (38, 38, 41, 34, 39)	0.711 (± 7.3113)	1.026 (± 5.5140)	-1.220 (± 25.5798)	1.588 (± 6.6017)
AST Week 40 (37, 38, 41, 34, 39)	0.946 (± 12.1494)	1.316 (± 5.5269)	0.244 (± 29.2701)	-0.647 (± 6.0597)
AST Week 44 (37, 38, 41, 34, 39)	2.838 (± 15.4641)	2.553 (± 7.9175)	-1.268 (± 28.4280)	-0.588 (± 7.7190)
AST Week 48 (38, 37, 41, 34, 40)	2.158 (± 9.7939)	3.459 (± 6.3403)	-1.927 (± 28.3182)	0.441 (± 6.6796)
GGT Week 1 (41, 38, 43, 41, 40)	0.171 (± 5.4447)	-2.737 (± 7.0354)	-0.535 (± 10.8745)	0.171 (± 5.0245)
GGT Week 2 (42, 39, 43, 41, 41)	-0.190 (± 5.8736)	-2.026 (± 7.6828)	-4.116 (± 25.7527)	-0.341 (± 5.2517)
GGT Week 4 (41, 39, 42, 41, 41)	-0.220 (± 7.2129)	-2.641 (± 9.9167)	-6.143 (± 35.5504)	1.171 (± 17.6265)
GGT Week 8 (41, 39, 43, 39, 41)	-1.829 (± 5.9745)	-4.410 (± 11.6319)	11.581 (± 103.8974)	-1.795 (± 5.7454)
GGT Week 12 (41, 39, 42, 38, 41)	-0.585 (± 5.9033)	-2.154 (± 10.7643)	-5.762 (± 34.8767)	-0.447 (± 8.3785)
GGT Week 16 (42, 38, 42, 38, 41)	-0.357 (± 9.6445)	-1.842 (± 13.4476)	-4.357 (± 34.0020)	-0.947 (± 8.1868)
GGT Week 20 (40, 39, 42, 37, 40)	-0.750 (± 9.5051)	-2.769 (± 13.0555)	-5.452 (± 32.1970)	-1.649 (± 5.5137)
GGT Week 24 (39, 39, 41, 36, 40)	-0.615 (± 12.4173)	-2.769 (± 10.9339)	-4.122 (± 36.6832)	-2.639 (± 9.4360)
GGT Week 28 (39, 38, 41, 35, 40)	-0.462 (± 11.5618)	-2.132 (± 11.7638)	-6.341 (± 36.7434)	-2.629 (± 7.6354)
GGT Week 32 (39, 39, 40, 34, 39)	0.359 (± 15.7872)	-1.538 (± 13.2463)	-7.875 (± 36.9103)	-3.676 (± 8.6435)
GGT Week 36 (38, 38, 41, 34, 39)	-0.026 (± 14.7162)	-4.289 (± 11.4559)	-8.195 (± 38.6899)	-2.735 (± 7.1236)
GGT Week 40 (37, 38, 41, 34, 40)	-2.568 (± 9.3676)	-3.842 (± 13.9275)	-9.073 (± 40.5792)	-4.088 (± 7.5573)
GGT Week 44 (37, 38, 41, 34, 39)	1.081 (± 23.2108)	-1.289 (± 21.3730)	-7.488 (± 34.4145)	-3.824 (± 7.0430)
GGT Week 48 (38, 38, 41, 34, 40)	1.474 (± 17.6723)	-2.184 (± 12.0850)	-7.805 (± 35.4924)	-2.941 (± 8.8247)

LDH Week 1 (41, 38, 43, 41, 40)	-7.000 (± 16.1509)	0.026 (± 19.6118)	-1.163 (± 33.1669)	-0.585 (± 16.6673)
LDH Week 2 (42, 39, 43, 41, 41)	-5.929 (± 18.4858)	-0.410 (± 14.9045)	-5.930 (± 32.8325)	-2.439 (± 19.2146)
LDH Week 4 (41, 39, 42, 41, 41)	-5.634 (± 25.5693)	4.846 (± 21.4372)	-6.190 (± 29.5265)	0.854 (± 26.6238)
LDH Week 8 (41, 39, 43, 39, 41)	-3.561 (± 17.3249)	0.026 (± 19.0449)	0.140 (± 38.8413)	3.513 (± 18.6503)
LDH Week 12 (41, 39, 42, 38, 41)	-0.927 (± 28.3058)	4.077 (± 21.0905)	2.119 (± 27.5134)	3.342 (± 17.0346)
LDH Week 16 (42, 38, 42, 38, 41)	0.881 (± 26.0180)	15.447 (± 62.0267)	-4.381 (± 35.9600)	0.474 (± 19.8967)
LDH Week 20 (40, 39, 42, 37, 40)	1.200 (± 35.1817)	2.154 (± 22.8825)	2.500 (± 31.6145)	0.676 (± 20.9206)
LDH Week 24 (39, 39, 41, 36, 40)	4.462 (± 31.9282)	1.333 (± 22.1862)	2.878 (± 44.9662)	1.944 (± 23.5638)
LDH Week 28 (39, 38, 41, 35, 40)	1.436 (± 21.1122)	-4.763 (± 21.2138)	-2.902 (± 34.3590)	8.143 (± 44.0929)
LDH Week 32 (39, 39, 40, 34, 39)	-6.333 (± 23.0587)	-6.410 (± 23.8324)	-4.525 (± 35.2762)	-2.971 (± 27.9171)
LDH Week 36 (38, 38, 41, 34, 39)	0.553 (± 37.3889)	-4.658 (± 16.8383)	-7.585 (± 35.0442)	-6.147 (± 21.6895)
LDH Week 40 (37, 38, 41, 34, 40)	-0.216 (± 34.5214)	-8.289 (± 17.4896)	-6.366 (± 36.6898)	-10.618 (± 24.4293)
LDH Week 44 (37, 38, 41, 34, 40)	-0.757 (± 32.2847)	-5.316 (± 21.4805)	-5.000 (± 34.6259)	-5.059 (± 22.2683)
LDH Week 48 (38, 38, 41, 34, 40)	4.447 (± 34.3493)	-1.395 (± 23.8061)	-4.707 (± 38.6654)	-7.441 (± 23.0443)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: U/L				
arithmetic mean (standard deviation)				
ALT Week 1 (41, 38, 43, 41, 40)	0.700 (± 9.5868)			
ALT Week 2 (42, 39, 43, 41, 41)	1.171 (± 10.2978)			
ALT Week 4 (41, 38, 42, 41, 41)	-1.561 (± 10.1392)			
ALT Week 8 (41, 39, 43, 39, 41)	-1.659 (± 11.1009)			
ALT Week 12 (41, 39, 42, 38, 41)	-1.390 (± 8.1941)			
ALT Week 16 (42, 38, 42, 38, 41)	0.829 (± 11.5432)			
ALT Week 20 (40, 39, 42, 37, 40)	-1.350 (± 10.5479)			
ALT Week 24 (39, 38, 41, 36, 40)	-3.475 (± 8.6202)			
ALT Week 28 (39, 38, 41, 35, 40)	-2.775 (± 10.4280)			
ALT Week 32 (39, 39, 40, 34, 39)	-0.821 (± 11.5482)			
ALT Week 36 (38, 38, 41, 34, 39)	-1.103 (± 10.6296)			

ALT Week 40 (37, 38, 41, 34, 38)	-1.385 (± 13.1061)			
ALT Week 44 (37, 38, 41, 34, 36)	-2.692 (± 10.2525)			
ALT Week 48 (38, 37, 41, 34, 40)	-0.575 (± 9.6181)			
ALP Week 1 (41, 38, 43, 41, 40)	-4.275 (± 7.1360)			
ALP Week 2 (42, 39, 43, 41, 41)	-3.585 (± 8.8430)			
ALP Week 4 (41, 39, 42, 41, 41)	-4.829 (± 10.9268)			
ALP Week 8 (41, 39, 43, 39, 41)	-3.585 (± 9.8336)			
ALP Week 12 (41, 39, 42, 38, 41)	-3.146 (± 17.2476)			
ALP Week 16 (42, 38, 42, 38, 41)	-1.512 (± 25.7722)			
ALP Week 20 (40, 39, 42, 37, 40)	-6.650 (± 14.8143)			
ALP Week 24 (39, 39, 41, 36, 40)	-7.225 (± 18.4231)			
ALP Week 28 (39, 38, 41, 35, 40)	-8.525 (± 16.8523)			
ALP Week 32 (39, 39, 41, 35, 40)	-8.385 (± 17.5988)			
ALP Week 36 (38, 38, 41, 34, 39)	-6.487 (± 19.2434)			
ALP Week 40 (37, 38, 41, 34, 38)	-8.175 (± 17.8884)			
ALP Week 44 (37, 38, 41, 34, 40)	-8.950 (± 18.3162)			
ALP Week 48 (38, 38, 41, 34, 40)	-7.875 (± 20.1370)			
AST Week 1 (41, 38, 43, 41, 40)	0.475 (± 5.2963)			
AST Week 2 (42, 39, 43, 41, 41)	0.780 (± 6.1746)			
AST Week 4 (41, 38, 42, 41, 41)	-1.195 (± 4.2791)			
AST Week 8 (41, 39, 43, 39, 41)	0.366 (± 6.1877)			
AST Week 12 (41, 39, 42, 38, 41)	1.122 (± 6.2897)			
AST Week 16 (42, 38, 42, 38, 41)	2.122 (± 6.1733)			
AST Week 20 (40, 39, 42, 37, 40)	0.500 (± 4.8569)			
AST Week 24 (39, 38, 41, 36, 40)	0.325 (± 4.3759)			
AST Week 28 (39, 38, 41, 35, 40)	0.175 (± 4.1255)			
AST Week 32 (39, 39, 40, 34, 39)	2.051 (± 4.9997)			
AST Week 36 (38, 38, 41, 34, 39)	1.667 (± 6.0755)			
AST Week 40 (37, 38, 41, 34, 39)	2.462 (± 8.4972)			
AST Week 44 (37, 38, 41, 34, 39)	1.590 (± 6.9347)			
AST Week 48 (38, 37, 41, 34, 40)	2.900 (± 6.2339)			

GGT Week 1 (41, 38, 43, 41, 40)	-2.300 (± 6.2684)			
GGT Week 2 (42, 39, 43, 41, 41)	-1.268 (± 7.8773)			
GGT Week 4 (41, 39, 42, 41, 41)	0.512 (± 16.3968)			
GGT Week 8 (41, 39, 43, 39, 41)	-1.805 (± 9.0698)			
GGT Week 12 (41, 39, 42, 38, 41)	3.244 (± 21.8229)			
GGT Week 16 (42, 38, 42, 38, 41)	15.024 (± 77.1617)			
GGT Week 20 (40, 39, 42, 37, 40)	1.475 (± 22.2722)			
GGT Week 24 (39, 39, 41, 36, 40)	-2.625 (± 10.3272)			
GGT Week 28 (39, 38, 41, 35, 40)	-0.200 (± 11.5585)			
GGT Week 32 (39, 39, 40, 34, 39)	2.795 (± 21.1501)			
GGT Week 36 (38, 38, 41, 34, 39)	1.410 (± 18.0200)			
GGT Week 40 (37, 38, 41, 34, 40)	0.925 (± 20.1066)			
GGT Week 44 (37, 38, 41, 34, 39)	-0.949 (± 11.5643)			
GGT Week 48 (38, 38, 41, 34, 40)	2.525 (± 20.6112)			
LDH Week 1 (41, 38, 43, 41, 40)	-1.075 (± 18.4341)			
LDH Week 2 (42, 39, 43, 41, 41)	0.537 (± 19.7270)			
LDH Week 4 (41, 39, 42, 41, 41)	-4.293 (± 17.4732)			
LDH Week 8 (41, 39, 43, 39, 41)	1.439 (± 24.0230)			
LDH Week 12 (41, 39, 42, 38, 41)	1.049 (± 22.9303)			
LDH Week 16 (42, 38, 42, 38, 41)	1.488 (± 21.8325)			
LDH Week 20 (40, 39, 42, 37, 40)	2.025 (± 23.0401)			
LDH Week 24 (39, 39, 41, 36, 40)	8.550 (± 25.3093)			
LDH Week 28 (39, 38, 41, 35, 40)	1.250 (± 22.0962)			
LDH Week 32 (39, 39, 40, 34, 39)	-1.615 (± 24.8052)			
LDH Week 36 (38, 38, 41, 34, 39)	5.436 (± 30.0436)			
LDH Week 40 (37, 38, 41, 34, 40)	0.000 (± 29.3852)			
LDH Week 44 (37, 38, 41, 34, 40)	1.675 (± 24.9588)			
LDH Week 48 (38, 38, 41, 34, 40)	4.500 (± 37.8120)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in biochemistry parameters during the study (albumin)

End point title	Changes from Baseline in biochemistry parameters during the study (albumin)

End point description:

Albumin was measured in grams per liter (g/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: g/L				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-1.000 (± 1.7464)	-0.079 (± 2.1357)	0.279 (± 1.8038)	-0.439 (± 1.8715)
Week 2 (42, 39, 43, 41, 41)	-0.500 (± 2.0982)	0.051 (± 1.5719)	0.419 (± 1.9908)	-0.537 (± 2.0988)
Week 4 (41, 39, 42, 41, 41)	-0.683 (± 2.4743)	0.538 (± 2.1007)	0.595 (± 1.9514)	-0.171 (± 1.9862)
Week 8 (41, 39, 43, 39, 41)	-0.634 (± 2.0094)	0.154 (± 2.1829)	0.581 (± 2.0843)	0.077 (± 2.2051)
Week 12 (41, 39, 42, 38, 41)	0.073 (± 2.4020)	0.538 (± 2.1986)	0.857 (± 1.8685)	0.211 (± 1.9474)
Week 16 (42, 38, 42, 38, 41)	0.833 (± 1.8468)	1.132 (± 2.2800)	0.881 (± 2.0025)	0.316 (± 2.0678)
Week 20 (40, 39, 42, 37, 40)	0.175 (± 1.9333)	0.487 (± 2.4047)	0.976 (± 1.7873)	-0.081 (± 2.1000)
Week 24 (39, 39, 41, 36, 40)	0.385 (± 1.7262)	0.949 (± 2.3164)	1.341 (± 1.8790)	0.722 (± 2.2502)
Week 28 (39, 38, 41, 35, 40)	-0.462 (± 2.0881)	0.632 (± 2.1362)	0.976 (± 1.9169)	0.114 (± 1.9819)
Week 32 (39, 39, 40, 34, 39)	-0.179 (± 1.7452)	0.359 (± 1.8706)	0.700 (± 1.9897)	-0.235 (± 1.6341)
Week 36 (38, 38, 41, 34, 39)	-0.289 (± 2.6397)	0.816 (± 1.7220)	0.659 (± 1.6064)	-0.029 (± 2.0815)
Week 40 (37, 38, 41, 34, 40)	-0.108 (± 2.0109)	0.763 (± 1.9650)	0.805 (± 1.8196)	0.000 (± 1.8749)
Week 44 (37, 38, 41, 34, 40)	-0.297 (± 2.0120)	0.132 (± 2.3269)	0.659 (± 2.2429)	-0.206 (± 1.9661)
Week 48 (38, 38, 41, 34, 40)	0.132 (± 2.2800)	0.632 (± 2.9903)	0.366 (± 3.1682)	0.088 (± 2.6671)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: g/L				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.350 (± 1.6259)			
Week 2 (42, 39, 43, 41, 41)	-0.073 (± 1.8220)			
Week 4 (41, 39, 42, 41, 41)	0.220 (± 1.9687)			
Week 8 (41, 39, 43, 39, 41)	0.195 (± 1.7638)			
Week 12 (41, 39, 42, 38, 41)	0.415 (± 2.1210)			
Week 16 (42, 38, 42, 38, 41)	0.683 (± 1.9422)			
Week 20 (40, 39, 42, 37, 40)	0.575 (± 1.8659)			
Week 24 (39, 39, 41, 36, 40)	0.875 (± 2.3004)			
Week 28 (39, 38, 41, 35, 40)	0.525 (± 2.0999)			
Week 32 (39, 39, 40, 34, 39)	0.667 (± 1.9912)			
Week 36 (38, 38, 41, 34, 39)	0.436 (± 1.9166)			
Week 40 (37, 38, 41, 34, 40)	0.400 (± 1.9716)			
Week 44 (37, 38, 41, 34, 40)	0.175 (± 2.2858)			
Week 48 (38, 38, 41, 34, 40)	0.150 (± 2.3044)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in biochemistry parameters during the study (bilirubin, creatinine, urate)

End point title	Changes from Baseline in biochemistry parameters during the study (bilirubin, creatinine, urate)

End point description:

Bilirubin, creatinine, urate were measured in micromols per liter (µmol/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: µmol/L				
arithmetic mean (standard deviation)				
Bilirubin Week 1 (41, 38, 43, 41, 40)	-0.841 (± 2.8968)	-1.195 (± 3.1083)	-0.465 (± 3.4868)	0.471 (± 3.0332)
Bilirubin Week 2 (42, 39, 43, 41, 41)	-0.762 (± 2.9415)	0.492 (± 3.1202)	0.516 (± 2.7030)	0.978 (± 2.9538)
Bilirubin Week 4 (41, 38, 42, 41, 41)	-0.290 (± 3.4900)	0.789 (± 2.8952)	-0.119 (± 3.2318)	1.066 (± 3.4454)
Bilirubin Week 8 (41, 39, 43, 39, 41)	-0.776 (± 3.7242)	0.541 (± 3.1822)	0.442 (± 3.8005)	0.972 (± 3.4557)
Bilirubin Week 12 (41, 39, 42, 38, 41)	-0.261 (± 2.6113)	0.341 (± 3.0050)	0.095 (± 2.5793)	0.629 (± 3.2367)
Bilirubin Week 16 (42, 38, 42, 38, 41)	0.607 (± 3.7361)	0.637 (± 3.7786)	0.740 (± 3.2505)	1.092 (± 3.7662)
Bilirubin Week 20 (40, 39, 42, 37, 40)	-0.007 (± 3.3543)	0.136 (± 3.4239)	1.062 (± 3.8164)	1.030 (± 3.8636)
Bilirubin Week 24 (39, 38, 41, 36, 40)	0.146 (± 3.2508)	0.592 (± 4.4981)	0.383 (± 3.1235)	1.081 (± 2.8708)
Bilirubin Week 28 (39, 38, 41, 35, 40)	-0.200 (± 3.6974)	-0.068 (± 3.8885)	0.105 (± 2.5550)	0.449 (± 3.4106)
Bilirubin Week 32 (39, 39, 40, 34, 39)	0.233 (± 3.2668)	0.262 (± 3.7358)	0.655 (± 3.1125)	0.994 (± 2.6879)
Bilirubin Week 36 (38, 38, 41, 34, 39)	0.942 (± 3.6870)	0.776 (± 4.3703)	0.078 (± 3.8443)	1.012 (± 3.5311)
Bilirubin Week 40 (37, 38, 41, 34, 39)	0.600 (± 3.8064)	0.679 (± 3.4707)	0.415 (± 3.3481)	1.065 (± 3.1718)
Bilirubin Week 44 (37, 38, 41, 34, 39)	-0.019 (± 3.6800)	-0.276 (± 3.1827)	-0.102 (± 3.1253)	0.871 (± 2.8347)
Bilirubin Week 48 (38, 37, 41, 34, 40)	0.716 (± 4.0370)	0.559 (± 3.2460)	0.285 (± 3.8393)	1.124 (± 3.2882)
Creatinine Week 1 (41, 38, 43, 41, 40)	-0.512 (± 6.6788)	0.368 (± 7.3757)	2.442 (± 7.8628)	1.366 (± 8.9044)
Creatinine Week 2 (42, 39, 43, 41, 41)	2.310 (± 11.1300)	0.026 (± 6.1194)	2.093 (± 8.4426)	2.537 (± 6.8304)
Creatinine Week 4 (41, 39, 42, 41, 41)	0.854 (± 10.2508)	1.256 (± 7.0812)	1.762 (± 8.8229)	-0.561 (± 7.3418)
Creatinine Week 8 (41, 39, 43, 39, 41)	1.366 (± 8.3269)	1.487 (± 8.3756)	3.674 (± 10.1997)	1.590 (± 7.9131)
Creatinine Week 12 (41, 39, 42, 38, 41)	1.268 (± 8.0282)	0.949 (± 8.6113)	6.214 (± 9.5062)	1.947 (± 9.1236)
Creatinine Week 16 (42, 38, 42, 38, 41)	1.833 (± 8.4678)	1.421 (± 10.7945)	3.738 (± 7.7964)	0.658 (± 8.7897)
Creatinine Week 20 (40, 39, 42, 37, 40)	3.150 (± 8.3468)	1.051 (± 7.7966)	4.976 (± 10.5818)	2.270 (± 8.5461)
Creatinine Week 24 (39, 39, 41, 36, 40)	1.359 (± 8.1741)	0.103 (± 6.8817)	3.829 (± 11.4256)	1.972 (± 9.3914)
Creatinine Week 28 (38, 38, 41, 35, 40)	2.921 (± 7.0227)	1.737 (± 7.4858)	4.634 (± 8.9576)	1.371 (± 8.3634)
Creatinine Week 32 (39, 39, 40, 34, 39)	1.718 (± 8.8227)	2.462 (± 9.1360)	2.500 (± 8.9299)	4.118 (± 12.0825)
Creatinine Week 36 (38, 38, 41, 34, 39)	0.289 (± 7.5656)	1.632 (± 7.1600)	1.024 (± 8.8218)	1.853 (± 10.8492)

Creatinine Week 40 (37, 38, 41, 34, 40)	3.838 (± 9.5205)	2.974 (± 7.3796)	4.122 (± 9.7575)	0.647 (± 10.7672)
Creatinine Week 44 (35, 36, 41, 33, 40)	4.543 (± 10.6670)	4.250 (± 8.7876)	3.659 (± 8.5311)	3.364 (± 10.6853)
Creatinine Week 48 (35, 33, 39, 33, 39)	3.000 (± 10.3299)	4.667 (± 8.5355)	3.923 (± 7.7371)	2.879 (± 9.8513)
Urate Week 1 (41, 38, 43, 41, 40)	-1.220 (± 37.4503)	-0.237 (± 43.0100)	11.953 (± 60.5652)	8.732 (± 39.4088)
Urate Week 2 (42, 39, 43, 41, 41)	12.405 (± 47.5795)	-2.974 (± 44.8826)	9.791 (± 61.4009)	9.073 (± 39.3430)
Urate Week 4 (41, 39, 42, 41, 41)	10.171 (± 41.5493)	0.308 (± 47.3193)	13.452 (± 49.1633)	5.659 (± 31.2591)
Urate Week 8 (41, 39, 43, 39, 41)	5.415 (± 42.9500)	-6.231 (± 40.4198)	11.791 (± 64.9910)	3.410 (± 33.9518)
Urate Week 12 (41, 39, 42, 38, 41)	10.707 (± 40.2208)	6.795 (± 54.4814)	13.881 (± 55.3332)	7.553 (± 33.4904)
Urate Week 16 (42, 38, 42, 38, 41)	25.810 (± 44.1965)	8.079 (± 50.0062)	15.357 (± 59.0311)	14.026 (± 40.5173)
Urate Week 20 (40, 39, 42, 37, 40)	28.950 (± 53.8602)	4.692 (± 59.0420)	16.048 (± 63.4346)	10.622 (± 42.1567)
Urate Week 24 (39, 39, 41, 36, 40)	17.410 (± 45.0045)	9.923 (± 54.9648)	3.683 (± 58.6977)	6.667 (± 45.2580)
Urate Week 28 (39, 38, 41, 35, 40)	-0.897 (± 29.4331)	9.447 (± 59.8655)	18.976 (± 62.4894)	-6.371 (± 40.1227)
Urate Week 32 (39, 39, 40, 34, 39)	17.026 (± 47.8185)	2.821 (± 48.9042)	5.800 (± 56.2017)	3.971 (± 45.1103)
Urate Week 36 (38, 38, 41, 34, 39)	0.211 (± 37.5630)	-4.868 (± 49.1419)	-10.927 (± 59.4228)	4.735 (± 42.4309)
Urate Week 40 (37, 38, 41, 34, 40)	9.730 (± 43.5295)	15.605 (± 53.8931)	9.976 (± 62.8739)	-5.029 (± 41.2630)
Urate Week 44 (37, 38, 41, 34, 40)	20.541 (± 57.9164)	7.605 (± 64.3342)	-8.854 (± 67.3523)	1.382 (± 47.9558)
Urate Week 48 (38, 38, 41, 34, 40)	8.684 (± 53.6208)	3.895 (± 48.5831)	-3.220 (± 64.9282)	1.853 (± 54.8762)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: µmol/L				
arithmetic mean (standard deviation)				
Bilirubin Week 1 (41, 38, 43, 41, 40)	0.385 (± 2.2726)			
Bilirubin Week 2 (42, 39, 43, 41, 41)	1.395 (± 4.0672)			
Bilirubin Week 4 (41, 38, 42, 41, 41)	1.344 (± 3.7625)			
Bilirubin Week 8 (41, 39, 43, 39, 41)	0.639 (± 2.8243)			
Bilirubin Week 12 (41, 39, 42, 38, 41)	2.073 (± 4.0034)			
Bilirubin Week 16 (42, 38, 42, 38, 41)	2.024 (± 3.7217)			
Bilirubin Week 20 (40, 39, 42, 37, 40)	1.225 (± 2.9632)			
Bilirubin Week 24 (39, 38, 41, 36, 40)	1.128 (± 2.8112)			

Bilirubin Week 28 (39, 38, 41, 35, 40)	1.595 (± 3.4093)			
Bilirubin Week 32 (39, 39, 40, 34, 39)	1.669 (± 4.0868)			
Bilirubin Week 36 (38, 38, 41, 34, 39)	1.095 (± 2.3971)			
Bilirubin Week 40 (37, 38, 41, 34, 39)	1.433 (± 3.3425)			
Bilirubin Week 44 (37, 38, 41, 34, 39)	1.851 (± 3.7976)			
Bilirubin Week 48 (38, 37, 41, 34, 40)	1.160 (± 3.9493)			
Creatinine Week 1 (41, 38, 43, 41, 40)	1.300 (± 6.7300)			
Creatinine Week 2 (42, 39, 43, 41, 41)	3.317 (± 6.7470)			
Creatinine Week 4 (41, 39, 42, 41, 41)	2.171 (± 6.9279)			
Creatinine Week 8 (41, 39, 43, 39, 41)	3.073 (± 5.7810)			
Creatinine Week 12 (41, 39, 42, 38, 41)	2.220 (± 8.2417)			
Creatinine Week 16 (42, 38, 42, 38, 41)	3.976 (± 8.2719)			
Creatinine Week 20 (40, 39, 42, 37, 40)	4.525 (± 7.4144)			
Creatinine Week 24 (39, 39, 41, 36, 40)	4.650 (± 7.2627)			
Creatinine Week 28 (38, 38, 41, 35, 40)	4.900 (± 7.2388)			
Creatinine Week 32 (39, 39, 40, 34, 39)	4.974 (± 7.7408)			
Creatinine Week 36 (38, 38, 41, 34, 39)	3.462 (± 6.8127)			
Creatinine Week 40 (37, 38, 41, 34, 40)	3.200 (± 7.0208)			
Creatinine Week 44 (35, 36, 41, 33, 40)	3.925 (± 8.0012)			
Creatinine Week 48 (35, 33, 39, 33, 39)	3.256 (± 7.0290)			
Urate Week 1 (41, 38, 43, 41, 40)	11.650 (± 61.0924)			
Urate Week 2 (42, 39, 43, 41, 41)	15.610 (± 49.0693)			
Urate Week 4 (41, 39, 42, 41, 41)	-4.293 (± 47.5753)			
Urate Week 8 (41, 39, 43, 39, 41)	8.024 (± 44.0043)			
Urate Week 12 (41, 39, 42, 38, 41)	2.805 (± 37.6651)			
Urate Week 16 (42, 38, 42, 38, 41)	21.683 (± 41.1670)			
Urate Week 20 (40, 39, 42, 37, 40)	10.600 (± 44.3262)			
Urate Week 24 (39, 39, 41, 36, 40)	6.950 (± 45.8638)			
Urate Week 28 (39, 38, 41, 35, 40)	1.250 (± 45.8972)			
Urate Week 32 (39, 39, 40, 34, 39)	17.077 (± 40.3089)			
Urate Week 36 (38, 38, 41, 34, 39)	5.846 (± 49.4259)			

Urate Week 40 (37, 38, 41, 34, 40)	7.255 (± 46.0833)			
Urate Week 44 (37, 38, 41, 34, 40)	10.675 (± 50.8963)			
Urate Week 48 (38, 38, 41, 34, 40)	8.050 (± 49.1956)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in biochemistry parameters during the study (calcium, chloride, cholesterol, glucose, magnesium, potassium, sodium)

End point title	Changes from Baseline in biochemistry parameters during the study (calcium, chloride, cholesterol, glucose, magnesium, potassium, sodium)

End point description:

Calcium, chloride, cholesterol, glucose, magnesium, potassium, sodium were measured in millimoles per liter (mmol/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: mmol/L				
arithmetic mean (standard deviation)				
Calcium Week 1 (41, 38, 43, 41, 40)	-0.034 (± 0.0810)	-0.017 (± 0.0984)	-0.008 (± 0.0858)	-0.002 (± 0.0990)
Calcium Week 2 (42, 39, 43, 41, 41)	-0.021 (± 0.0951)	0.002 (± 0.0973)	0.009 (± 0.1304)	-0.024 (± 0.1001)
Calcium Week 4 (41, 39, 42, 41, 41)	-0.029 (± 0.1079)	-0.011 (± 0.1015)	-0.021 (± 0.0973)	-0.047 (± 0.1147)
Calcium Week 8 (41, 39, 43, 39, 41)	-0.024 (± 0.0942)	-0.006 (± 0.0926)	0.008 (± 0.1260)	-0.004 (± 0.1105)
Calcium Week 12 (41, 39, 42, 38, 41)	-0.021 (± 0.1009)	-0.025 (± 0.1090)	0.021 (± 0.1057)	-0.020 (± 0.1088)
Calcium Week 16 (42, 38, 42, 38, 41)	0.004 (± 0.0826)	-0.006 (± 0.1079)	0.023 (± 0.1334)	-0.004 (± 0.1027)
Calcium Week 20 (40, 39, 42, 37, 40)	0.002 (± 0.0931)	0.000 (± 0.1013)	0.017 (± 0.0999)	-0.008 (± 0.0948)
Calcium Week 24 (39, 39, 41, 36, 40)	0.011 (± 0.1019)	-0.002 (± 0.1028)	0.015 (± 0.0845)	0.004 (± 0.0896)
Calcium Week 28 (39, 38, 41, 35, 40)	-0.027 (± 0.1117)	0.002 (± 0.0877)	0.009 (± 0.1068)	0.008 (± 0.0909)

Calcium Week 32 (39, 39, 40, 34, 39)	-0.023 (± 0.1069)	0.000 (± 0.0952)	0.001 (± 0.1074)	-0.017 (± 0.0932)
Calcium Week 36 (38, 38, 41, 34, 39)	-0.013 (± 0.1172)	0.007 (± 0.0804)	-0.005 (± 0.1096)	0.001 (± 0.0972)
Calcium Week 40 (37, 38, 41, 34, 40)	0.003 (± 0.0905)	0.001 (± 0.0807)	-0.007 (± 0.1084)	-0.019 (± 0.0809)
Calcium Week 44 (37, 38, 41, 34, 40)	-0.027 (± 0.0920)	-0.018 (± 0.0861)	-0.008 (± 0.1023)	-0.019 (± 0.0839)
Calcium Week 48 (38, 38, 41, 34, 40)	-0.010 (± 0.0881)	-0.009 (± 0.1033)	-0.014 (± 0.1126)	-0.014 (± 0.0912)
Chloride Week 1 (41, 38, 43, 41, 40)	-0.195 (± 2.1121)	-0.105 (± 2.5446)	-0.674 (± 4.1388)	-0.244 (± 2.5572)
Chloride Week 2 (42, 39, 43, 41, 41)	-0.214 (± 2.1131)	0.308 (± 2.6273)	0.093 (± 2.7500)	0.415 (± 2.5296)
Chloride Week 4 (41, 39, 42, 41, 41)	-0.293 (± 1.9525)	-0.333 (± 2.2750)	0.000 (± 2.4792)	0.024 (± 2.6409)
Chloride Week 8 (41, 39, 43, 39, 41)	-0.537 (± 2.1920)	0.615 (± 2.4346)	0.047 (± 2.6988)	0.538 (± 2.3038)
Chloride Week 12 (41, 39, 42, 38, 41)	0.341 (± 2.2205)	-0.282 (± 2.3946)	0.548 (± 2.5681)	-0.211 (± 2.3499)
Chloride Week 16 (42, 38, 42, 38, 41)	-0.310 (± 1.8934)	0.026 (± 2.2837)	0.190 (± 2.0864)	-0.184 (± 2.2644)
Chloride Week 20 (40, 39, 42, 37, 40)	-0.325 (± 2.4640)	-0.538 (± 2.1502)	0.262 (± 2.3484)	0.162 (± 2.6616)
Chloride Week 24 (39, 39, 41, 36, 40)	-0.615 (± 2.0081)	-0.128 (± 2.5462)	-0.390 (± 2.6351)	-0.306 (± 2.1885)
Chloride Week 28 (39, 38, 41, 35, 40)	0.128 (± 2.3190)	0.000 (± 2.6913)	0.195 (± 2.3154)	0.086 (± 2.5365)
Chloride Week 32 (39, 39, 40, 34, 39)	-0.154 (± 2.2069)	0.436 (± 2.3708)	0.500 (± 2.2072)	0.794 (± 2.3196)
Chloride Week 36 (38, 38, 41, 34, 39)	0.237 (± 1.9923)	0.684 (± 2.4285)	0.732 (± 1.9239)	0.294 (± 2.5999)
Chloride Week 40 (37, 38, 41, 34, 40)	-0.054 (± 2.5380)	0.263 (± 2.6271)	0.707 (± 2.4418)	0.824 (± 2.4676)
Chloride Week 44 (37, 38, 41, 34, 40)	0.135 (± 1.9027)	0.579 (± 2.6977)	0.756 (± 2.1069)	0.882 (± 2.8044)
Chloride Week 48 (38, 38, 41, 34, 40)	0.605 (± 2.0994)	0.737 (± 2.8158)	1.024 (± 2.4545)	0.971 (± 2.5044)
Cholesterol Week 1 (41, 38, 43, 41, 40)	-0.254 (± 0.4371)	0.032 (± 0.4307)	0.244 (± 0.5220)	0.105 (± 0.4690)
Cholesterol Week 2 (42, 39, 43, 41, 41)	-0.224 (± 0.4154)	0.108 (± 0.5132)	0.295 (± 0.5178)	0.054 (± 0.5441)
Cholesterol Week 4 (41, 39, 42, 41, 41)	-0.198 (± 0.6334)	-0.023 (± 0.5905)	0.210 (± 0.8027)	0.093 (± 0.6525)
Cholesterol Week 8 (41, 39, 43, 39, 41)	-0.190 (± 0.6935)	-0.023 (± 0.5770)	0.284 (± 0.8012)	0.074 (± 0.7920)
Cholesterol Week 12 (41, 39, 42, 38, 41)	-0.124 (± 0.6719)	0.013 (± 0.7473)	0.117 (± 0.7616)	0.005 (± 0.6045)
Cholesterol Week 16 (42, 38, 42, 38, 41)	0.095 (± 0.6811)	0.184 (± 0.6378)	0.138 (± 0.6814)	0.068 (± 0.6014)
Cholesterol Week 20 (40, 39, 42, 37, 40)	0.053 (± 0.7609)	0.126 (± 0.6889)	0.186 (± 0.9669)	0.116 (± 0.7101)
Cholesterol Week 24 (39, 39, 41, 36, 40)	0.041 (± 0.8729)	0.013 (± 0.8673)	0.127 (± 1.0682)	-0.003 (± 0.6984)
Cholesterol Week 28 (39, 38, 41, 35, 40)	-0.044 (± 0.9797)	-0.037 (± 0.8930)	0.076 (± 1.1434)	-0.037 (± 0.5801)
Cholesterol Week 32 (39, 39, 40, 34, 39)	-0.085 (± 0.8540)	-0.079 (± 0.8918)	0.175 (± 1.0895)	-0.050 (± 0.5945)
Cholesterol Week 36 (38, 38, 41, 34, 39)	0.005 (± 0.7322)	0.024 (± 0.7951)	0.117 (± 0.8408)	-0.038 (± 0.6597)
Cholesterol Week 40 (37, 38, 41, 34, 40)	-0.103 (± 0.7541)	-0.118 (± 0.9109)	0.183 (± 0.8947)	-0.135 (± 0.7454)

Cholesterol Week 44 (37, 38, 41, 34, 39)	-0.170 (± 0.8082)	-0.176 (± 1.0874)	0.071 (± 0.9341)	-0.218 (± 0.9150)
Cholesterol Week 48 (38, 38, 41, 34, 40)	-0.282 (± 0.7891)	-0.279 (± 0.8348)	0.012 (± 0.8883)	-0.253 (± 0.6653)
Glucose Week 1 (41, 38, 43, 41, 40)	0.307 (± 1.3942)	0.103 (± 0.7027)	0.077 (± 1.1366)	0.173 (± 1.0232)
Glucose Week 2 (42, 39, 43, 41, 41)	0.062 (± 0.6681)	0.013 (± 0.8348)	0.221 (± 0.9652)	0.129 (± 1.2364)
Glucose Week 4 (41, 39, 42, 41, 41)	0.298 (± 0.8575)	0.015 (± 0.6888)	0.248 (± 0.7693)	0.249 (± 1.0659)
Glucose Week 8 (41, 39, 43, 39, 41)	0.112 (± 0.9127)	0.308 (± 0.7696)	0.258 (± 0.9254)	0.344 (± 0.6939)
Glucose Week 12 (41, 39, 42, 38, 41)	0.110 (± 0.9146)	0.005 (± 0.6117)	0.188 (± 0.7533)	0.111 (± 0.6455)
Glucose Week 16 (42, 37, 42, 38, 41)	0.176 (± 0.8363)	0.195 (± 0.6316)	0.424 (± 1.1521)	0.276 (± 0.8280)
Glucose Week 20 (40, 39, 42, 37, 40)	0.208 (± 1.0560)	0.315 (± 1.0225)	0.267 (± 1.0132)	0.632 (± 0.9741)
Glucose Week 24 (39, 39, 40, 36, 40)	0.018 (± 1.1856)	0.092 (± 0.7747)	0.328 (± 0.8554)	0.061 (± 1.0462)
Glucose Week 28 (39, 38, 41, 35, 40)	0.246 (± 1.1812)	0.263 (± 0.9371)	0.322 (± 1.1372)	0.263 (± 1.0053)
Glucose Week 32 (39, 39, 40, 34, 39)	0.333 (± 1.2671)	0.236 (± 0.7013)	0.570 (± 1.0301)	0.356 (± 1.1021)
Glucose Week 36 (38, 38, 41, 34, 39)	0.089 (± 0.9061)	0.342 (± 0.9406)	0.234 (± 1.0379)	0.174 (± 1.0175)
Glucose Week 40 (37, 38, 41, 34, 40)	0.143 (± 1.0885)	0.245 (± 1.1081)	0.507 (± 1.1257)	0.203 (± 0.7420)
Glucose Week 44 (37, 38, 41, 34, 39)	0.222 (± 1.4919)	0.200 (± 1.0950)	0.185 (± 0.8688)	0.303 (± 1.2760)
Glucose Week 48 (38, 38, 41, 34, 40)	-0.013 (± 1.2512)	0.045 (± 0.8472)	0.141 (± 0.9341)	0.276 (± 1.0841)
Magnesium Week 1 (41, 38, 43, 41, 40)	-0.010 (± 0.0672)	-0.007 (± 0.0676)	0.002 (± 0.0694)	-0.014 (± 0.0573)
Magnesium Week 2 (42, 39, 43, 41, 41)	-0.004 (± 0.0795)	0.008 (± 0.0745)	-0.011 (± 0.0771)	-0.019 (± 0.0624)
Magnesium Week 4 (41, 39, 42, 41, 41)	-0.022 (± 0.0606)	0.009 (± 0.0725)	-0.012 (± 0.0789)	-0.020 (± 0.0712)
Magnesium Week 8 (41, 39, 43, 39, 41)	-0.016 (± 0.0706)	-0.008 (± 0.0593)	-0.013 (± 0.0819)	-0.015 (± 0.0706)
Magnesium Week 12 (41, 39, 42, 38, 41)	0.010 (± 0.0797)	0.008 (± 0.0847)	-0.011 (± 0.0733)	-0.001 (± 0.0660)
Magnesium Week 16 (42, 38, 42, 38, 41)	-0.002 (± 0.0742)	0.003 (± 0.0823)	-0.021 (± 0.0659)	-0.009 (± 0.0629)
Magnesium Week 20 (40, 39, 42, 37, 40)	-0.007 (± 0.0811)	-0.012 (± 0.0728)	-0.018 (± 0.0659)	-0.005 (± 0.0724)
Magnesium Week 24 (39, 39, 41, 36, 40)	-0.005 (± 0.0757)	-0.004 (± 0.0572)	-0.014 (± 0.0732)	-0.009 (± 0.0559)
Magnesium Week 28 (39, 38, 41, 35, 40)	-0.027 (± 0.0713)	-0.007 (± 0.0525)	-0.018 (± 0.0678)	-0.019 (± 0.0719)
Magnesium Week 32 (39, 39, 40, 34, 39)	-0.023 (± 0.0727)	-0.016 (± 0.0641)	-0.016 (± 0.0603)	-0.012 (± 0.0670)
Magnesium Week 36 (38, 38, 41, 34, 39)	-0.015 (± 0.0694)	-0.001 (± 0.0596)	-0.031 (± 0.0698)	-0.004 (± 0.0534)
Magnesium Week 40 (37, 38, 41, 34, 40)	-0.032 (± 0.0681)	-0.007 (± 0.0541)	-0.014 (± 0.0754)	-0.024 (± 0.0636)
Magnesium Week 44 (37, 38, 41, 34, 40)	-0.024 (± 0.0677)	-0.000 (± 0.0597)	-0.009 (± 0.0685)	-0.024 (± 0.0668)
Magnesium Week 48 (38, 38, 41, 34, 40)	-0.004 (± 0.0633)	-0.004 (± 0.0546)	-0.014 (± 0.0569)	-0.006 (± 0.0616)
Potassium Week 1 (41, 38, 43, 41, 40)	-0.095 (± 0.2701)	0.089 (± 0.3608)	0.081 (± 0.4289)	-0.017 (± 0.3098)

Potassium Week 2 (42, 39, 43, 41, 41)	-0.098 (± 0.2975)	0.085 (± 0.4095)	0.002 (± 0.3327)	-0.005 (± 0.3521)
Potassium Week 4 (41, 39, 42, 41, 41)	-0.080 (± 0.2522)	0.008 (± 0.3821)	0.026 (± 0.2632)	0.024 (± 0.4030)
Potassium Week 8 (41, 39, 43, 39, 41)	-0.056 (± 0.2907)	0.069 (± 0.3221)	0.014 (± 0.3306)	-0.010 (± 0.3135)
Potassium Week 12 (41, 39, 42, 38, 41)	-0.073 (± 0.3217)	0.033 (± 0.3398)	-0.024 (± 0.3192)	-0.082 (± 0.3074)
Potassium Week 16 (42, 36, 42, 38, 41)	-0.086 (± 0.3258)	0.083 (± 0.3112)	0.012 (± 0.3651)	-0.037 (± 0.3035)
Potassium Week 20 (40, 39, 42, 37, 40)	-0.092 (± 0.3846)	0.031 (± 0.3381)	0.055 (± 0.3494)	-0.019 (± 0.3627)
Potassium Week 24 (39, 39, 40, 36, 40)	-0.095 (± 0.3308)	-0.072 (± 0.3052)	0.030 (± 0.3844)	-0.094 (± 0.3414)
Potassium Week 28 (39, 38, 41, 35, 40)	-0.077 (± 0.3141)	0.105 (± 0.3616)	0.063 (± 0.4265)	-0.003 (± 0.3312)
Potassium Week 32 (39, 39, 40, 34, 39)	-0.062 (± 0.3306)	0.069 (± 0.3621)	0.023 (± 0.4154)	0.056 (± 0.2688)
Potassium Week 36 (38, 38, 41, 34, 39)	-0.092 (± 0.3388)	0.045 (± 0.3689)	0.066 (± 0.4316)	0.003 (± 0.3205)
Potassium Week 40 (37, 38, 41, 34, 40)	-0.092 (± 0.3616)	0.089 (± 0.3826)	0.024 (± 0.3484)	-0.003 (± 0.3407)
Potassium Week 44 (37, 38, 41, 34, 40)	-0.119 (± 0.2933)	0.029 (± 0.3571)	0.068 (± 0.4344)	0.094 (± 0.3084)
Potassium Week 48 (38, 38, 41, 34, 40)	-0.137 (± 0.3627)	-0.053 (± 0.3244)	-0.032 (± 0.3274)	0.003 (± 0.4123)
Sodium Week 1 (41, 38, 43, 41, 40)	-0.146 (± 1.5582)	-0.184 (± 1.7531)	0.000 (± 2.0471)	-0.610 (± 2.0722)
Sodium Week 2 (42, 39, 43, 41, 41)	-0.500 (± 1.6417)	-0.513 (± 1.8191)	-0.209 (± 1.9341)	-0.244 (± 2.0221)
Sodium Week 4 (41, 39, 42, 41, 41)	-0.732 (± 1.8442)	-0.385 (± 1.6482)	-0.214 (± 2.3430)	-0.707 (± 2.0155)
Sodium Week 8 (41, 39, 43, 39, 41)	-0.854 (± 2.0070)	-0.410 (± 1.3711)	-0.860 (± 2.2316)	-0.359 (± 1.7394)
Sodium Week 12 (41, 39, 42, 38, 41)	-0.512 (± 1.8858)	-0.513 (± 1.4845)	-0.619 (± 2.0357)	-0.632 (± 2.1738)
Sodium Week 16 (42, 38, 42, 38, 41)	-0.738 (± 1.8086)	-0.211 (± 1.7423)	-0.714 (± 1.7708)	-0.842 (± 2.3656)
Sodium Week 20 (40, 39, 42, 37, 40)	-0.675 (± 1.7155)	-0.538 (± 1.4482)	-0.857 (± 2.1928)	-0.595 (± 2.1661)
Sodium Week 24 (39, 39, 41, 36, 40)	-0.821 (± 1.7751)	-0.487 (± 1.5196)	-0.463 (± 2.0137)	-0.472 (± 1.8124)
Sodium Week 28 (39, 38, 41, 35, 40)	-0.462 (± 2.2924)	-0.658 (± 1.8494)	-0.683 (± 1.8767)	-0.457 (± 2.3307)
Sodium Week 32 (39, 39, 40, 34, 39)	-1.077 (± 1.8692)	-0.128 (± 1.9219)	-0.525 (± 1.8809)	-0.441 (± 1.6732)
Sodium Week 36 (38, 38, 41, 34, 39)	-0.711 (± 2.0122)	-0.263 (± 1.8986)	-0.512 (± 1.8725)	-0.618 (± 1.9850)
Sodium Week 40 (37, 38, 41, 34, 40)	-0.432 (± 2.1153)	-0.474 (± 1.6397)	-0.512 (± 2.1578)	-0.882 (± 1.9812)
Sodium Week 44 (37, 38, 41, 34, 40)	-0.486 (± 1.8352)	-0.737 (± 2.0492)	-0.878 (± 1.9390)	-0.647 (± 1.8238)
Sodium Week 48 (38, 38, 41, 34, 40)	-0.237 (± 1.7772)	-0.763 (± 1.8074)	-0.732 (± 1.8845)	-0.706 (± 1.5281)

End point values	BKZ 320 mg (SS)			

Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: mmol/L				
arithmetic mean (standard deviation)				
Calcium Week 1 (41, 38, 43, 41, 40)	-0.014 (± 0.0897)			
Calcium Week 2 (42, 39, 43, 41, 41)	-0.022 (± 0.0938)			
Calcium Week 4 (41, 39, 42, 41, 41)	-0.020 (± 0.0917)			
Calcium Week 8 (41, 39, 43, 39, 41)	-0.022 (± 0.0975)			
Calcium Week 12 (41, 39, 42, 38, 41)	-0.025 (± 0.0923)			
Calcium Week 16 (42, 38, 42, 38, 41)	0.005 (± 0.0888)			
Calcium Week 20 (40, 39, 42, 37, 40)	-0.018 (± 0.0919)			
Calcium Week 24 (39, 39, 41, 36, 40)	0.003 (± 0.0974)			
Calcium Week 28 (39, 38, 41, 35, 40)	-0.021 (± 0.1043)			
Calcium Week 32 (39, 39, 40, 34, 39)	-0.008 (± 0.1024)			
Calcium Week 36 (38, 38, 41, 34, 39)	-0.015 (± 0.0936)			
Calcium Week 40 (37, 38, 41, 34, 40)	-0.025 (± 0.0947)			
Calcium Week 44 (37, 38, 41, 34, 40)	-0.042 (± 0.0972)			
Calcium Week 48 (38, 38, 41, 34, 40)	-0.034 (± 0.0861)			
Chloride Week 1 (41, 38, 43, 41, 40)	-0.125 (± 2.3986)			
Chloride Week 2 (42, 39, 43, 41, 41)	-0.439 (± 2.4192)			
Chloride Week 4 (41, 39, 42, 41, 41)	0.000 (± 2.6363)			
Chloride Week 8 (41, 39, 43, 39, 41)	0.683 (± 2.4025)			
Chloride Week 12 (41, 39, 42, 38, 41)	0.000 (± 2.4393)			
Chloride Week 16 (42, 38, 42, 38, 41)	-0.268 (± 2.1334)			
Chloride Week 20 (40, 39, 42, 37, 40)	0.075 (± 2.3685)			
Chloride Week 24 (39, 39, 41, 36, 40)	-0.050 (± 2.5415)			
Chloride Week 28 (39, 38, 41, 35, 40)	0.250 (± 2.5090)			
Chloride Week 32 (39, 39, 40, 34, 39)	0.282 (± 2.0641)			
Chloride Week 36 (38, 38, 41, 34, 39)	0.205 (± 2.4299)			
Chloride Week 40 (37, 38, 41, 34, 40)	0.500 (± 2.4495)			
Chloride Week 44 (37, 38, 41, 34, 40)	0.200 (± 2.5840)			
Chloride Week 48 (38, 38, 41, 34, 40)	0.725 (± 2.7826)			

Cholesterol Week 1 (41, 38, 43, 41, 40)	0.102 (± 0.3965)			
Cholesterol Week 2 (42, 39, 43, 41, 41)	0.222 (± 0.6101)			
Cholesterol Week 4 (41, 39, 42, 41, 41)	0.151 (± 0.4178)			
Cholesterol Week 8 (41, 39, 43, 39, 41)	0.061 (± 0.6268)			
Cholesterol Week 12 (41, 39, 42, 38, 41)	0.212 (± 0.7491)			
Cholesterol Week 16 (42, 38, 42, 38, 41)	0.249 (± 0.7075)			
Cholesterol Week 20 (40, 39, 42, 37, 40)	0.115 (± 0.7718)			
Cholesterol Week 24 (39, 39, 41, 36, 40)	0.077 (± 0.5686)			
Cholesterol Week 28 (39, 38, 41, 35, 40)	0.100 (± 0.5923)			
Cholesterol Week 32 (39, 39, 40, 34, 39)	0.256 (± 0.6920)			
Cholesterol Week 36 (38, 38, 41, 34, 39)	0.144 (± 0.7950)			
Cholesterol Week 40 (37, 38, 41, 34, 40)	0.110 (± 0.7824)			
Cholesterol Week 44 (37, 38, 41, 34, 39)	-0.000 (± 0.8407)			
Cholesterol Week 48 (38, 38, 41, 34, 40)	-0.083 (± 0.5817)			
Glucose Week 1 (41, 38, 43, 41, 40)	-0.060 (± 0.8445)			
Glucose Week 2 (42, 39, 43, 41, 41)	0.190 (± 0.8938)			
Glucose Week 4 (41, 39, 42, 41, 41)	0.134 (± 0.7428)			
Glucose Week 8 (41, 39, 43, 39, 41)	0.256 (± 0.7075)			
Glucose Week 12 (41, 39, 42, 38, 41)	-0.124 (± 0.6636)			
Glucose Week 16 (42, 37, 42, 38, 41)	0.398 (± 0.8332)			
Glucose Week 20 (40, 39, 42, 37, 40)	0.165 (± 1.0366)			
Glucose Week 24 (39, 39, 40, 36, 40)	0.037 (± 0.6295)			
Glucose Week 28 (39, 38, 41, 35, 40)	0.262 (± 0.6412)			
Glucose Week 32 (39, 39, 40, 34, 39)	0.203 (± 0.5945)			
Glucose Week 36 (38, 38, 41, 34, 39)	0.290 (± 0.7789)			
Glucose Week 40 (37, 38, 41, 34, 40)	0.125 (± 0.7016)			
Glucose Week 44 (37, 38, 41, 34, 39)	0.197 (± 0.8966)			
Glucose Week 48 (38, 38, 41, 34, 40)	0.100 (± 0.7835)			
Magnesium Week 1 (41, 38, 43, 41, 40)	-0.015 (± 0.0680)			
Magnesium Week 2 (42, 39, 43, 41, 41)	-0.007 (± 0.0680)			
Magnesium Week 4 (41, 39, 42, 41, 41)	-0.005 (± 0.0998)			

Magnesium Week 8 (41, 39, 43, 39, 41)	-0.006 (± 0.0624)			
Magnesium Week 12 (41, 39, 42, 38, 41)	0.003 (± 0.0730)			
Magnesium Week 16 (42, 38, 42, 38, 41)	-0.002 (± 0.0731)			
Magnesium Week 20 (40, 39, 42, 37, 40)	-0.009 (± 0.0636)			
Magnesium Week 24 (39, 39, 41, 36, 40)	-0.016 (± 0.0664)			
Magnesium Week 28 (39, 38, 41, 35, 40)	-0.017 (± 0.0565)			
Magnesium Week 32 (39, 39, 40, 34, 39)	-0.013 (± 0.0572)			
Magnesium Week 36 (38, 38, 41, 34, 39)	-0.007 (± 0.0563)			
Magnesium Week 40 (37, 38, 41, 34, 40)	-0.009 (± 0.0684)			
Magnesium Week 44 (37, 38, 41, 34, 40)	-0.016 (± 0.0667)			
Magnesium Week 48 (38, 38, 41, 34, 40)	-0.009 (± 0.0648)			
Potassium Week 1 (41, 38, 43, 41, 40)	-0.062 (± 0.3216)			
Potassium Week 2 (42, 39, 43, 41, 41)	0.027 (± 0.3074)			
Potassium Week 4 (41, 39, 42, 41, 41)	-0.063 (± 0.2853)			
Potassium Week 8 (41, 39, 43, 39, 41)	0.000 (± 0.2520)			
Potassium Week 12 (41, 39, 42, 38, 41)	-0.080 (± 0.2977)			
Potassium Week 16 (42, 36, 42, 38, 41)	-0.020 (± 0.2713)			
Potassium Week 20 (40, 39, 42, 37, 40)	0.000 (± 0.2774)			
Potassium Week 24 (39, 39, 40, 36, 40)	-0.062 (± 0.2967)			
Potassium Week 28 (39, 38, 41, 35, 40)	-0.030 (± 0.3480)			
Potassium Week 32 (39, 39, 40, 34, 39)	0.046 (± 0.3094)			
Potassium Week 36 (38, 38, 41, 34, 39)	0.033 (± 0.3359)			
Potassium Week 40 (37, 38, 41, 34, 40)	-0.017 (± 0.3456)			
Potassium Week 44 (37, 38, 41, 34, 40)	-0.035 (± 0.3009)			
Potassium Week 48 (38, 38, 41, 34, 40)	-0.027 (± 0.3250)			
Sodium Week 1 (41, 38, 43, 41, 40)	-0.375 (± 2.1326)			
Sodium Week 2 (42, 39, 43, 41, 41)	-0.341 (± 2.1167)			
Sodium Week 4 (41, 39, 42, 41, 41)	-0.805 (± 1.8196)			
Sodium Week 8 (41, 39, 43, 39, 41)	-0.463 (± 2.2924)			
Sodium Week 12 (41, 39, 42, 38, 41)	-0.854 (± 2.3512)			
Sodium Week 16 (42, 38, 42, 38, 41)	-0.780 (± 1.7250)			

Sodium Week 20 (40, 39, 42, 37, 40)	-0.775 (± 1.9147)			
Sodium Week 24 (39, 39, 41, 36, 40)	-0.725 (± 1.7393)			
Sodium Week 28 (39, 38, 41, 35, 40)	-0.575 (± 2.5609)			
Sodium Week 32 (39, 39, 40, 34, 39)	-0.667 (± 1.8257)			
Sodium Week 36 (38, 38, 41, 34, 39)	-0.436 (± 2.2337)			
Sodium Week 40 (37, 38, 41, 34, 40)	-0.950 (± 2.0248)			
Sodium Week 44 (37, 38, 41, 34, 40)	-1.000 (± 2.4179)			
Sodium Week 48 (38, 38, 41, 34, 40)	-0.750 (± 2.1334)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in biochemistry parameters during the study (urea nitrogen)

End point title	Changes from Baseline in biochemistry parameters during the study (urea nitrogen)

End point description:

Urea nitrogen was measured in millimoles per liter (mmol/L).
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	38	43	41
Units: mmol/L				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	-0.093 (± 1.0815)	0.126 (± 1.2116)	-0.123 (± 1.0989)	-0.012 (± 1.0900)
Week 2 (42, 39, 43, 41, 41)	0.386 (± 1.8183)	-0.208 (± 1.1329)	-0.047 (± 1.0359)	0.024 (± 1.1762)
Week 4 (41, 39, 42, 41, 41)	0.027 (± 1.3217)	0.013 (± 1.1307)	0.083 (± 1.1244)	-0.224 (± 1.1449)
Week 8 (41, 39, 43, 39, 41)	0.007 (± 0.9936)	0.023 (± 1.1685)	-0.070 (± 1.1143)	-0.379 (± 1.2316)
Week 12 (41, 39, 42, 38, 41)	-0.166 (± 1.2654)	-0.244 (± 1.1740)	-0.231 (± 1.3357)	-0.429 (± 1.1733)

Week 16 (42, 38, 42, 38, 41)	-0.133 (± 1.0656)	-0.087 (± 0.9793)	-0.200 (± 1.3083)	-0.218 (± 1.0747)
Week 20 (40, 39, 42, 37, 40)	-0.207 (± 1.2670)	-0.490 (± 1.0901)	-0.064 (± 1.2916)	-0.357 (± 1.1572)
Week 24 (39, 39, 41, 36, 40)	-0.256 (± 1.1378)	-0.523 (± 1.1235)	-0.232 (± 1.4951)	-0.289 (± 1.1369)
Week 28 (39, 38, 41, 35, 40)	-0.267 (± 1.3487)	-0.287 (± 1.0992)	0.012 (± 1.3020)	-0.263 (± 1.1835)
Week 32 (39, 39, 40, 34, 39)	-0.097 (± 1.0396)	-0.141 (± 1.3098)	-0.200 (± 1.1266)	-0.326 (± 1.1199)
Week 36 (38, 38, 41, 34, 39)	-0.203 (± 1.0579)	-0.308 (± 1.1757)	0.015 (± 1.1094)	-0.247 (± 1.1683)
Week 40 (37, 38, 41, 34, 40)	-0.214 (± 1.2537)	0.192 (± 1.3690)	0.068 (± 1.1230)	-0.132 (± 1.1834)
Week 44 (37, 38, 41, 34, 39)	-0.105 (± 1.3389)	-0.047 (± 1.3456)	-0.054 (± 1.1276)	-0.229 (± 1.1979)
Week 48 (38, 38, 41, 34, 40)	-0.111 (± 1.4431)	-0.113 (± 1.1796)	-0.222 (± 1.4085)	-0.285 (± 1.2611)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: mmol/L				
arithmetic mean (standard deviation)				
Week 1 (41, 38, 43, 41, 40)	0.173 (± 1.5513)			
Week 2 (42, 39, 43, 41, 41)	0.212 (± 1.3064)			
Week 4 (41, 39, 42, 41, 41)	0.007 (± 1.2384)			
Week 8 (41, 39, 43, 39, 41)	0.080 (± 1.1265)			
Week 12 (41, 39, 42, 38, 41)	-0.151 (± 1.2426)			
Week 16 (42, 38, 42, 38, 41)	0.012 (± 1.1996)			
Week 20 (40, 39, 42, 37, 40)	-0.035 (± 1.3202)			
Week 24 (39, 39, 41, 36, 40)	-0.138 (± 1.2245)			
Week 28 (39, 38, 41, 35, 40)	-0.082 (± 1.3239)			
Week 32 (39, 39, 40, 34, 39)	0.082 (± 1.1841)			
Week 36 (38, 38, 41, 34, 39)	-0.018 (± 1.1014)			
Week 40 (37, 38, 41, 34, 40)	0.283 (± 1.3435)			
Week 44 (37, 38, 41, 34, 39)	0.210 (± 1.2264)			
Week 48 (38, 38, 41, 34, 40)	0.088 (± 1.4580)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in urinalysis parameters during the study (erythrocytes, leukocytes, renal epithelial casts, squamous epithelial cells, transitional epithelial cells)

End point title	Changes from Baseline in urinalysis parameters during the study (erythrocytes, leukocytes, renal epithelial casts, squamous epithelial cells, transitional epithelial cells)

End point description:

Erythrocytes, leukocytes, renal epithelial casts, squamous epithelial cells, transitional epithelial cells were measured in cells per high power field (cells/HPF).
The SS consisted of all randomized study participants who received at least 1 dose of IMP. Number of participants reflect those with non-missing urinalysis results during the study.

Note 1: 999 is used as a placeholder for values not evaluable because only one participant was analyzed and for groups that had 0 participants analyzed.
Note 2: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	3	5
Units: cells/HPF				
arithmetic mean (standard deviation)				
Erythrocytes Week 1 (1, 4, 3, 5, 3)	-55.000 (± 999)	0.750 (± 0.9574)	0.333 (± 0.5774)	0.000 (± 0.0000)
Erythrocytes Week 2 (1, 4, 4, 4, 3)	-54.000 (± 999)	-0.500 (± 0.5774)	0.250 (± 0.5000)	0.000 (± 0.0000)
Erythrocytes Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	3.333 (± 5.7735)	0.000 (± 0.7071)	0.250 (± 0.5000)
Erythrocytes Week 8 (0, 3, 4, 2, 3)	999 (± 999)	0.000 (± 0.0000)	0.000 (± 0.8165)	0.000 (± 0.0000)
Erythrocytes Week 12 (1, 3, 5, 2, 3)	-23.000 (± 999)	0.000 (± 0.0000)	0.800 (± 1.3038)	0.000 (± 0.0000)
Erythrocytes Week 16 (1, 5, 4, 5, 2)	-55.000 (± 999)	0.800 (± 1.7889)	0.500 (± 1.7321)	0.000 (± 0.0000)
Erythrocytes Week 20 (2, 4, 5, 6, 4)	-30.000 (± 35.3553)	0.000 (± 0.0000)	0.400 (± 1.1402)	0.000 (± 0.0000)
Erythrocytes Week 24 (0, 4, 4, 7, 3)	999 (± 999)	-0.250 (± 0.5000)	0.250 (± 0.5000)	-0.143 (± 0.8997)
Erythrocytes Week 28 (1, 4, 5, 4, 3)	-5.000 (± 999)	0.000 (± 0.8165)	0.400 (± 1.5166)	0.000 (± 0.0000)
Erythrocytes Week 32 (2, 3, 4, 6, 3)	-27.500 (± 38.8909)	0.000 (± 0.0000)	0.250 (± 0.5000)	0.000 (± 0.0000)
Erythrocytes Week 36 (1, 6, 4, 1, 1)	-55.000 (± 999)	0.000 (± 0.0000)	0.250 (± 0.5000)	0.000 (± 999)
Erythrocytes Week 40 (0, 4, 4, 4, 2)	999 (± 999)	-0.250 (± 0.5000)	0.750 (± 1.5000)	-0.250 (± 0.5000)
Erythrocytes Week 44 (1, 5, 5, 4, 2)	-55.000 (± 999)	0.000 (± 0.0000)	0.400 (± 0.8944)	-0.250 (± 1.2583)

Erythrocytes Week 48 (2, 6, 4, 3, 4)	-27.500 (± 38.8909)	0.167 (± 0.4082)	1.750 (± 3.5000)	0.000 (± 0.0000)
Leukocytes Week 1 (1, 4, 3, 5, 3)	0.000 (± 999)	2.750 (± 6.1847)	-7.667 (± 13.2791)	-0.200 (± 1.0954)
Leukocytes Week 2 (1, 4, 4, 4, 3)	2.000 (± 999)	-2.500 (± 2.0817)	-3.000 (± 6.6833)	-0.250 (± 0.5000)
Leukocytes Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	-4.600 (± 10.2372)	0.250 (± 0.5000)
Leukocytes Week 8 (0, 2, 4, 2, 3))	999 (± 999)	0.000 (± 0.0000)	-1.500 (± 3.6968)	0.000 (± 0.0000)
Leukocytes Week 12 (1, 3, 4, 2, 3)	0.000 (± 999)	1.667 (± 4.7258)	13.500 (± 26.3376)	0.000 (± 0.0000)
Leukocytes Week 16 (1, 5, 4, 5, 2)	0.000 (± 999)	-0.200 (± 1.7889)	33.750 (± 67.5000)	-0.400 (± 0.8944)
Leukocytes Week 20 (2, 4, 5, 6, 4)	0.000 (± 2.8284)	3.000 (± 6.0000)	57.800 (± 145.4036)	0.667 (± 1.5055)
Leukocytes Week 24 (0, 4, 4, 7, 3)	999 (± 999)	2.750 (± 4.8563)	-6.500 (± 13.0000)	2.286 (± 4.8206)
Leukocytes Week 28 (1, 4, 5, 4, 3)	-2.000 (± 999)	-0.750 (± 0.9574)	-5.400 (± 12.0748)	0.000 (± 0.0000)
Leukocytes Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)	3.333 (± 5.7735)	-6.500 (± 13.0000)	-1.333 (± 1.6330)
Leukocytes Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)	0.667 (± 2.7325)	0.000 (± 0.0000)	24.000 (± 999)
Leukocytes Week 40 (0, 4, 4, 4, 2)	999 (± 999)	-0.500 (± 2.5166)	-7.500 (± 15.0000)	1.500 (± 3.0000)
Leukocytes Week 44 (1, 5, 5, 4, 2)	0.000 (± 999)	0.400 (± 0.8944)	-1.400 (± 3.1305)	-0.500 (± 1.0000)
Leukocytes Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)	8.000 (± 21.6148)	69.500 (± 139.0000)	-1.000 (± 1.7321)
Renal Casts Week 1 (1, 4, 3, 5, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 2 (1, 4, 4, 4, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 8 (0, 3, 4, 2, 3)	999 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 12 (1, 3, 5, 2, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 16 (1, 5, 4, 5, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 20 (2, 4, 5, 6, 4)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 24 (0, 4, 4, 7, 3)	999 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 28 (1, 4, 5, 4, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)	0.167 (± 0.4082)	0.000 (± 0.0000)	0.000 (± 999)
Renal Casts Week 40 (0, 4, 4, 4, 2)	999 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 44 (1, 5, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Renal Casts Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Squamous Cells Week 1 (1, 4, 3, 5, 3)	0.000 (± 999)	0.250 (± 1.2583)	3.000 (± 5.1962)	-0.200 (± 0.4472)
Squamous Cells Week 2 (1, 4, 4, 4, 3)	1.000 (± 999)	-8.000 (± 14.6969)	-0.250 (± 3.6856)	0.000 (± 0.0000)

Squamous Cells Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	-1.800 (± 7.1554)	0.000 (± 0.0000)
Squamous Cells Week 8 (0, 2, 4, 2, 3)	999 (± 999)	0.000 (± 0.0000)	0.500 (± 1.0000)	0.000 (± 0.0000)
Squamous Cells Week 12 (1, 3, 5, 2, 3)	0.000 (± 999)	-4.333 (± 7.5056)	-2.200 (± 5.4955)	0.000 (± 0.0000)
Squamous Cells Week 16 (1, 5, 4, 5, 2)	0.000 (± 999)	0.000 (± 0.0000)	-2.750 (± 5.5000)	-0.200 (± 0.4472)
Squamous Cells Week 20 (2, 4, 5, 6, 4)	1.000 (± 1.4142)	-2.750 (± 5.5000)	-1.400 (± 5.6391)	-0.167 (± 0.9832)
Squamous Cells Week 24 (0, 4, 4, 7, 3)	999 (± 999)	1.000 (± 1.4142)	1.000 (± 2.0000)	-0.286 (± 0.4880)
Squamous Cells Week 28 (1, 4, 5, 4, 3)	0.000 (± 999)	-3.000 (± 6.0000)	0.600 (± 1.3416)	-0.250 (± 0.5000)
Squamous Cells Week 32 (2, 2, 4, 6, 2)	0.500 (± 0.7071)	0.000 (± 0.0000)	0.500 (± 1.0000)	-0.667 (± 0.8165)
Squamous Cells Week 36 (1, 5, 4, 1, 1)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 999)
Squamous Cells Week 40 (0, 4, 4, 4, 2)	999 (± 999)	-2.750 (± 5.5000)	0.750 (± 1.5000)	0.000 (± 0.0000)
Squamous Cells Week 44 (1, 5, 5, 4, 2)	0.000 (± 999)	-1.000 (± 2.2361)	0.600 (± 1.3416)	-0.250 (± 0.5000)
Squamous Cells Week 48 (2, 6, 4, 3, 3)	0.000 (± 0.0000)	0.667 (± 1.6330)	1.250 (± 1.8930)	0.333 (± 0.5774)
Transitional Cells Week 1 (1, 4, 3, 5, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 2 (1, 4, 4, 4, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 8 (0, 3, 4, 2, 3)	999 (± 999)	1.000 (± 1.7321)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 12 (1, 3, 5, 2, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.200 (± 0.4472)	0.000 (± 0.0000)
Transitional Cells Week 16 (1, 5, 4, 5, 2)	0.000 (± 999)	0.400 (± 0.8944)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 20 (2, 4, 5, 6, 4)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 24 (0, 4, 4, 7, 3)	999 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 28 (1, 4, 5, 4, 3)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)	0.167 (± 0.4082)	0.000 (± 0.0000)	0.000 (± 999)
Transitional Cells Week 40 (0, 4, 4, 4, 2)	999 (± 999)	0.250 (± 0.5000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 44 (1, 5, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)
Transitional Cells Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: cells/HPF				

arithmetic mean (standard deviation)				
Erythrocytes Week 1 (1, 4, 3, 5, 3)	0.333 (± 0.5774)			
Erythrocytes Week 2 (1, 4, 4, 4, 3)	1.333 (± 2.5166)			
Erythrocytes Week 4 (1, 3, 5, 4, 2)	-0.500 (± 0.7071)			
Erythrocytes Week 8 (0, 3, 4, 2, 3)	0.000 (± 1.0000)			
Erythrocytes Week 12 (1, 3, 5, 2, 3)	-0.333 (± 0.5774)			
Erythrocytes Week 16 (1, 5, 4, 5, 2)	2.500 (± 3.5355)			
Erythrocytes Week 20 (2, 4, 5, 6, 4)	0.250 (± 0.5000)			
Erythrocytes Week 24 (0, 4, 4, 7, 3)	1.000 (± 2.6458)			
Erythrocytes Week 28 (1, 4, 5, 4, 3)	2.333 (± 5.7735)			
Erythrocytes Week 32 (2, 3, 4, 6, 3)	2.000 (± 3.4641)			
Erythrocytes Week 36 (1, 6, 4, 1, 1)	-1.000 (± 999)			
Erythrocytes Week 40 (0, 4, 4, 4, 2)	0.000 (± 0.0000)			
Erythrocytes Week 44 (1, 5, 5, 4, 2)	0.000 (± 0.0000)			
Erythrocytes Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.8165)			
Leukocytes Week 1 (1, 4, 3, 5, 3)	0.667 (± 1.1547)			
Leukocytes Week 2 (1, 4, 4, 4, 3)	0.000 (± 0.0000)			
Leukocytes Week 4 (1, 3, 5, 4, 2)	2.000 (± 2.8284)			
Leukocytes Week 8 (0, 2, 4, 2, 3))	4.000 (± 6.9282)			
Leukocytes Week 12 (1, 3, 4, 2, 3)	0.000 (± 0.0000)			
Leukocytes Week 16 (1, 5, 4, 5, 2)	0.500 (± 0.7071)			
Leukocytes Week 20 (2, 4, 5, 6, 4)	-6.750 (± 14.8633)			
Leukocytes Week 24 (0, 4, 4, 7, 3)	0.333 (± 0.5774)			
Leukocytes Week 28 (1, 4, 5, 4, 3)	2.333 (± 4.0415)			
Leukocytes Week 32 (2, 3, 4, 6, 3)	1.333 (± 2.3094)			
Leukocytes Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)			
Leukocytes Week 40 (0, 4, 4, 4, 2)	0.000 (± 0.0000)			
Leukocytes Week 44 (1, 5, 5, 4, 2)	0.000 (± 0.0000)			
Leukocytes Week 48 (2, 6, 4, 3, 4)	0.250 (± 0.5000)			
Renal Casts Week 1 (1, 4, 3, 5, 3)	0.000 (± 0.0000)			
Renal Casts Week 2 (1, 4, 4, 4, 3)	0.000 (± 0.0000)			
Renal Casts Week 4 (1, 3, 5, 4, 2)	0.000 (± 0.0000)			

Renal Casts Week 8 (0, 3, 4, 2, 3)	0.000 (± 0.0000)			
Renal Casts Week 12 (1, 3, 5, 2, 3)	0.000 (± 0.0000)			
Renal Casts Week 16 (1, 5, 4, 5, 2)	0.000 (± 0.0000)			
Renal Casts Week 20 (2, 4, 5, 6, 4)	0.000 (± 0.0000)			
Renal Casts Week 24 (0, 4, 4, 7, 3)	0.000 (± 0.0000)			
Renal Casts Week 28 (1, 4, 5, 4, 3)	0.000 (± 0.0000)			
Renal Casts Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)			
Renal Casts Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)			
Renal Casts Week 40 (0, 4, 4, 4, 2)	0.000 (± 0.0000)			
Renal Casts Week 44 (1, 5, 5, 4, 2)	0.000 (± 0.0000)			
Renal Casts Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)			
Squamous Cells Week 1 (1, 4, 3, 5, 3)	-0.333 (± 0.5774)			
Squamous Cells Week 2 (1, 4, 4, 4, 3)	-1.667 (± 1.5275)			
Squamous Cells Week 4 (1, 3, 5, 4, 2)	1.000 (± 1.4142)			
Squamous Cells Week 8 (0, 2, 4, 2, 3)	0.333 (± 0.5774)			
Squamous Cells Week 12 (1, 3, 5, 2, 3)	0.333 (± 0.5774)			
Squamous Cells Week 16 (1, 5, 4, 5, 2)	0.000 (± 0.0000)			
Squamous Cells Week 20 (2, 4, 5, 6, 4)	-0.750 (± 0.9574)			
Squamous Cells Week 24 (0, 4, 4, 7, 3)	1.333 (± 4.1633)			
Squamous Cells Week 28 (1, 4, 5, 4, 3)	-1.667 (± 1.5275)			
Squamous Cells Week 32 (2, 2, 4, 6, 2)	-0.500 (± 0.7071)			
Squamous Cells Week 36 (1, 5, 4, 1, 1)	0.000 (± 999)			
Squamous Cells Week 40 (0, 4, 4, 4, 2)	-0.500 (± 0.7071)			
Squamous Cells Week 44 (1, 5, 5, 4, 2)	-0.500 (± 0.7071)			
Squamous Cells Week 48 (2, 6, 4, 3, 3)	-1.000 (± 1.0000)			
Transitional Cells Week 1 (1, 4, 3, 5, 3)	0.000 (± 0.0000)			
Transitional Cells Week 2 (1, 4, 4, 4, 3)	0.000 (± 0.0000)			
Transitional Cells Week 4 (1, 3, 5, 4, 2)	0.000 (± 0.0000)			
Transitional Cells Week 8 (0, 3, 4, 2, 3)	0.000 (± 0.0000)			
Transitional Cells Week 12 (1, 3, 5, 2, 3)	0.000 (± 0.0000)			
Transitional Cells Week 16 (1, 5, 4, 5, 2)	0.000 (± 0.0000)			
Transitional Cells Week 20 (2, 4, 5, 6, 4)	0.000 (± 0.0000)			

Transitional Cells Week 24 (0, 4, 4, 7, 3)	0.000 (± 0.0000)			
Transitional Cells Week 28 (1, 4, 5, 4, 3)	0.000 (± 0.0000)			
Transitional Cells Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)			
Transitional Cells Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)			
Transitional Cells Week 40 (0, 4, 4, 4, 2)	0.000 (± 0.0000)			
Transitional Cells Week 44 (1, 5, 5, 4, 2)	0.000 (± 0.0000)			
Transitional Cells Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in urinalysis parameters during the study (hyaline casts)

End point title	Changes from Baseline in urinalysis parameters during the study (hyaline casts)

End point description:

Hyaline casts was measured in cells per low power field (cells/LPF).
The SS consisted of all randomized study participants who received at least 1 dose of IMP. Number of participants reflect those with non-missing urinalysis results during the study.

Note 1: 999 is used as a placeholder for values not evaluable because only one participant was analyzed and for groups that had 0 participants analyzed.
Note 2: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg).

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	4	3	5
Units: cells/LPF				
arithmetic mean (standard deviation)				
Week 1 (1, 4, 3, 5, 3)	0.000 (± 999)	0.000 (± 0.0000)	1.000 (± 1.7321)	-0.200 (± 0.4472)
Week 2 (1, 4, 4, 4, 3)	0.000 (± 999)	0.250 (± 0.5000)	1.000 (± 1.1547)	-0.250 (± 0.5000)
Week 4 (1, 3, 5, 4, 2)	0.000 (± 999)	0.000 (± 0.0000)	-0.800 (± 1.0954)	-0.250 (± 0.5000)
Week 8 (0, 3, 4, 2, 3)	999 (± 999)	0.333 (± 0.5774)	0.250 (± 0.5000)	0.000 (± 0.0000)
Week 12 (1, 3, 5, 2, 3)	0.000 (± 999)	0.000 (± 0.0000)	5.000 (± 11.1803)	0.000 (± 0.0000)

Week 16 (1, 5, 4, 5, 2)	0.000 (± 999)	0.000 (± 0.0000)	0.500 (± 1.0000)	0.000 (± 0.0000)
Week 20 (2, 4, 5, 6, 4)	0.000 (± 0.0000)	0.000 (± 0.0000)	-0.600 (± 0.8944)	1.500 (± 3.6742)
Week 24 (0, 4, 4, 7, 3)	999 (± 999)	0.000 (± 0.0000)	-0.250 (± 0.5000)	0.857 (± 2.2678)
Week 28 (1, 4, 5, 4, 3)	0.000 (± 999)	0.000 (± 0.0000)	-0.400 (± 0.8944)	0.000 (± 0.0000)
Week 32 (2, 3, 4, 6, 3)	0.000 (± 0.0000)	0.000 (± 0.0000)	1.250 (± 2.5000)	0.000 (± 0.0000)
Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 999)
Week 40 (0, 4, 4, 4, 2)	999 (± 999)	0.000 (± 0.0000)	-0.500 (± 1.0000)	0.000 (± 0.0000)
Week 44 (1, 5, 5, 4, 2)	0.000 (± 999)	0.400 (± 0.8944)	-0.400 (± 0.8944)	0.000 (± 0.0000)
Week 48 (2, 6, 4, 3, 4)	0.000 (± 0.0000)	1.167 (± 2.8577)	0.000 (± 0.0000)	0.000 (± 0.0000)

End point values	BKZ 320 mg (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: cells/LPF				
arithmetic mean (standard deviation)				
Week 1 (1, 4, 3, 5, 3)	0.000 (± 0.0000)			
Week 2 (1, 4, 4, 4, 3)	0.333 (± 0.5774)			
Week 4 (1, 3, 5, 4, 2)	0.000 (± 0.0000)			
Week 8 (0, 3, 4, 2, 3)	0.000 (± 0.0000)			
Week 12 (1, 3, 5, 2, 3)	0.000 (± 0.0000)			
Week 16 (1, 5, 4, 5, 2)	0.500 (± 0.7071)			
Week 20 (2, 4, 5, 6, 4)	-0.750 (± 1.5000)			
Week 24 (0, 4, 4, 7, 3)	0.333 (± 0.5774)			
Week 28 (1, 4, 5, 4, 3)	0.000 (± 0.0000)			
Week 32 (2, 3, 4, 6, 3)	13.333 (± 23.0940)			
Week 36 (1, 6, 4, 1, 1)	0.000 (± 999)			
Week 40 (0, 4, 4, 4, 2)	0.000 (± 0.0000)			
Week 44 (1, 5, 5, 4, 2)	0.000 (± 0.0000)			
Week 48 (2, 6, 4, 3, 4)	-0.250 (± 0.5000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in urinalysis parameters during the study (pH)

End point title	Changes from Baseline in urinalysis parameters during the study (pH)

End point description:

Urine pH was measured on a pH scale.
The SS consisted of all randomized study participants who received at least 1 dose of IMP.

Note: The number of participants analyzed for each timepoint is presented in parentheses following this model (PBO, BKZ 16 mg, BKZ 160 mg, BKZ 160 mg LD, BKZ 320 mg)

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44 and Week 48

End point values	Placebo (SS)	BKZ 16 mg (SS)	BKZ 160 mg (SS)	BKZ 160 mg LD (SS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	38	43	41
Units: pH				
arithmetic mean (standard deviation)				
Week 1 (40, 38, 43, 41, 40)	-0.138 (± 0.9198)	0.197 (± 0.5875)	0.023 (± 0.8014)	0.085 (± 0.6011)
Week 2 (42, 39, 43, 41, 41)	-0.155 (± 0.9072)	0.154 (± 0.7708)	-0.081 (± 0.7149)	0.134 (± 0.8293)
Week 4 (41, 38, 41, 40, 41)	-0.195 (± 0.9211)	0.026 (± 0.6571)	-0.134 (± 0.8368)	0.063 (± 0.6620)
Week 8 (41, 39, 42, 38, 41)	0.000 (± 0.7826)	0.077 (± 0.7393)	-0.024 (± 0.8762)	0.263 (± 0.7235)
Week 12 (40, 38, 43, 38, 41)	-0.100 (± 1.0203)	0.237 (± 0.7600)	-0.047 (± 0.6971)	0.211 (± 0.6641)
Week 16 (42, 38, 41, 38, 40)	-0.107 (± 0.8449)	0.092 (± 0.7957)	-0.122 (± 0.8199)	0.118 (± 0.7207)
Week 20 (40, 39, 42, 37, 40)	-0.113 (± 0.7884)	0.269 (± 0.8649)	-0.012 (± 0.8300)	-0.054 (± 0.6539)
Week 24 (39, 38, 41, 35, 39)	-0.154 (± 0.9400)	-0.013 (± 0.8011)	-0.085 (± 0.6605)	0.100 (± 0.4820)
Week 28 (39, 38, 41, 35, 40)	-0.090 (± 0.8419)	-0.053 (± 0.6657)	-0.122 (± 0.7313)	0.086 (± 0.6122)
Week 32 (39, 38, 40, 34, 39)	-0.218 (± 0.8335)	-0.079 (± 0.7491)	0.063 (± 0.8784)	-0.103 (± 0.6717)
Week 36 (38, 38, 41, 34, 39)	-0.211 (± 0.8353)	0.118 (± 0.7300)	-0.195 (± 0.8506)	-0.118 (± 0.6038)
Week 40 (37, 37, 40, 34, 39)	-0.216 (± 0.9394)	-0.041 (± 0.6388)	-0.188 (± 0.8525)	-0.191 (± 0.5643)
Week 44 (36, 38, 41, 33, 38)	-0.458 (± 0.7780)	-0.171 (± 0.7002)	-0.159 (± 0.9044)	-0.167 (± 0.6693)
Week 48 (38, 36, 40, 33, 40)	-0.092 (± 1.0771)	-0.014 (± 0.7318)	-0.200 (± 0.8533)	-0.015 (± 0.7855)

End point values	BKZ 320 mg (SS)			

Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: pH				
arithmetic mean (standard deviation)				
Week 1 (40, 38, 43, 41, 40)	0.000 (± 0.8321)			
Week 2 (42, 39, 43, 41, 41)	-0.012 (± 0.7541)			
Week 4 (41, 38, 41, 40, 41)	-0.098 (± 0.6729)			
Week 8 (41, 39, 42, 38, 41)	0.024 (± 0.7579)			
Week 12 (40, 38, 43, 38, 41)	0.073 (± 0.8843)			
Week 16 (42, 38, 41, 38, 40)	0.088 (± 0.7240)			
Week 20 (40, 39, 42, 37, 40)	0.063 (± 0.8929)			
Week 24 (39, 38, 41, 35, 39)	-0.026 (± 0.6973)			
Week 28 (39, 38, 41, 35, 40)	-0.088 (± 0.6783)			
Week 32 (39, 38, 40, 34, 39)	-0.269 (± 0.5718)			
Week 36 (38, 38, 41, 34, 39)	-0.077 (± 0.7569)			
Week 40 (37, 37, 40, 34, 39)	-0.154 (± 0.7448)			
Week 44 (36, 38, 41, 33, 38)	-0.171 (± 0.7285)			
Week 48 (38, 36, 40, 33, 40)	-0.100 (± 0.7528)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from Baseline until the Safety Follow-Up Visit (up to Week 68)

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 or BKZ 320 mg at Baseline were not re-randomized at Week 12 and remained on their treatment. The Safety Set is based on actual treatment, other populations are based on planned treatment. 160mg LD is considered 160mg.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo (SS) - up to Wk 12

Reporting group description:

This arm consisted of all participants who received Placebo at any time in the study (up to Week 12). Participants formed the Safety Set (SS).

Reporting group title	BKZ 320 mg (SS) - up to Wk 68

Reporting group description:

This arm consisted of all participants who received Bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) at any time in the study (up to Week 68). Participants formed the SS.

Reporting group title	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68

Reporting group description:

This arm consisted of all participants who received Bimekizumab (BKZ) 320 mg at Baseline followed by 160 mg every 4 weeks (Q4W) and Bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) at any time in the study (up to Week 68). Participants formed the SS.

Reporting group title	BKZ 16 mg (SS) - up to Wk 12

Reporting group description:

This arm consisted of all participants who received Bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS.

Serious adverse events	Placebo (SS) - up to Wk 12	BKZ 320 mg (SS) - up to Wk 68	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)	0 / 80 (0.00%)	8 / 126 (6.35%)
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)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 80 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			

subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BKZ 16 mg (SS) - up to Wk 12		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Osteoarthritis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media chronic			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis E			
subjects affected / exposed	0 / 39 (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	Placebo (SS) - up to Wk 12	BKZ 320 mg (SS) - up to Wk 68	BKZ 160 mg & 160 mg LD (SS) - up to Wk 68
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 42 (19.05%)	29 / 80 (36.25%)	40 / 126 (31.75%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 42 (9.52%)	2 / 80 (2.50%)	0 / 126 (0.00%)
occurrences (all)	4	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 42 (0.00%)	3 / 80 (3.75%)	0 / 126 (0.00%)
occurrences (all)	0	4	0

Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	3 / 42 (7.14%)	1 / 80 (1.25%)	2 / 126 (1.59%)
occurrences (all)	4	1	2
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	2 / 80 (2.50%)	8 / 126 (6.35%)
occurrences (all)	0	3	8
Bronchitis			
subjects affected / exposed	1 / 42 (2.38%)	3 / 80 (3.75%)	7 / 126 (5.56%)
occurrences (all)	1	3	8
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	11 / 80 (13.75%)	12 / 126 (9.52%)
occurrences (all)	0	11	15
Pharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	7 / 80 (8.75%)	4 / 126 (3.17%)
occurrences (all)	0	7	4
Upper respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	8 / 80 (10.00%)	12 / 126 (9.52%)
occurrences (all)	0	10	12

Non-serious adverse events	BKZ 16 mg (SS) - up to Wk 12		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 39 (23.08%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Psychiatric disorders			

Insomnia			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2018	Protocol Amendment 2 was a substantial amendment dated 09 Mar 2018. The purpose of this protocol amendment was the following: •To update the study contact details for the sponsor study physician and clinical trial biostatistician. •To revise the withdrawal criteria Section to provide instructions for the management of 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). A total of 308 study participants were screened and 206 study participants were randomized at the time of this amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Biomarker assays were not rigorously validated, thus it was not possible to use results for PD as a secondary objective. The results were interpreted with caution for exploratory purpose, and thus are not shared in this report.

Notes: