Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study Evaluating the Efficacy and Safety of Bimekizumab in Study Participants With Moderate to Severe Hidradenitis Suppurativa

Summary

EudraCT number	2019-002551-42
Trial protocol	DE IE FR GB HU CZ ES BG
Global end of trial date	28 September 2022

Results information

Result version number	v2 (current)
This version publication date	02 November 2023
First version publication date	13 October 2023
Version creation reason	• Correction of full data set Corrected the sequence of endpoints.

Trial information

Trial identification

Sponsor protocol code	HS0004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04242498
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2021
Global end of trial reached?	Yes
Global end of trial date	28 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of bimekizumab in study participants with moderate to severe Hidradenitis Suppurativa (HS)

Protection of trial subjects:

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

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	02 March 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Bulgaria: 61
Country: Number of subjects enrolled	Canada: 36
Country: Number of subjects enrolled	Czechia: 23
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Japan: 27
Country: Number of subjects enrolled	Poland: 124
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 113
Worldwide total number of subjects	509
EEA total number of subjects	321

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)	499
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in March 2020 and concluded in September 2022.

Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set (RS) and Maintenance Set (MS).

Period 1

Period 1 title	Initial Treatment Period: Week 0-16
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo during the 16-weeks Initial Treatment Period.

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

Dosage and administration details:

Participants received placebo at prespecified time points.

Arm title	BKZ Dosing Regimen 1

Arm description:

Participants received Bimekizumab (BKZ) dosing regimen 1 subcutaneously (SC) during the 16-weeks Initial Treatment 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:

Participants received BKZ dosing regimen 1 at prespecified time points.

Arm title	BKZ Dosing Regimen 2

Arm description:

Participants received BKZ dosing regimen 2 SC during the 16-weeks Initial Treatment 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:

Participants received BKZ dosing regimen 2 at prespecified time points.

Number of subjects in period 1	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2
Started	74	144	291
Completed	69	133	262
Not completed	5	11	29
Subject Moved Long Distance From Clinic (Abroad)	-	-	1
Adverse event, non-fatal	1	1	9
Consent withdrawn by subject, not due to AE	2	8	12
Lost to follow-up	1	-	3
Withdrawn by investigator's decision	-	-	1
Randomized, not treated	-	2	1
Protocol deviation	1	-	1
Lack of efficacy	-	-	1

Period 2

Period 2 title	Maintenance Treatment Period: Week 16-48
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/BKZ Dosing Regimen 2

Arm description:

After the 16-weeks Initial Treatment Period, participants initially randomized to placebo received BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

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:

Participants received BKZ dosing regimen 2 at prespecified time points.

Arm title	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1

Arm description:

After the 16-weeks Initial Treatment Period, participants initially randomized to BKZ dosing regimen 1 continued to receive BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

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:

Participants received BKZ dosing regimen 1 at prespecified time points.

Arm title	BKZ Dosing regimen 2/BKZ Dosing regimen 1

Arm description:

After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 received BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

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:

Participants received BKZ dosing regimen 1 at prespecified time points.

Arm title	BKZ Dosing regimen 2/BKZ Dosing regimen 2

Arm description:

After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 continued to receive BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

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:

Participants received BKZ dosing regimen 2 at prespecified time points.

Number of subjects in period 2[1]	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 1
Started	69	133	130
Completed	61	109	107
Not completed	8	24	23
Adverse event, non-fatal	-	7	6
Change In Address-Patient Not Wanting To Continue	-	1	-
Consent withdrawn by subject, not due to AE	6	9	10
Subject Relocated	-	-	1
Lost to follow-up	2	3	1
Visits Too Time-Consuming, Only Sfu Will Be Done	-	-	1
Lack of efficacy	-	4	2
Protocol deviation	-	-	2

Number of subjects in period 2[1]	BKZ Dosing regimen 2/BKZ Dosing regimen 2
Started	131
Completed	110
Not completed	21
Adverse event, non-fatal	4
Change In Address-Patient Not Wanting To Continue	-
Consent withdrawn by subject, not due to AE	11
Subject Relocated	1
Lost to follow-up	2
Visits Too Time-Consuming, Only Sfu Will Be Done	-
Lack of efficacy	2
Protocol deviation	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant completed the 16-Week Initial Treatment Period but did not enter the Maintenance Treatment Period because of the below reason: consent withdrawn by subject (not due to adverse event).

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo during the 16-weeks Initial Treatment Period.	
Reporting group title	BKZ Dosing Regimen 1
Reporting group description:	
Participants received Bimekizumab (BKZ) dosing regimen 1 subcutaneously (SC) during the 16-weeks Initial Treatment Period.	
Reporting group title	BKZ Dosing Regimen 2
Reporting group description:	
Participants received BKZ dosing regimen 2 SC during the 16-weeks Initial Treatment Period.	

Reporting group values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2
Number of subjects	74	144	291
Age Categorical Units: Participants			
<=18 years	0	7	10
Between 18 and 65 years	70	135	277
>=65 years	4	2	4
Age Continuous Units: Years			
arithmetic mean	38.1	35.2	36.9
standard deviation	± 13.2	± 11.9	± 12.3
Sex: Female, Male Units: Participants			
Female	31	77	150
Male	43	67	141

Reporting group values	Total		
Number of subjects	509		
Age Categorical Units: Participants			
<=18 years	17		
Between 18 and 65 years	482		
>=65 years	10		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	258		
Male	251		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo during the 16-weeks Initial Treatment Period.	
Reporting group title	BKZ Dosing Regimen 1
Reporting group description:	
Participants received Bimekizumab (BKZ) dosing regimen 1 subcutaneously (SC) during the 16-weeks Initial Treatment Period.	
Reporting group title	BKZ Dosing Regimen 2
Reporting group description:	
Participants received BKZ dosing regimen 2 SC during the 16-weeks Initial Treatment Period.	
Reporting group title	Placebo/BKZ Dosing Regimen 2
Reporting group description:	
After the 16-weeks Initial Treatment Period, participants initially randomized to placebo received BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).	
Reporting group title	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1
Reporting group description:	
After the 16-weeks Initial Treatment Period, participants initially randomized to BKZ dosing regimen 1 continued to receive BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).	
Reporting group title	BKZ Dosing regimen 2/BKZ Dosing regimen 1
Reporting group description:	
After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 received BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).	
Reporting group title	BKZ Dosing regimen 2/BKZ Dosing regimen 2
Reporting group description:	
After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 continued to receive BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).	

Primary: Percentage of participants achieving clinical response as measured by Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at Week 16

End point title	Percentage of participants achieving clinical response as measured by Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at Week 16
End point description:	
HiSCR50 was defined as at least a 50 percent (%) reduction from Baseline in the total abscess and inflammatory nodule (AN) count, with no increase from Baseline in abscess or draining tunnel count. Intermittent missing data are imputed using multiple imputation with Markov Chain Monte Carlo (MCMC) method followed by monotone regression for monotone missing data. Lesion counts are imputed and then dichotomized to obtain the response status. Participants who experienced an intercurrent event were treated as nonresponders following the intercurrent event. An intercurrent event was defined as receipt of systemic antibiotic rescue medication or discontinuation of study treatment due to an adverse event (AE) or lack of efficacy. Percentages of participants shown do not account for model effects using the logistic regression model. The RS consisted of all study participants randomized into the study.	
End point type	Primary
End point timeframe:	
Week 16	

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	144	291	
Units: percentage of participants				
number (confidence interval 95%)	32.2 (21.4 to 42.9)	53.8 (45.4 to 62.1)	52.0 (46.1 to 57.8)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.287
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.22
upper limit	4.291

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.422
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.221
upper limit	4.804

Secondary: Percentage of participants achieving clinical response as measured by Hidradenitis Suppurativa Clinical Response 75 (HiSCR75) at Week 16

End point title	Percentage of participants achieving clinical response as measured by Hidradenitis Suppurativa Clinical Response 75 (HiSCR75) at Week 16

End point description:

HiSCR75 was defined as at least a 75% reduction from Baseline in the total AN count, with no increase from Baseline in abscess or draining tunnel count. Intermittent missing data were imputed using multiple imputation with MCMC method followed by monotone regression for monotone missing data. Lesion counts were imputed and then dichotomized to obtain the response status. Participants who experienced an intercurrent event were treated as nonresponders following the intercurrent event. An intercurrent event was defined as receipt of systemic antibiotic rescue medication or discontinuation of study treatment due to an AE or lack of efficacy. Percentages of participants shown do not account for model effects using the logistic regression model. The RS consisted of all study participants randomized into the study.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	144	291	
Units: percentage of participants				
number (confidence interval 95%)	15.6 (7.2 to 24.0)	33.7 (25.7 to 41.7)	35.7 (30.1 to 41.3)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.007
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.374
upper limit	6.581

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.722
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.182
upper limit	6.267

Secondary: Percentage of participants with Flare by Week 16

End point title	Percentage of participants with Flare by Week 16

End point description:

Flare was defined as a greater than or equal to (>=) 25% increase in AN count with an absolute increase in AN count of >= 2 relative to Baseline. Intermittent missing data were imputed using multiple imputation with MCMC method followed by monotone regression for monotone missing data. Lesion counts were imputed and then dichotomized to obtain the response status. Participants who experienced an intercurrent event prior to experiencing a flare were treated as having experienced a flare at all flare assessments on and after the intercurrent event date. An intercurrent event was defined as receipt of systemic antibiotic rescue medication or discontinuation of study treatment due to an AE or lack of efficacy. Percentages of participants shown do not account for model effects using the logistic regression model. The RS consisted of all study participants randomized into the study.

End point type	Secondary

End point timeframe:

From Baseline to Week 16

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	144	291	
Units: percentage of participants				
number (confidence interval 95%)	28.0 (17.6 to 38.4)	23.6 (16.5 to 30.7)	28.8 (23.5 to 34.1)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.497
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.798
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.378
upper limit	1.683

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.868
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.541
upper limit	2.041

Secondary: Absolute change from Baseline in Dermatology Life Quality Index (DLQI) Total Score at Week 16

End point title	Absolute change from Baseline in Dermatology Life Quality Index (DLQI) Total Score at Week 16

End point description:

DLQI is patient-reported questionnaire designed for use in adult participants with skin diseases and HS. DLQI: skin disease-specific questionnaire aimed at evaluation of how symptoms and treatment affect patients' health related quality of life (HRQoL), with recall period of 7 days. This instrument asks participants 10 questions about symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Scoring of each answer for DLQI is on scale range of 0 (not at all) to 3(very much). DLQI total score was calculated by adding score of each question. Max score is 30, and min score is 0. Higher score, more quality of life is impaired. Those who experienced intercurrent event were treated as missing following intercurrent event and imputed using multiple imputation method for missing data. RS consisted of all study participants randomized into study. Mean values shown do not account for model effects using the analysis of covariance (ANCOVA) model.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	144	291	
Units: score on a scale				
arithmetic mean (standard error)	-3.2 (± 0.6)	-4.7 (± 0.5)	-4.6 (± 0.3)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.309
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.705
upper limit	-0.914

Notes:

[1] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.393
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.92
upper limit	-0.867

Notes:

[2] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

Secondary: Absolute change from Baseline in Worst Skin Pain score at Week 16

End point title	Absolute change from Baseline in Worst Skin Pain score at

	Week 16

End point description:

Absolute change from Baseline in worst Skin Pain score at Week 16 was assessed using worst skin pain item in Hidradenitis Suppurativa Symptom Daily Diary (HSSDD). Worst skin pain during past 24 hours was assessed daily using 11-point numeric rating scale ranges from 0 (no skin pain) to 10 (skin pain as bad as you can imagine). Worst skin pain score was derived from weekly average of daily scores, defined as sum of scored item over course of study week divided by number of days in which item completed, relative to each respective visit date. Intermittent missing data imputed using multiple imputation with MCMC method followed by monotone regression for monotone missing data. Those who experienced intercurrent event were treated as missing following intercurrent event and imputed using multiple imputation method for missing data. RS consisted of all study participants randomized into study. Mean values shown do not account for model effects using the ANCOVA model.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	144	291	
Units: score on a scale				
arithmetic mean (standard error)	-0.36 (± 0.30)	-1.44 (± 0.24)	-1.83 (± 0.17)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.265
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.978
upper limit	-0.552

Notes:

[3] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [4]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.898
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.684
upper limit	-0.113

Notes:

[4] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

Secondary: Percentage of participants achieving Skin Pain response at Week 16

End point title	Percentage of participants achieving Skin Pain response at Week 16

End point description:

Skin pain response at Week 16, as assessed by the "worst skin pain" item in the HSSDD, was defined as an improvement in the weekly worst skin pain score of at least 3 points versus Baseline. Intermittent missing data were imputed using multiple imputation with MCMC method followed by monotone regression for monotone missing data. Weekly pain scores were imputed and then dichotomized to obtain the response status. Participants who experienced an intercurrent event were treated as nonresponders following the intercurrent event. An intercurrent event was defined as receipt of systemic antibiotic rescue medication or discontinuation of study treatment due to an AE or lack of efficacy. The RS consisted of all study participants randomized into the study. Here, number of participants analyzed included RS with worst skin pain score >=3 at Baseline. Percentages of participants shown do not account for model effects using the logistic regression model.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	108	209	
Units: percentage of participants				
number (confidence interval 95%)	10.9 (1.7 to 20.1)	28.6 (19.5 to 37.8)	31.8 (25.1 to 38.4)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2

Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.756
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.189
upper limit	11.867

Notes:

[5] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028 [6]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.273
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.974
upper limit	10.997

Notes:

[6] - Nominal p-value only due to the testing hierarchy failing on the flare endpoint.

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

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

End point description:

An AE is 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 could 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. Treatment-emergent AEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week Safety Follow-Up [SFU] period). The Safety Set (SS) consisted of all study participants who received at least 1 dose (full or partial) of IMP. The MS consisted of all study participants who received at least 1 dose (full or partial) of BKZ in the Maintenance Treatment Period.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 71)

End point values	Placebo	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	69	142	133
Units: percentage of participants				
number (not applicable)	56.8	71.0	51.4	72.2

End point values	BKZ Dosing Regimen 2	BKZ Dosing regimen 2/BKZ Dosing regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	290	130	131	
Units: percentage of participants				
number (not applicable)	64.5	77.7	77.1	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: Results in death; Is life-threatening, Requires inpatient hospitalization or prolongation of existing hospitalization; Results in persistent disability/incapacity; Is a congenital anomaly/birth defect; Important medical events. Treatment-emergent AEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week SFU period). The SS consisted of all study participants who received at least 1 dose (full or partial) of IMP. The MS consisted of all study participants who received at least 1 dose (full or partial) of BKZ in the Maintenance Treatment Period.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 71)

End point values	Placebo	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	69	142	133
Units: percentage of participants				
number (not applicable)	0	2.9	2.1	3.0

End point values	BKZ Dosing Regimen 2	BKZ Dosing regimen 2/BKZ Dosing regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	290	130	131	
Units: percentage of participants				
number (not applicable)	3.1	2.3	3.1	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of IMP, whether or not considered related to the IMP. An AE could 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. Treatment-emergent AEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week SFU period). TEAEs leading to discontinuation of the study are reported. The SS consisted of all study participants who received at least 1 dose (full or partial) of IMP. The MS consisted of all study participants who received at least 1 dose (full or partial) of BKZ in the Maintenance Treatment Period.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 71)

End point values	Placebo	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	69	142	133
Units: percentage of participants				
number (not applicable)	0	0	2.1	4.5

End point values	BKZ Dosing Regimen 2	BKZ Dosing regimen 2/BKZ Dosing regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 2	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	290	130	131	
Units: percentage of participants				
number (not applicable)	4.1	3.1	1.5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) until Safety Follow-Up (up to Week 71)

Adverse event reporting additional description:

Treatment-emergent AEs are defined as those AEs that have a start date on or following the first dose of study treatment through the final dose of study treatment + 140 days (covering the 20-week SFU period). TEAEs were analyzed and reported for Initial Treatment Period (SS) and Maintenance Treatment Period (MS) separately.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo during the 16-weeks Initial Treatment Period.

Reporting group title	BKZ Dosing Regimen 1

Reporting group description:

Participants received Bimekizumab (BKZ) dosing regimen 1 subcutaneously (SC) during the 16-weeks Initial Treatment Period.

Reporting group title	BKZ Dosing Regimen 2

Reporting group description:

Participants received BKZ dosing regimen 2 SC during the 16-weeks Initial Treatment Period.

Reporting group title	Placebo/BKZ Dosing Regimen 2

Reporting group description:

After the 16-weeks Initial Treatment Period, participants initially randomized to placebo received BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

Reporting group title	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1

Reporting group description:

After the 16-weeks Initial Treatment Period, participants initially randomized to BKZ dosing regimen 1 continued to receive BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

Reporting group title	BKZ Dosing regimen 2/BKZ Dosing regimen 1

Reporting group description:

After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 received BKZ dosing regimen 1 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

Reporting group title	BKZ Dosing regimen 2/BKZ Dosing regimen 2

Reporting group description:

After the 16-week Initial Treatment Period, participants initially randomized to BKZ dosing regimen 2 continued to receive BKZ dosing regimen 2 SC during the 32-weeks Maintenance Treatment Period (up to Week 48).

Serious adverse events	Placebo	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 74 (0.00%)	3 / 142 (2.11%)	9 / 290 (3.10%)
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)			
Breast cancer			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 74 (0.00%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 74 (0.00%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphoedema			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy on contraceptive			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Colitis ulcerative			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
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			
Cholelithiasis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholecystitis acute			
subjects affected / exposed	0 / 74 (0.00%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hidradenitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	2 / 290 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	1 / 290 (0.34%)
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			
Appendicitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholinitis			

subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pustular			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 142 (0.00%)	0 / 290 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 1
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 69 (2.90%)	4 / 133 (3.01%)	3 / 130 (2.31%)
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)			
Breast cancer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphoedema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy on contraceptive			
subjects affected / exposed	0 / 69 (0.00%)	1 / 133 (0.75%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			

subjects affected / exposed	0 / 69 (0.00%)	1 / 133 (0.75%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 133 (0.00%)	0 / 130 (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
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 69 (0.00%)	1 / 133 (0.75%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hidradenitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 133 (0.75%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	1 / 130 (0.77%)
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			
Rhabdomyolysis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 133 (0.00%)	0 / 130 (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
Gastroenteritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholinitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pustular			
subjects affected / exposed	0 / 69 (0.00%)	0 / 133 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 133 (0.75%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BKZ Dosing regimen 2/BKZ Dosing regimen 2		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	4 / 131 (3.05%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy on contraceptive			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			

subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Irritable bowel syndrome			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fissure			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hidradenitis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bartholinitis			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash pustular			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Corona virus infection			
subjects affected / exposed	0 / 131 (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	BKZ Dosing Regimen 1	BKZ Dosing Regimen 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 74 (24.32%)	40 / 142 (28.17%)	101 / 290 (34.83%)
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 74 (9.46%)	7 / 142 (4.93%)	18 / 290 (6.21%)
occurrences (all)	9	9	21
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 74 (8.11%)	5 / 142 (3.52%)	18 / 290 (6.21%)
occurrences (all)	7	6	21
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	5 / 74 (6.76%)	13 / 142 (9.15%)	23 / 290 (7.93%)
occurrences (all)	6	15	27
Eczema			

subjects affected / exposed	1 / 74 (1.35%)	1 / 142 (0.70%)	9 / 290 (3.10%)
occurrences (all)	1	1	10
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 74 (0.00%)	5 / 142 (3.52%)	24 / 290 (8.28%)
occurrences (all)	0	5	26
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 74 (0.00%)	8 / 142 (5.63%)	1 / 290 (0.34%)
occurrences (all)	0	8	1
Nasopharyngitis			
subjects affected / exposed	0 / 74 (0.00%)	3 / 142 (2.11%)	11 / 290 (3.79%)
occurrences (all)	0	3	11
Folliculitis			
subjects affected / exposed	0 / 74 (0.00%)	5 / 142 (3.52%)	8 / 290 (2.76%)
occurrences (all)	0	5	9
Corona virus infection			
subjects affected / exposed	0 / 74 (0.00%)	3 / 142 (2.11%)	11 / 290 (3.79%)
occurrences (all)	0	3	11
Rhinitis			
subjects affected / exposed	1 / 74 (1.35%)	1 / 142 (0.70%)	0 / 290 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 74 (1.35%)	0 / 142 (0.00%)	5 / 290 (1.72%)
occurrences (all)	1	0	6

Non-serious adverse events	Placebo/BKZ Dosing Regimen 2	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 69 (37.68%)	49 / 133 (36.84%)	57 / 130 (43.85%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 69 (4.35%)	7 / 133 (5.26%)	4 / 130 (3.08%)
occurrences (all)	3	10	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 69 (2.90%)	6 / 133 (4.51%)	4 / 130 (3.08%)
occurrences (all)	3	8	5

Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	7 / 69 (10.14%)	16 / 133 (12.03%)	24 / 130 (18.46%)
occurrences (all)	11	19	33
Eczema			
subjects affected / exposed	4 / 69 (5.80%)	5 / 133 (3.76%)	5 / 130 (3.85%)
occurrences (all)	4	6	5
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	3 / 69 (4.35%)	11 / 133 (8.27%)	16 / 130 (12.31%)
occurrences (all)	3	13	18
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 69 (1.45%)	2 / 133 (1.50%)	3 / 130 (2.31%)
occurrences (all)	1	3	4
Nasopharyngitis			
subjects affected / exposed	2 / 69 (2.90%)	6 / 133 (4.51%)	8 / 130 (6.15%)
occurrences (all)	2	6	9
Folliculitis			
subjects affected / exposed	2 / 69 (2.90%)	5 / 133 (3.76%)	6 / 130 (4.62%)
occurrences (all)	2	8	6
Corona virus infection			
subjects affected / exposed	4 / 69 (5.80%)	2 / 133 (1.50%)	7 / 130 (5.38%)
occurrences (all)	4	2	7
Rhinitis			
subjects affected / exposed	1 / 69 (1.45%)	1 / 133 (0.75%)	2 / 130 (1.54%)
occurrences (all)	1	1	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 69 (5.80%)	7 / 133 (5.26%)	5 / 130 (3.85%)
occurrences (all)	4	7	6

Non-serious adverse events	BKZ Dosing regimen 2/BKZ Dosing regimen 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 131 (48.85%)		
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	7 / 131 (5.34%) 7		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 3 / 131 (2.29%) 3		
Skin and subcutaneous tissue disorders Hidradenitis subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all)	 15 / 131 (11.45%) 15 3 / 131 (2.29%) 3		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) Vulvovaginal candidiasis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Folliculitis subjects affected / exposed occurrences (all) Corona virus infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 14 / 131 (10.69%) 17 3 / 131 (2.29%) 3 11 / 131 (8.40%) 15 9 / 131 (6.87%) 11 8 / 131 (6.11%) 8 7 / 131 (5.34%) 7 3 / 131 (2.29%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2021	Protocol Amendment 3 was dated 09 Feb 2021, and approximately 300 study participants were enrolled at the time of the amendment. The purpose of this substantial amendment was to update the protocol based on Regulatory Agency feedback and provide procedural clarifications. Key changes included the following: • Order of secondary efficacy endpoints was aligned for closed testing procedure • Removal of 30% cap on enrollment for the Baseline antibiotic therapy strata • Aligned the final Independent Data Monitoring Committee (DMC) Charter and the DMC Statistical Analysis Plan (SAP) for the planned unblinded futility analysis for the DMC • Update and clarifications to Schedule of Activities, inclusion criteria, exclusion criteria, and severe acute respiratory syndrome. Necessary protocol revisions due to the coronavirus disease 2019 (COVID-19) pandemic • Removal of depression as a safety topic of interest while maintaining collection of data to monitor for this potential effect • Added lesion care section and updated wound care section • Clarified and updated prohibited medications and associated washout periods • Addition of specific infection-related Investigational Medicinal Product (IMP) interruption criterion.
06 May 2022	Protocol Amendment 4 was dated 06 May 2022, and all study participants were enrolled at the time of the amendment. The purpose of this substantial amendment was to align with Food and Drug Administration (FDA) recommendations. It was recommended that a threshold for within patient clinically meaningful change to define treatment success be used in order to establish efficacy for skin pain in Phase 3 studies of patients with moderate to severe HS. The Sponsor conducted analyses to determine the threshold for within-patient clinically meaningful change that was applied in the final analysis for a responder definition based on the Hidradenitis Suppurativa Symptom Daily Diary (HSSDD) worst skin pain item score using established guidelines and analytical methods. Pain response status at Week 16 using this definition was added as a secondary endpoint to the study. This change also resulted in an addition to the sample size section, including assumptions on response rates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	Pause in recruitment due to Covid-19 pandemic.	02 June 2020

Notes:

Limitations and caveats

None reported