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	2019-002550-23
Trial protocol	DE GR BE NL DK ES IT
Global end of trial date	19 February 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	HS0003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04242446
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	10 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 April 2022
Global end of trial reached?	Yes
Global end of trial date	19 February 2023
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	19 February 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: 22
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Greece: 45
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Türkiye: 17
Country: Number of subjects enrolled	United States: 206
Worldwide total number of subjects	505
EEA total number of subjects	223

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)	497
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in February 2020 and concluded in February 2023.

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	72	144	289
Completed	65	127	259
Not completed	7	17	30
Adverse event, non-fatal	1	5	7
Consent withdrawn by subject, not due to AE	4	6	14
Withdrawn based to Exclusion Criterion	-	-	1
Lost to follow-up	1	3	2
Per Sponsors Request Due To Covid 19 Pandemic	-	-	1
Randomized, not treated	-	1	3
Country Relocation	1	-	-
Protocol deviation	-	2	2

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	65	125	129
Completed	44	87	104
Not completed	21	38	25
Relocation	-	1	-
Sponsor's Decision	-	-	-
Subject Withdrew Due To Custody Issue & Relocation	-	1	-
Study Schedule Too Demanding, Clashing With Work	-	1	-
Consent withdrawn by subject, not due to AE	7	12	11
Patient Relocated And Withdrew Consent	-	1	-
Patient Relocated Last Minute Decision	-	-	1
Subject Moved A Long Distance From Clinic	-	1	-
Subject Is Moving A Long Distance From Clinic	1	-	-
Patient Move Away	-	-	1
Adverse event, non-fatal	9	7	5
Needs Systemic Therapy Incompatible With Protocol	-	-	-
Lost to follow-up	2	5	3
Develop Illness Would Interfere With Participation	-	-	-
Lack of efficacy	1	7	3
Protocol deviation	1	2	1

Number of subjects in period 2[1]	BKZ Dosing regimen 2/BKZ Dosing regimen 2
Started	129
Completed	98
Not completed	31
Relocation	-
Sponsor's Decision	1
Subject Withdrew Due To Custody Issue & Relocation	-
Study Schedule Too Demanding, Clashing With Work	-
Consent withdrawn by subject, not due to AE	14
Patient Relocated And Withdrew Consent	-
Patient Relocated Last Minute Decision	-
Subject Moved A Long Distance From Clinic	-
Subject Is Moving A Long Distance From Clinic	-

Patient Move Away	-
Adverse event, non-fatal	6
Needs Systemic Therapy Incompatible With Protocol	1
Lost to follow-up	3
Develop Illness Would Interfere With Participation	1
Lack of efficacy	3
Protocol deviation	2

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: 2 participants completed the 16-Week Initial Treatment Period but did not enter the Maintenance Treatment Period because of the reason: Adverse event and Consent withdrawn by subject (not due to adverse event) of BKZ Dosing Regimen 1/BKZ Dosing Regimen 1 arm. 1 participant completed the 16-Week Initial Treatment Period but did not enter the Maintenance Treatment Period because of the reason: Protocol violation of BKZ Dosing regimen 2/BKZ Dosing regimen 1 arm.

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	72	144	289
Age Categorical Units: Participants			
18 years - <65 years	71	143	283
65 years - <85 years	1	1	6
Age Continuous Units: Years			
arithmetic mean	36.4	36.3	36.9
standard deviation	± 12.4	± 11.2	± 12.4
Sex: Female, Male Units: Participants			
Female	44	98	176
Male	28	46	113

Reporting group values	Total		
Number of subjects	505		
Age Categorical Units: Participants			
18 years - <65 years	497		
65 years - <85 years	8		
Age Continuous Units: Years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Participants			
Female	318		
Male	187		

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 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 adverse event (AE) or lack of efficacy. Percentage of participants shown do not account for model effects using the logistic regression model. The RS consisted of all 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	72	144	289	
Units: percentage of participants				
number (confidence interval 95%)	28.7 (18.1 to 39.3)	45.3 (36.8 to 53.8)	47.8 (41.8 to 53.7)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.979
upper limit	4.089

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.234
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.159
upper limit	4.307

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. Percentage of participants shown do not account for model effects using the logistic regression model. The RS consisted of all 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	72	144	289	
Units: percentage of participants				
number (confidence interval 95%)	18.4 (9.3 to 27.5)	24.7 (17.3 to 32.1)	33.4 (27.8 to 39.1)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.175
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.021
upper limit	4.635

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

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.416
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.615
upper limit	3.26

Notes:

[1] - Nominal p-value only due to the testing hierarchy failing on the HISCR50 outcome.

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	72	144	289	
Units: score on a scale				
arithmetic mean (standard error)	-2.7 (± 0.9)	-5.5 (± 0.6)	-5.0 (± 0.4)	

Statistical analyses

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

Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.682
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.394
upper limit	-0.97

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [2]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.574
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.472
upper limit	-0.675

Notes:

[2] - Nominal p-value only due to the testing hierarchy failing on the HISCR50 outcome.

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	72	144	289	
Units: score on a scale				
arithmetic mean (standard error)	-0.99 (± 0.38)	-1.56 (± 0.26)	-2.00 (± 0.17)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.201 [3]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.551
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.521
upper limit	0.418

Notes:

[3] - Nominal p-value only due to the testing hierarchy failing on the HISCR50 outcome.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.186
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.05
upper limit	-0.322

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

End point title	Percentage of participants achieving Worst 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. Percentage 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	46	103	190	
Units: percentage of participants				
number (confidence interval 95%)	15.0 (3.6 to 26.5)	22.1 (12.7 to 31.4)	32.3 (25.1 to 39.5)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BKZ Dosing Regimen 1
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.618
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.489
upper limit	5.352

Notes:

[4] - Nominal p-value only due to the testing hierarchy failing on the HISCR50 outcome.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v BKZ Dosing Regimen 2
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.757

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.909
upper limit	8.364

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. TEAEs are defined as 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	72	65	143	125
Units: percentage of participants				
number (not applicable)	66.7	81.5	65.7	76.0

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	286	129	129	
Units: percentage of participants				
number (not applicable)	67.1	79.1	81.4	

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. TEAEs are defined as 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	72	65	143	125
Units: percentage of participants				
number (not applicable)	0	9.2	2.8	8.0

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	286	129	129	
Units: percentage of participants				
number (not applicable)	2.1	5.4	7.8	

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. TEAEs are defined as 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. TEAEs leading to discontinuation of the study are reported.

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	72	65	143	125
Units: percentage of participants				
number (not applicable)	1.4	13.8	4.2	4.8

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	286	129	129	
Units: percentage of participants				
number (not applicable)	3.5	1.6	4.7	

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:

TEAEs are defined as 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	BKZ Dosing Regimen 2

Reporting group description:

Participants received BKZ dosing regimen 2 SC 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	Placebo

Reporting group description:

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

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 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 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).

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).

Serious adverse events	BKZ Dosing Regimen 2	BKZ Dosing Regimen 1	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 286 (2.10%)	4 / 143 (2.80%)	0 / 72 (0.00%)
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)			
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Thrombophlebitis superficial			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 286 (0.00%)	1 / 143 (0.70%)	0 / 72 (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
Pregnancy, puerperium and perinatal conditions			
Pregnancy on contraceptive			
subjects affected / exposed	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (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
Abortion spontaneous			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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			
Genital erythema			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Psychiatric disorders			

Suicidal ideation			
subjects affected / exposed	0 / 286 (0.00%)	1 / 143 (0.70%)	0 / 72 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Road traffic accident			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Laceration			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Acute coronary syndrome			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Atrial fibrillation			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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

Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 286 (0.00%)	1 / 143 (0.70%)	0 / 72 (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
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 286 (0.00%)	1 / 143 (0.70%)	0 / 72 (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
Colitis ulcerative			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Aphthous ulcer			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (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
Drug-induced liver injury			

subjects affected / exposed	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (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
Intertrigo			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Diabetic foot			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Diabetic ulcer			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Ureterolithiasis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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			
Cellulitis			
subjects affected / exposed	1 / 286 (0.35%)	0 / 143 (0.00%)	0 / 72 (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

Peritonitis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Genital candidiasis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Tooth abscess			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Groin infection			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Bronchitis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Sepsis			
subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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
Wound infection staphylococcal			

subjects affected / exposed	0 / 286 (0.00%)	0 / 143 (0.00%)	0 / 72 (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	BKZ Dosing regimen 2/BKZ Dosing regimen 1	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 2
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 129 (5.43%)	10 / 125 (8.00%)	10 / 129 (7.75%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Abortion spontaneous			

subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (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			
Genital erythema			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Road traffic accident			
subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (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
Laceration			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Cardiac failure congestive			

subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute coronary syndrome			
subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (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
Atrial fibrillation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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			
Small intestinal obstruction			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Colitis ulcerative			

subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphthous ulcer			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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			
Hidradenitis			
subjects affected / exposed	0 / 129 (0.00%)	3 / 125 (2.40%)	2 / 129 (1.55%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intertrigo			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Diabetic foot			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ulcer			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 125 (0.80%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	0 / 129 (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
Genital candidiasis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 125 (0.80%)	0 / 129 (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
Tooth abscess			
subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin infection			

subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (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
Sepsis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 125 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	1 / 129 (0.78%)	0 / 125 (0.00%)	0 / 129 (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

Serious adverse events	Placebo/BKZ Dosing Regimen 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 65 (9.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis superficial			

subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy on contraceptive			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Genital erythema			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			

subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laceration			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Eye disorders			
Keratitis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aphthous ulcer			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intertrigo			

subjects affected / exposed	0 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				
subjects affected / exposed	0 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ulcer				
subjects affected / exposed	0 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrolithiasis				
subjects affected / exposed	0 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 65 (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 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 65 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
subjects affected / exposed	1 / 65 (1.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Genital candidiasis				

subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Groin infection			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection staphylococcal			
subjects affected / exposed	0 / 65 (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	BKZ Dosing Regimen 2	BKZ Dosing Regimen 1	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 286 (32.87%)	52 / 143 (36.36%)	23 / 72 (31.94%)
Investigations			
Psychiatric evaluation abnormal			
subjects affected / exposed	2 / 286 (0.70%)	7 / 143 (4.90%)	2 / 72 (2.78%)
occurrences (all)	2	7	2
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 286 (7.69%)	8 / 143 (5.59%)	3 / 72 (4.17%)
occurrences (all)	27	14	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 286 (6.29%)	12 / 143 (8.39%)	1 / 72 (1.39%)
occurrences (all)	21	14	1
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	18 / 286 (6.29%)	12 / 143 (8.39%)	10 / 72 (13.89%)
occurrences (all)	21	15	11
Eczema			
subjects affected / exposed	5 / 286 (1.75%)	3 / 143 (2.10%)	1 / 72 (1.39%)
occurrences (all)	5	3	1
Seborrhoeic dermatitis			
subjects affected / exposed	6 / 286 (2.10%)	4 / 143 (2.80%)	0 / 72 (0.00%)
occurrences (all)	6	4	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 286 (2.45%)	0 / 143 (0.00%)	6 / 72 (8.33%)
occurrences (all)	7	0	6
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	17 / 286 (5.94%)	2 / 143 (1.40%)	0 / 72 (0.00%)
occurrences (all)	18	2	0
Corona virus infection			
subjects affected / exposed	9 / 286 (3.15%)	2 / 143 (1.40%)	2 / 72 (2.78%)
occurrences (all)	9	2	2
Fungal skin infection			

subjects affected / exposed	2 / 286 (0.70%)	3 / 143 (2.10%)	1 / 72 (1.39%)
occurrences (all)	2	3	1
Influenza			
subjects affected / exposed	3 / 286 (1.05%)	0 / 143 (0.00%)	2 / 72 (2.78%)
occurrences (all)	3	0	2
Nasopharyngitis			
subjects affected / exposed	12 / 286 (4.20%)	7 / 143 (4.90%)	3 / 72 (4.17%)
occurrences (all)	14	10	5
Upper respiratory tract infection			
subjects affected / exposed	4 / 286 (1.40%)	0 / 143 (0.00%)	0 / 72 (0.00%)
occurrences (all)	4	0	0
Urinary tract infection			
subjects affected / exposed	4 / 286 (1.40%)	4 / 143 (2.80%)	1 / 72 (1.39%)
occurrences (all)	4	4	1

Non-serious adverse events	BKZ Dosing regimen 2/BKZ Dosing regimen 1	BKZ Dosing Regimen 1/BKZ Dosing Regimen 1	BKZ Dosing regimen 2/BKZ Dosing regimen 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 129 (53.49%)	63 / 125 (50.40%)	63 / 129 (48.84%)
Investigations			
Psychiatric evaluation abnormal			
subjects affected / exposed	2 / 129 (1.55%)	4 / 125 (3.20%)	1 / 129 (0.78%)
occurrences (all)	2	4	1
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 129 (6.20%)	4 / 125 (3.20%)	5 / 129 (3.88%)
occurrences (all)	8	9	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 129 (3.88%)	6 / 125 (4.80%)	6 / 129 (4.65%)
occurrences (all)	6	7	9
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	19 / 129 (14.73%)	27 / 125 (21.60%)	17 / 129 (13.18%)
occurrences (all)	25	38	32
Eczema			

subjects affected / exposed	5 / 129 (3.88%)	7 / 125 (5.60%)	7 / 129 (5.43%)
occurrences (all)	5	7	7
Seborrhoeic dermatitis			
subjects affected / exposed	7 / 129 (5.43%)	3 / 125 (2.40%)	1 / 129 (0.78%)
occurrences (all)	7	3	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 129 (0.78%)	4 / 125 (3.20%)	2 / 129 (1.55%)
occurrences (all)	1	4	2
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	10 / 129 (7.75%)	11 / 125 (8.80%)	11 / 129 (8.53%)
occurrences (all)	13	12	17
Corona virus infection			
subjects affected / exposed	19 / 129 (14.73%)	14 / 125 (11.20%)	18 / 129 (13.95%)
occurrences (all)	20	14	18
Fungal skin infection			
subjects affected / exposed	7 / 129 (5.43%)	3 / 125 (2.40%)	4 / 129 (3.10%)
occurrences (all)	7	3	5
Influenza			
subjects affected / exposed	2 / 129 (1.55%)	2 / 125 (1.60%)	2 / 129 (1.55%)
occurrences (all)	3	2	2
Nasopharyngitis			
subjects affected / exposed	10 / 129 (7.75%)	6 / 125 (4.80%)	4 / 129 (3.10%)
occurrences (all)	12	6	4
Upper respiratory tract infection			
subjects affected / exposed	7 / 129 (5.43%)	7 / 125 (5.60%)	7 / 129 (5.43%)
occurrences (all)	8	8	10
Urinary tract infection			
subjects affected / exposed	9 / 129 (6.98%)	3 / 125 (2.40%)	8 / 129 (6.20%)
occurrences (all)	9	3	8

Non-serious adverse events	Placebo/BKZ Dosing Regimen 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 65 (58.46%)		

Investigations Psychiatric evaluation abnormal subjects affected / exposed occurrences (all)	 4 / 65 (6.15%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 5 / 65 (7.69%) 5		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 6 / 65 (9.23%) 7		
Skin and subcutaneous tissue disorders Hidradenitis subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	 11 / 65 (16.92%) 13 2 / 65 (3.08%) 2 3 / 65 (4.62%) 4		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 0 / 65 (0.00%) 0		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) Corona virus infection subjects affected / exposed occurrences (all) Fungal skin infection subjects affected / exposed occurrences (all) Influenza	 3 / 65 (4.62%) 4 9 / 65 (13.85%) 9 2 / 65 (3.08%) 2		

subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	7		
Upper respiratory tract infection			
subjects affected / exposed	2 / 65 (3.08%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2021	Protocol Amendment 3 was dated 03 Feb 2021, and approximately 162 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 IMP interruption criterion.
09 May 2022	Protocol Amendment 4 was dated 09 May 2022, and all 505 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.
27 September 2022	Protocol Amendment 5 was dated 27 Sep 2022, and all 505 study participants were enrolled at the time of the amendment. The purpose of this substantial amendment was to remove the flare (secondary) endpoint from the statistical testing procedure. The rationale for the amendment was the lack of unanimous consensus on the definition of HS flare, including the flare definition used in previous and ongoing clinical studies (outside of and independent of HS0003), the continued lack of published validation studies of a flare endpoint, and inconsistent data on the flare endpoint observed both within the bimekizumab program and in recently published data from another experimental HS treatment. (Kimball et al, 2022). Flare was included as an "Other" endpoint in the study.

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