Clinical trial results:
A Phase 2b Pivotal Study to Evaluate the Efficacy and Safety of Izokibep in Subjects with Moderate to Severe Hidradenitis Suppurativa

Summary

EudraCT number	2021-005713-13
Trial protocol	DE ES HU
Global end of trial date	21 February 2024

Results information

Result version number	v1 (current)
This version publication date	09 March 2025
First version publication date	09 March 2025

Trial information

Trial identification

Sponsor protocol code	21102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05355805
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ACELYRIN
Sponsor organisation address	4149 Liberty Canyon Rd, Agoura Hills, United States, 91301
Public contact	Clinical Trial Information Desk, ACELYRIN, INC., +1 805-456-4393, clinicaltrials@acelyrin.com
Scientific contact	Clinical Trial Information Desk, ACELYRIN, INC., +1 805-456-4393, clinicaltrials@acelyrin.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	21 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study were, to explore the efficacy of izokibep as measured by Hidradenitis Suppurativa
Clinical Response 75 (HiSCR75) at Week 12, and to demonstrate that one or both treatment regimens of izokibep was efficacious compared to placebo, as measured by HiSCR75 at Week 16.

Protection of trial subjects:

This study was conducted in compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) (CPMP/ICH/135/95), the Declaration of Helsinki, and other applicable local regulations; documents were retained per ICH GCP, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 May 2022
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	Poland: 44
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	United States: 90
Worldwide total number of subjects	205
EEA total number of subjects	97

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)	202
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at different centers in the United States, Canada, Germany, Hungary, Poland, and Spain, and participated from May 2022 to February 2024.

Pre-assignment

Screening details:

Part A was a single-arm, open-label, proof-of-concept investigation to explore preliminary efficacy and safety of izokibep. Part B was a randomized, double-blind, placebo-controlled, parallel-group, dose-finding investigation to evaluate the efficacy, safety, and immunogenicity of izokibep.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study was characterized by an open-label, non-randomized design for the Part A arm, while the Part B arms followed a double-blinded (participants, investigators, and sponsor), randomized design.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Izokibep 160 mg QW

Arm description:

Participants with moderate to severe Hidradenitis Suppurativa (HS) received open label izokibep 160 mg by subcutaneous (SC) injection once every week (QW) in Part A for up to 31 weeks.

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

Dosage and administration details:

Participants received izokibep 160 mg QW for 31 weeks.

Arm title	Part B Placebo/Izokibep QW/Q2W

Arm description:

Participants with moderate to severe HS received placebo by SC injection either QW or every 2 weeks (Q2W) up to 16 weeks. After Week 16, participants who received placebo QW switched to izokibep QW through Week 31. Participants who received placebo Q2W switched to izokibep Q2W through Week 30.

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 either Placebo QW for 16 weeks followed by Izokibep 160 mg QW for 16 weeks, or Placebo Q2W for 15 weeks followed by Izokibep 160 mg Q2W for 14 weeks.

Investigational medicinal product name	Izokibep
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who received Placebo QW for 16 weeks switched to izokibep 160 mg QW for an additional 15 weeks. Participants who received Placebo Q2W for 16 weeks switched to izokibep 160 mg Q2W for an additional 14 weeks.

Arm title	Part B Izokibep 160 mg QW

Arm description:

Participants with moderate to severe HS received izokibep 160 mg QW by SC injection for 31 weeks.

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

Dosage and administration details:

Participants received izokibep 160 mg QW for 31 weeks.

Arm title	Part B Izokibep 160 mg Q2W

Arm description:

Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection for 30 weeks.

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

Dosage and administration details:

Participants received izokibep 160 mg Q2W for 30 weeks.

Number of subjects in period 1	Part A Izokibep 160 mg QW	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW
Started	30	59	57
Switched to Izokibep 160 mg QW	0 [1]	24 [2]	0 [3]
Switched to Izokibep 160 mg Q2W	0 [4]	24 [5]	0 [6]
Completed	17	34	31
Not completed	13	25	26
Consent withdrawn by subject	7	14	15
Decision by Sponsor	-	-	1
Lost to follow-up	6	11	10

Number of subjects in period 1	Part B Izokibep 160 mg Q2W
Started	59
Switched to Izokibep 160 mg QW	0 [7]
Switched to Izokibep 160 mg Q2W	0 [8]

Completed	40
Not completed	19
Consent withdrawn by subject	13
Decision by Sponsor	-
Lost to follow-up	6

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg QW.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Indicates the number of participants that moved from placebo QW or Q2W to izokibep QW or Q2W.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg QW.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg QW.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Indicates the number of participants that moved from placebo QW or Q2W to izokibep QW or Q2W.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg QW.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg Q2W.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants only received izokibep 160mg Q2W.

Baseline characteristics

Reporting groups	
Reporting group title	Part A Izokibep 160 mg QW
Reporting group description:	
Participants with moderate to severe Hidradenitis Suppurativa (HS) received open label izokibep 160 mg by subcutaneous (SC) injection once every week (QW) in Part A for up to 31 weeks.	
Reporting group title	Part B Placebo/Izokibep QW/Q2W
Reporting group description:	
Participants with moderate to severe HS received placebo by SC injection either QW or every 2 weeks (Q2W) up to 16 weeks. After Week 16, participants who received placebo QW switched to izokibep QW through Week 31. Participants who received placebo Q2W switched to izokibep Q2W through Week 30.	
Reporting group title	Part B Izokibep 160 mg QW
Reporting group description:	
Participants with moderate to severe HS received izokibep 160 mg QW by SC injection for 31 weeks.	
Reporting group title	Part B Izokibep 160 mg Q2W
Reporting group description:	
Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection for 30 weeks.	

Reporting group values	Part A Izokibep 160 mg QW	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW
Number of subjects	30	59	57
Age categorical Units: Subjects			
Age continuous Units: years			
median	38.3	37.2	53.3
standard deviation	± 9.68	± 11.45	± 11.66
Gender categorical Units: Subjects			
Female	21	40	39
Male	9	19	18
Ethnicity Units: Subjects			
Hispanic or Latino	4	9	11
Not Hispanic or Latino	26	50	46
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	0	1	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	14	9	7
White	16	47	45
More than one race	0	2	1
Unknown or Not Reported	0	0	0

Abscess Count			
Units: Abcesses			
arithmetic mean	1.75	1.8	1.9
standard deviation	± 2.18	± 2.10	± 3.57
Inflammatory Nodule Count			
Units: Nodules			
arithmetic mean	8.8	7.5	10.0
standard deviation	± 7.20	± 5.10	± 8.45
Draining Fistula Count			
Units: Fistulas			
arithmetic mean	1.75	3.5	3.0
standard deviation	± 2.35	± 5.18	± 3.97
Abscess and Inflammatory Nodule (AN) Count			
Units: Total Abcess/ Nodules			
arithmetic mean	10.5	9.3	11.9
standard deviation	± 7.64	± 5.24	± 9.50

Reporting group values	Part B Izokibep 160 mg Q2W	Total	
Number of subjects	59	205	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median	40.3		
standard deviation	± 10.04	-	
Gender categorical			
Units: Subjects			
Female	36	136	
Male	23	69	
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	31	
Not Hispanic or Latino	52	174	
Unknown or Not Reported	0	0	
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	6	36	
White	51	159	
More than one race	2	5	
Unknown or Not Reported	0	0	
Abscess Count			
Units: Abcesses			
arithmetic mean	1.9		
standard deviation	± 4.86	-	
Inflammatory Nodule Count			
Units: Nodules			

arithmetic mean	7.9		
standard deviation	± 4.21	-	
Draining Fistula Count			
Units: Fistulas			
arithmetic mean	2.6		
standard deviation	± 3.38	-	
Abscess and Inflammatory Nodule (AN) Count			
Units: Total Abcess/ Nodules			
arithmetic mean	9.9		
standard deviation	± 6.85	-	

Subject analysis sets

Subject analysis set title	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received izokibep QW in a blinded manner for weeks 16-31.	
Subject analysis set title	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received izokibep Q2W in a blinded manner for weeks 16-30.	
Subject analysis set title	Part B: Izokibep 160 mg QW (Week 16 to 31)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with moderate to severe HS received izokibep 160 mg QW by SC injection during weeks 16-31.	
Subject analysis set title	Part B: Izokibep 160 mg Q2W (Week 16 to 30)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection during weeks 16-30.	

Reporting group values	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)	Part B: Izokibep 160 mg QW (Week 16 to 31)
Number of subjects	24	24	42
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median			
standard deviation	±	±	±
Gender categorical			
Units: Subjects			
Female			
Male			
Ethnicity			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			

Unknown or Not Reported			
Race Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Abscess Count Units: Abcesses			
arithmetic mean	1.7	1.8	1.9
standard deviation	± 2.18	± 2.10	± 3.57
Inflammatory Nodule Count Units: Nodules			
arithmetic mean			
standard deviation	±	±	±
Draining Fistula Count Units: Fistulas			
arithmetic mean			
standard deviation	±	±	±
Abscess and Inflammatory Nodule (AN) Count Units: Total Abcess/ Nodules			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Part B: Izokibep 160 mg Q2W (Week 16 to 30)		
Number of subjects	53		
Age categorical Units: Subjects			
Age continuous Units: years			
median			
standard deviation	±		
Gender categorical Units: Subjects			
Female Male			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Race Units: Subjects			
American Indian or Alaska Native Asian			

Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Abscess Count Units: Abcesses arithmetic mean standard deviation	 1.9 ± 4.86		
Inflammatory Nodule Count Units: Nodules arithmetic mean standard deviation	 ±		
Draining Fistula Count Units: Fistulas arithmetic mean standard deviation	 ±		
Abscess and Inflammatory Nodule (AN) Count Units: Total Abcess/ Nodules arithmetic mean standard deviation	 ±		

End points

End points reporting groups

Reporting group title	Part A Izokibep 160 mg QW
Reporting group description:	
Participants with moderate to severe Hidradenitis Suppurativa (HS) received open label izokibep 160 mg by subcutaneous (SC) injection once every week (QW) in Part A for up to 31 weeks.	
Reporting group title	Part B Placebo/Izokibep QW/Q2W
Reporting group description:	
Participants with moderate to severe HS received placebo by SC injection either QW or every 2 weeks (Q2W) up to 16 weeks. After Week 16, participants who received placebo QW switched to izokibep QW through Week 31. Participants who received placebo Q2W switched to izokibep Q2W through Week 30.	
Reporting group title	Part B Izokibep 160 mg QW
Reporting group description:	
Participants with moderate to severe HS received izokibep 160 mg QW by SC injection for 31 weeks.	
Reporting group title	Part B Izokibep 160 mg Q2W
Reporting group description:	
Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection for 30 weeks.	
Subject analysis set title	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received izokibep QW in a blinded manner for weeks 16-31.	
Subject analysis set title	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received izokibep Q2W in a blinded manner for weeks 16-30.	
Subject analysis set title	Part B: Izokibep 160 mg QW (Week 16 to 31)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with moderate to severe HS received izokibep 160 mg QW by SC injection during weeks 16-31.	
Subject analysis set title	Part B: Izokibep 160 mg Q2W (Week 16 to 30)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection during weeks 16-30.	

Primary: Part A: Percentage of Participants Who Achieved HiSCR75 at Week 12

End point title	Part A: Percentage of Participants Who Achieved HiSCR75 at Week 12[1][2]
End point description:	
HiSCR75 was defined as at least a 75% reduction from baseline in the total abscess and inflammatory nodule count, with no increase from baseline in abscess or draining fistula count. Full analysis set (FAS), Part A: all participants who received at lease one dose of study drug in Part A.	
End point type	Primary
End point timeframe:	
Part A: Baseline and Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No additional statistical analysis was pre-specified for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part A Izokibep 160 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)	40			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Percentage of Participants Who Achieved HiSCR75 at Week 16

End point title	Part B: Percentage of Participants Who Achieved HiSCR75 at Week 16[3]

End point description:

HiSCR75 was defined as at least a 75% reduction from baseline in the total abscess and inflammatory nodule count, with no increase from baseline in abscess or draining fistula count. FAS, Part B: all participants randomized in Part B.

End point type	Primary

End point timeframe:

Part B: Baseline to Week 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Percentage of participants				
number (not applicable)	27.1	36.8	32.2	

Statistical analyses

Statistical analysis title	Participants Who Achieved HiSCR75 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/Janus Kinase (JAK) inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error was estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting. Non-response imputation was used for participants with missing HiSCR75.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg QW

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.148 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - Risk Difference (RD) = -13.6
Standard Error of the Mean = 0.093
[5] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants Who Achieved HiSCR75 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error was estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR75.

Comparison groups	Part B Izokibep 160 mg Q2W v Part B Placebo/Izokibep QW/Q2W
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.7556 [7]
Method	Cochran-Mantel-Haenszel
Variability estimate	Standard error of the mean

Notes:

[6] - RD = -2.92
Standard Error of the Mean = 0.094

[7] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part A: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Part A: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs)[8]

End point description:

An adverse event (AE) referred to any untoward medical occurrence in a clinical study participant, regardless of a causal relationship with the study treatment. TEAEs included any event occurring after the participant received the study treatment. Clinically significant changes in vital signs, electrocardiograms, and laboratory tests recorded after treatment administration were documented as TEAEs. Serious TEAEs (SAEs) were untoward medical occurrences after the first dose, irrespective of a causal link to the study treatment, that led to death, were life-threatening, required hospitalization or its prolongation, caused significant disability, resulted in congenital anomalies, or were considered other medically important events.

Part A, safety analysis set (SAS): all participants who received at lease one dose of study drug in Part A of the study.

End point type	Secondary

End point timeframe:

Part A: Screening (Day -28) to Follow-up (Week 45), for a total of 49 weeks

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part A Izokibep 160 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)				
Any TEAE	86.67			
Any SAE	6.67			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants Testing Positive for Anti-drug Antibodies (ADAs)

End point title	Part A: Percentage of Participants Testing Positive for Anti-drug Antibodies (ADAs)[9]

End point description:

Blood samples were collected at different time points throughout the study. ADA Analysis Set: all participants who received at lease one dose of study drug and had both baseline ADA and at least one post-dose ADA measurement in Part A.

End point type	Secondary

End point timeframe:

Baseline, Week 16, Week 32, Week 39

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part A Izokibep 160 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percentage of participants				
number (not applicable)				
Baseline (N = 25)	48			
Week 16 (N = 18)	61.1			
Week 32 (N = 18)	83.3			
Week 39 (N = 18)	94.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Who Achieved HiSCR90 At Week 16

End point title	Part B: Percentage of Participants Who Achieved HiSCR90 At Week 16[10]

End point description:

HiSCR90 was defined as at least a 90% reduction from baseline in the total abscess and inflammatory nodule count, with no increase from baseline in abscess or draining fistula count.

FAS, Part B: all participants randomized in Part B.

End point type	Secondary

End point timeframe:

Part B: Baseline to Week 16

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Percentage of participants				
number (not applicable)	15.3	26.3	20.3	

Statistical analyses

Statistical analysis title	Participants Who Achieved HiSCR90 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR90.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg QW
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0933 [12]
Method	Cochran-Mantel-Haenszel

Notes:

[11] - RD = -14.8
Standard Error of the Mean = 0.087
[12] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants Who Achieved HiSCR90 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting. Non-response imputation was used for participants with missing HiSCR90.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg Q2W

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.6018 [14]
Method	Cochran-Mantel-Haenszel

Notes:

[13] - RD = -4.30
Standard Error of the Mean = 0.084
[14] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part B: Percentage of Participants Who Achieved HiSCR100 at Week 16

End point title	Part B: Percentage of Participants Who Achieved HiSCR100 at Week 16[15]

End point description:

HiSCR100 was defined as at least a 100% reduction from baseline in the total abscess and inflammatory nodule count, with no increase from baseline in abscess or draining fistula count.

FAS, Part B: all participants randomized in Part B.

End point type	Secondary

End point timeframe:

Part B: Baseline to Week 16

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Percentage of participants				
number (not applicable)	11.9	26.3	18.6	

Statistical analyses

Statistical analysis title	Participants Who Achieved HiSCR100 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR100.

Comparison groups	Part B Izokibep 160 mg QW v Part B Placebo/Izokibep QW/Q2W

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.0273 [17]
Method	Cochran-Mantel-Haenszel

Notes:

[16] - RD = -19.2
Standard Error of the Mean = 0.086
[17] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants Who Achieved HiSCR100 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR100.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg Q2W
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.3989 [19]
Method	Cochran-Mantel-Haenszel

Notes:

[18] - RD = -6.55
Standard Error of the Mean = 0.078
[19] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part B: Percentage of Participants Who Achieved HiSCR50 at Week 16

End point title	Part B: Percentage of Participants Who Achieved HiSCR50 at Week 16[20]

End point description:

HiSCR50 was defined as at least a 50% reduction from baseline in the total abscess and inflammatory nodule count, with no increase from baseline in abscess or draining fistula count.

FAS, Part B: all participants randomized in Part B.

End point type	Secondary

End point timeframe:

Part B: Baseline to Week 16

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Percentage of participants				
number (not applicable)	37.3	45.6	44.1	

Statistical analyses

Statistical analysis title	Participants Who Achieved HiSCR50 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR50.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg QW
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.1281 [22]
Method	Cochran-Mantel-Haenszel

Notes:

[21] - RD = -15.2
Standard Error of the Mean = 0.098
[22] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants Who Achieved HiSCR50 at Week 16

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.
Non-response imputation was used for participants with missing HiSCR50.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg Q2W
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.5428 [24]
Method	Cochran-Mantel-Haenszel

Notes:

[23] - RD = -5.87
Standard Error of the Mean = 0.095
[24] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part B: Number of Participants Who Experienced ≥ 1 Disease Flare Through 16 Weeks of Treatment

End point title	Part B: Number of Participants Who Experienced ≥ 1 Disease Flare Through 16 Weeks of Treatment[25]

End point description:

A flare was defined as ≥ 25% increase in AN count with a minimum increase of 2 AN relative to baseline.
Missing data of abscess and inflammatory nodules counts at scheduled visits are imputed assuming

monotone missingness pattern. Predictors in the regression model for missing values at Week 4 are Baseline Hurley stage, baseline abscess count, baseline inflammatory nodule count, baseline draining fistula count, sex, race, age, body mass index (BMI) and prior Biologic/JAK inhibitor use for HS. Predictors in the regression model for missing values after Week 4 are all of these variables, plus counts of abscess, inflammatory nodule, and draining fistula at prior scheduled assessment. Missing flare values in both the placebo and izokibep groups are imputed using observed data from the placebo group only. FAS, Part B: all participants randomized in Part B.

End point type	Secondary

End point timeframe:

Part B: Day 1 through to Week 16

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Imputed number of participants				
number (not applicable)	13.17	8.51	10.79	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants With Hurley Stage II at Baseline Who Achieved AN Count of 0, 1, or 2

End point title	Part B: Percentage of Participants With Hurley Stage II at Baseline Who Achieved AN Count of 0, 1, or 2[26]

End point description:

The percentage of participants with baseline Hurley Stage II who achieved AN count of 0, 1, or 2 at Week 16.
Hurley stages:
Stage 1 – solitary or multiple, isolated abscess formation without scarring or sinus tracts Stage 2 – recurrent abscesses, single or multiple widely separated lesions, with sinus tract formation Stage 3 – diffuse or broad involvement, with multiple interconnected sinus tracts and abscesses.

FAS, Part B: all participants randomized in Part B, inclusive only of participants with Hurley Stage II at baseline.

End point type	Secondary

End point timeframe:

Part B: Week 16

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	35	36	
Units: Percentage of participants				
number (not applicable)	44.1	51.4	38.9	

Statistical analyses

Statistical analysis title	Participants With Hurley Stage II

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg QW
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.4067 [28]
Method	Cochran-Mantel-Haenszel

Notes:

[27] - RD = -11.1
Standard Error of the Mean = 0.132
[28] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants With Hurley Stage II

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg Q2W
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.5893 [30]
Method	Cochran-Mantel-Haenszel

Notes:

[29] - RD = 7.28
Standard Error of the Mean = 0.133
[30] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part B: Percentage of Participants Who Achieved at Least a 3-Point Reduction From Baseline in Numeric Rating Scale (NRS) in Patient Global Assessment of Skin Pain at Its Worst at Week 16 Among Participants With Baseline NRS ≥ 4

End point title	Part B: Percentage of Participants Who Achieved at Least a 3-Point Reduction From Baseline in Numeric Rating Scale (NRS)

	in Patient Global Assessment of Skin Pain at Its Worst at Week 16 Among Participants With Baseline NRS ≥ 4[31]

End point description:

The Patient Global Assessment of Skin Pain is a NRS that consists of scores from 0 to 10 with 0 indicating "no skin pain" and 10 indicating "pain as bad as you can imagine".

FAS, Part B: all participants randomized in Part B who had a baseline NRS ≥ 4.

End point type	Secondary

End point timeframe:

Part B: Baseline to Week 16

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	29	29	
Units: Percentage of participants				
number (not applicable)	12.9	17.2	31.0	

Statistical analyses

Statistical analysis title	Participants Who Achieved at Least a 3-Point NRS

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg QW arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg QW
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.208 [33]
Method	Cochran-Mantel-Haenszel

Notes:

[32] - RD = -16.9
Standard Error of the Mean = 0.133
[33] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Statistical analysis title	Participants Who Achieved at Least a 3-Point NRS

Statistical analysis description:

The common risk difference between placebo QW/Q2W and the izokibep 160 mg Q2W arm among the four strata, prior biologic/JAK inhibitor use for HS (Yes/No) and Hurley Stage (II or III), used for randomization and associated standard error will be estimated by combining the observed risk differences using Cochran-Mantel-Haenszel weighting.

Comparison groups	Part B Placebo/Izokibep QW/Q2W v Part B Izokibep 160 mg Q2W

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	= 0.0571 [35]
Method	Cochran-Mantel-Haenszel

Notes:

[34] - RD = -25.2
Standard Error of the Mean = 0.124
[35] - The estimated risk difference divided by the standard error was used as the test statistic and a p-value calculated assuming that the test statistic follows a standard normal distribution under the null hypothesis.

Secondary: Part B: Percentage of Participants With TEAEs

End point title	Part B: Percentage of Participants With TEAEs[36]

End point description:

An AE referred to any untoward medical occurrence in a clinical study participant, regardless of a causal relationship with the study treatment. TEAEs included any event occurring after the participant received the study treatment. Clinically significant changes in vital signs, electrocardiograms, and laboratory tests recorded after treatment administration were documented as TEAEs. SAEs were untoward medical occurrences after the first dose, irrespective of a causal link to the study treatment, that led to death, were life-threatening, required hospitalization or its prolongation, caused significant disability, resulted in congenital anomalies, or were considered other medically important events.

Part B, SAS: all randomized participants who received at least one dose of study drug in Part B of the study.

End point type	Secondary

End point timeframe:

Part B: Screening (Day -28) to Follow-up (Week 45), for a total of 49 weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	59	57	59	24
Units: Percentage of participants				
number (not applicable)				
Any TEAE	67.8	86.0	83.1	70.8
Any SAE	5.1	3.5	1.7	8.3

End point values	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)	Part B: Izokibep 160 mg QW (Week 16 to 31)	Part B: Izokibep 160 mg Q2W (Week 16 to 30)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	42	53	
Units: Percentage of participants				
number (not applicable)				

Any TEAE	58.3	57.1	43.4	
Any SAE	0	2.4	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Testing Positive for ADAs

End point title	Part B: Percentage of Participants Testing Positive for ADAs[37]

End point description:

Blood samples were collected at different time points throughout the study.
ADA Analysis Set: all participants who received at lease one dose of study drug and had both baseline ADA and at least one post-dose ADA measurement in Part B.

End point type	Secondary

End point timeframe:

Up to 39 weeks

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	54	53	
Units: Percentage of participants				
number (not applicable)				
Baseline (N = 54, 54, 53)	5.0	53.7	67.9	
Week 16 (N = 47, 41, 49)	44.7	70.7	79.6	
Week 32 (N = 20, 46, 19)	65.0	76.1	63.1	
Week 39 (N = 18, 40, 18)	94.4	80.0	83.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants With TEAEs of Special Interest

End point title	Part B: Percentage of Participants With TEAEs of Special Interest[38]

End point description:

Adverse events of special interest were adverse events in the following categories: candida infection, inflammatory bowel disease, suicidal ideation, malignancies, major cardiovascular and cerebrovascular events, tuberculosis, infections, cytopenias and hypersensitivity reactions.
Part B, SAS: all randomized participants who received at least one dose of study drug in Part B of the study.

End point type	Secondary

End point timeframe:

Part B: Screening (Day -28) to Follow-up (Week 45), for a total of 49 weeks

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No additional statistical analysis was pre-specified for this endpoint.

End point values	Part B Placebo/Izokibep QW/Q2W	Part B Izokibep 160 mg QW	Part B Izokibep 160 mg Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	57	59	
Units: Percentage of participants				
number (not applicable)	10.2	1.8	3.4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: Screening (Day -28) to Follow-up (Week 45), for a total of 49 weeks. Part B: Screening (Day -28) to Follow-up (Week 45), for a total of 49 weeks.

Adverse event reporting additional description:

SAS: all randomized participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Part A Izokibep 160 mg QW (Openlabel)

Reporting group description:

Participants with moderate to severe Hidradenitis Suppurativa (HS) received open label izokibep 160 mg by subcutaneous (SC) injection once every week (QW) in Part A for up to 31 weeks.

Reporting group title	Part B Placebo QW/Q2W (Up to Week 16)

Reporting group description:

Participants with moderate to severe HS received placebo by SC injection either QW or every 2 weeks (Q2W) for up to 16 weeks. After Week 16, participants who received placebo QW switched to izokibep QW for up to Week 31. Participants who received placebo Q2W switched to izokibep Q2W for up to Week 30.

Reporting group title	Part B Izokibep 160 mg QW (Up to Week 16)

Reporting group description:

Participants with moderate to severe HS received izokibep 160 mg QW by SC injection for 31 weeks.

Reporting group title	Part B Izokibep 160 mg Q2W (Up to Week 16)

Reporting group description:

Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection for 30 weeks.

Reporting group title	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)

Reporting group description:

Participants received izokibep Q2W in a blinded manner for weeks 16-30.

Reporting group title	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)

Reporting group description:

Participants received izokibep QW in a blinded manner for weeks 16-31.

Reporting group title	Part B: Izokibep 160 mg Q2W (Week 16 to 30)

Reporting group description:

Participants with moderate to severe HS received izokibep 160 mg Q2W by SC injection during weeks 16-30.

Reporting group title	Part B: Izokibep 160 mg QW (Week 16 to 31)

Reporting group description:

Participants with moderate to severe HS received izokibep 160 mg QW by SC injection during weeks 16-31.

Serious adverse events	Part A Izokibep 160 mg QW (Openlabel)	Part B Placebo QW/Q2W (Up to Week 16)	Part B Izokibep 160 mg QW (Up to Week 16)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)	3 / 59 (5.08%)	2 / 57 (3.51%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	0 / 57 (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			
Crohn's disease			
subjects affected / exposed	1 / 30 (3.33%)	0 / 59 (0.00%)	0 / 57 (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
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	0 / 57 (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			
Cutaneous vasculitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	1 / 57 (1.75%)
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			
Arthritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Still's disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	0 / 57 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 59 (1.69%)	0 / 57 (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

Colonic abscess			
subjects affected / exposed	1 / 30 (3.33%)	0 / 59 (0.00%)	0 / 57 (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
Epstein-Barr virus infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 59 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal abscess			
subjects affected / exposed	0 / 30 (0.00%)	1 / 59 (1.69%)	0 / 57 (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
Sepsis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 59 (1.69%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 30 (0.00%)	1 / 59 (1.69%)	0 / 57 (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	Part B Izokibep 160 mg Q2W (Up to Week 16)	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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			
Crohn's disease			

subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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			
Drug-induced liver injury			
subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	0 / 24 (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
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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			
Arthritis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Still's disease			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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
Colonic abscess			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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
Epstein-Barr virus infection			

subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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
Scrotal abscess			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (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	Part B: Izokibep 160 mg Q2W (Week 16 to 30)	Part B: Izokibep 160 mg QW (Week 16 to 31)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Drug-induced liver injury			

subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Still's disease			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic abscess			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A Izokibep 160 mg QW (Openlabel)	Part B Placebo QW/Q2W (Up to Week 16)	Part B Izokibep 160 mg QW (Up to Week 16)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 30 (80.00%)	27 / 59 (45.76%)	43 / 57 (75.44%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)	3 / 59 (5.08%)	0 / 57 (0.00%)
occurrences (all)	2	4	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 30 (3.33%)	8 / 59 (13.56%)	9 / 57 (15.79%)
occurrences (all)	1	15	14
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	12 / 30 (40.00%)	2 / 59 (3.39%)	31 / 57 (54.39%)
occurrences (all)	38	2	60
Injection site induration			
subjects affected / exposed	1 / 30 (3.33%)	1 / 59 (1.69%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Injection site pain			
subjects affected / exposed	3 / 30 (10.00%)	2 / 59 (3.39%)	3 / 57 (5.26%)
occurrences (all)	9	16	19
Injection site pruritus			
subjects affected / exposed	8 / 30 (26.67%)	1 / 59 (1.69%)	17 / 57 (29.82%)
occurrences (all)	23	1	31

Injection site reaction			
subjects affected / exposed	4 / 30 (13.33%)	0 / 59 (0.00%)	1 / 57 (1.75%)
occurrences (all)	13	0	1
Injection site swelling			
subjects affected / exposed	6 / 30 (20.00%)	0 / 59 (0.00%)	9 / 57 (15.79%)
occurrences (all)	19	0	12
Injection site warmth			
subjects affected / exposed	5 / 30 (16.67%)	0 / 59 (0.00%)	1 / 57 (1.75%)
occurrences (all)	6	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 30 (6.67%)	0 / 59 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	2 / 30 (6.67%)	1 / 59 (1.69%)	1 / 57 (1.75%)
occurrences (all)	2	1	1
Nausea			
subjects affected / exposed	2 / 30 (6.67%)	1 / 59 (1.69%)	2 / 57 (3.51%)
occurrences (all)	2	1	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 30 (3.33%)	1 / 59 (1.69%)	3 / 57 (5.26%)
occurrences (all)	1	1	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 30 (6.67%)	1 / 59 (1.69%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 30 (0.00%)	5 / 59 (8.47%)	1 / 57 (1.75%)
occurrences (all)	0	5	1
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 59 (3.39%)	3 / 57 (5.26%)
occurrences (all)	0	2	3
Infections and infestations			

COVID-19 treatment			
subjects affected / exposed	2 / 30 (6.67%)	2 / 59 (3.39%)	1 / 57 (1.75%)
occurrences (all)	2	2	1
Nasopharyngitis			
subjects affected / exposed	0 / 30 (0.00%)	5 / 59 (8.47%)	9 / 57 (15.79%)
occurrences (all)	0	6	10
Upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	6 / 59 (10.17%)	6 / 57 (10.53%)
occurrences (all)	0	7	7

Non-serious adverse events	Part B Izokibep 160 mg Q2W (Up to Week 16)	Part B Placebo/Izokibep 160 mg Q2W (Week 16 to 30)	Part B Placebo/Izokibep 160 mg QW (Week 16 to 31)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 59 (57.63%)	7 / 24 (29.17%)	14 / 24 (58.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 59 (10.17%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	6	0	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	24 / 59 (40.68%)	5 / 24 (20.83%)	12 / 24 (50.00%)
occurrences (all)	47	9	75
Injection site induration			
subjects affected / exposed	1 / 59 (1.69%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Injection site pain			
subjects affected / exposed	3 / 59 (5.08%)	2 / 24 (8.33%)	3 / 24 (12.50%)
occurrences (all)	4	2	20
Injection site pruritus			
subjects affected / exposed	7 / 59 (11.86%)	3 / 24 (12.50%)	5 / 24 (20.83%)
occurrences (all)	10	3	24
Injection site reaction			

subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Injection site swelling			
subjects affected / exposed	7 / 59 (11.86%)	1 / 24 (4.17%)	3 / 24 (12.50%)
occurrences (all)	8	2	20
Injection site warmth			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 59 (3.39%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 59 (5.08%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 59 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19 treatment			

subjects affected / exposed	0 / 59 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	5 / 59 (8.47%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	5	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 59 (3.39%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	2	0	1

Non-serious adverse events	Part B: Izokibep 160 mg Q2W (Week 16 to 30)	Part B: Izokibep 160 mg QW (Week 16 to 31)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 53 (16.98%)	11 / 42 (26.19%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 53 (0.00%)	5 / 42 (11.90%)	
occurrences (all)	0	6	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	4 / 53 (7.55%)	2 / 42 (4.76%)	
occurrences (all)	12	16	
Injection site induration			
subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	2	
Injection site pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	7	
Injection site pruritus			
subjects affected / exposed	2 / 53 (3.77%)	1 / 42 (2.38%)	
occurrences (all)	3	3	
Injection site reaction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	

Injection site swelling			
subjects affected / exposed	2 / 53 (3.77%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
Injection site warmth			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 53 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 42 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 53 (1.89%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Infections and infestations			
COVID-19 treatment			
subjects affected / exposed	1 / 53 (1.89%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			

subjects affected / exposed	1 / 53 (1.89%)	4 / 42 (9.52%)	
occurrences (all)	1	4	
Upper respiratory tract infection			
subjects affected / exposed	4 / 53 (7.55%)	1 / 42 (2.38%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 July 2022	The following changes were subject to this amendment: - Storage conditions of the placebo in Table 3 were clarified. - The timing for contacting the medical monitor for unblinding a participant's treatment assignment was clarified. - Procedures for rescreening were clarified. - An additional description of monitoring was provided. - It was clarified that concomitant medications should have been used in alignment with the approved label in the respective country and per doses outlined in the protocol. - It was specified that approximately 30% of enrolled participants were allowed to be on stable doses of oral antibiotics for at least 4 weeks prior to baseline. - It was specified that investigators should have considered the effects on the metabolism of cytochrome P450 substrates with narrow therapeutic indices when the study drug was initiated or discontinued. - The process for missed or delayed doses was clarified. - It was clarified that the investigator should have determined whether another rescue medication would have been more appropriate for a participant who was previously intolerant or had a contraindication to both minocycline and doxycycline. - The reasons for discontinuation of the study drug were updated. - It was specified that instructions for collecting and handling biological samples were provided in the laboratory manual. - Procedures for the collection of samples for exploratory biomarker analysis (US only) were added. - The sample storage and shipping flow for ADA samples was added. - Duplicate sections describing the data monitoring committee structure were removed. - The schedule of assessments for HIV testing, ECG assessments, vital signs, fasting lipid levels, and evaluation for symptoms of clinical depression was modified. - The list of AEs of special interest was expanded. - For the primary endpoint, the reduction was changed from 30% to 50%. - Information on handling data security breaches was provided.
28 July 2022	The following changes were subject to this amendment: - Measures were added to ensure the protection of personal data and ensure confidentiality. - Text was added to further define source documents. - Requirements for participant competency with dosing at home were clarified. - The SAE process and the location for recording AE/SAE information were clarified. - Procedures for the assessment and follow-up for liver safety were updated. - The regions to be assessed for the degree of erythema were updated. - It was clarified that the PGIC assessment at week 16 asked the participant about pain since treatment began in the study. - The version and date were added to the header and title page.

28 July 2022	The following changes were subject to this amendment: - "Pivotal" was added to the study protocol title. - The term “study intervention” was changed to “study drug” when referring to the investigational product. - The rationale and background information were updated to specify indications that were currently being studied. - The observation period was modified to include weeks 16 and 17 for QW and weeks 16 and 18 for Q2W. - The number of days pain diaries needed to be completed for a participant to be randomized was clarified. - It was clarified that after a delayed or missed dose, participants should have returned to the original visit and dosing schedule. - For trough concentrations, “serum” was replaced with “plasma.” - The secondary pain endpoint was moved to be the last secondary endpoint. - The Patient Global Assessment of Skin Pain endpoint was changed from a 30% reduction to a 3-point reduction. - The disease flare endpoint was modified to be through 16 weeks of treatment. - The description of DMC membership was clarified. - The rationale for the placebo-controlled period was added. - Inclusion criterion 5 was revised from a total abscess and inflammatory nodule count of ≥3 to ≥5. - Legally authorized representatives were removed as being able to sign the informed consent. - Exclusion criterion 4 was revised to only exclude inflammatory bowel disease. - Exclusion criterion 6 was revised to clarify moderate to severe for both renal disease and liver disease. - Exclusion criterion 11 was removed as it duplicated Exclusion criterion 9. - Exclusion criterion 12 was reworded to clarify that it was not a separate criterion. - Exclusion criterion 22 was revised for clarity and to exclude laser or intense light therapy in anatomic areas of HS lesions. - The definition of renal impairment in Exclusion criterion 31 was modified. - Lifestyle considerations regarding alcohol consumption were added.
26 April 2023	The following changes were subject to this amendment: - The legal registered address for the sponsor was updated. - The sponsor signatory was updated. - The overall approximate number of participants to be enrolled for the study overall and in Part B, along with the approximate study power, was updated. - The timepoint for the primary objective and endpoint in Part A was updated. - The primary objective and endpoint in Part B were changed from HiSCR to HiSCR75. - The percentages of participants who achieved HiSCR90/100/50 at Week 16 were added as secondary objectives and endpoints in Part B. - The HiSCR percentage definition was revised. - The percentages of participants who achieved HiSCR75/90/100/50 at Weeks 2, 4, 8, 12, and 32 were added to exploratory objectives and endpoints in Part B. - The NRS Patient Global Assessment Skin Pain was added as a screening assessment. - It was clarified that participants randomized to Q2W arms did not need to complete the Week 17 visit. - Grammatical changes were made. - The version and date for the header and title page were revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported