Clinical trial results:
Randomized, double-blind, placebo-controlled, study of spesolimab in patients with moderate to severe hidradenitis suppurativa

Summary

EudraCT number	2020-003672-40
Trial protocol	FR HU CZ BE NL DE GR IT ES
Global end of trial date	21 April 2022

Results information

Result version number	v1 (current)
This version publication date	07 May 2023
First version publication date	07 May 2023

Trial information

Trial identification

Sponsor protocol code	1368-0052

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04762277
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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	01 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2022
Global end of trial reached?	Yes
Global end of trial date	21 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to estimate the effect of spesolimab compared to placebo for the mean percent change from baseline in total abscess and inflammatory nodule (AN) count at Week 12 in patients with moderate to severe hidradenitis suppurativa (HS).
Secondary objectives of this trial were the evaluation of efficacy of spesolimab on secondary endpoints versus placebo.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	28 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	63
EEA total number of subjects	41

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)	63
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an international, phase IIa multi-center, double-blind, placebo-controlled trial assessing the efficacy and safety of spesolimab in patients with moderate to severe Hidradenitis suppurativa (HS).

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.

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

Dosage and administration details:

Patients received placebo administered subcutaneously at Weeks 4, 6, 8, and 10.

Investigational medicinal product name	Placebo matching to spesolimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2.

Arm title	Spesolimab

Arm description:

Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.

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

Dosage and administration details:

Patients received 1200 mg of spesolimab administered subcutaneously injection at Weeks 4, 6, 8, and

10.

Investigational medicinal product name	Spesolimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2.

Number of subjects in period 1[1]	Placebo	Spesolimab
Started	17	35
Completed	16	32
Not completed	1	3
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	-
Protocol deviation	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 63 patients which were screened only 52 were randomized to receive "placebo" or "spesolimab".

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	
Reporting group title	Spesolimab
Reporting group description:	
Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	

Reporting group values	Placebo	Spesolimab	Total
Number of subjects	17	35	52
Age categorical			
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	35	52
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug.			
Units: years			
arithmetic mean	34.1	35.7	
standard deviation	± 11.0	± 11.3	-
Sex: Female, Male			
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug.			
Units: Participants			
Female	10	21	31
Male	7	14	21
Race (NIH/OMB)			
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	4	6
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	2	2	4
White	12	23	35
More than one race	0	0	0

Unknown or Not Reported	1	5	6
Ethnicity (NIH/OMB)			
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	15	29	44
Unknown or Not Reported	1	5	6
Total number of abscesses and inflammatory nodules			
Total number of abscesses and inflammatory nodules at baseline.			
Units: abscesses and inflammatory nodules			
arithmetic mean	18.9	11.6	
standard deviation	± 15.7	± 9.3	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	
Reporting group title	Spesolimab
Reporting group description:	
Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	
Subject analysis set title	Spesolimab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.	

Primary: Percent change from baseline in total abscess and inflammatory nodule count at Week 12

End point title	Percent change from baseline in total abscess and inflammatory nodule count at Week 12
End point description:	
Percent change from baseline in total abscess and inflammatory nodule count at Week 12= [(Total Abscess at Week 12 + Total Inflammatory Nodule at Week 12) - (Total Abscess at baseline + Total Inflammatory Nodule at baseline)] *100/ (Total Abscess at baseline + Total Inflammatory Nodule at baseline). Percent change from baseline in total abscess and inflammatory nodule count at Week 12 was modelled using mixed effects model for repeated measures (MMRM) accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to tumor necrosis factor inhibitor (TNFi)-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit (Weeks 1, 2, 4, 6, 8, 10, and 12). The Least Squares Mean (Standard Error) at Week 12 is reported.	
End point type	Primary
End point timeframe:	
Baseline (Week 0) and at Weeks 1, 2, 4, 6, 8, 10, and 12 after first drug administration.	

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[1]	30[2]		
Units: percent change				
least squares mean (standard error)	-34.7 (± 11.1)	-38.8 (± 7.5)		

Notes:

[1] - Safety Analysis Set (SAF)

[2] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.7
upper limit	23.4

Secondary: Percent change from baseline in draining fistula count at Week 12

End point title	Percent change from baseline in draining fistula count at Week 12

End point description:

Percent change from baseline in draining fistula at Week 12 was calculated as: [(total draining fistula at Week 12) - (total draining fistula at baseline)] * 100 %/ (total draining fistula at baseline).

Percent change from baseline in draining fistula count at Week 12 was modelled using mixed effects model for repeated measures (MMRM) accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to tumor necrosis factor inhibitor (TNFi)-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit (Weeks 1, 2, 4, 6, 8, 10, and 12). The Least Squares Mean (Standard Error) at Week 12 is reported.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and at Weeks 1, 2, 4, 6, 8, 10, and 12 after first drug administration.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[3]	24[4]		
Units: percent change				
least squares mean (standard deviation)	56.6 (± 23.0)	-40.1 (± 16.8)		

Notes:

[3] - Safety Analysis Set (SAF)

[4] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each

visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-96.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-154.5
upper limit	-38.8

Secondary: Achievement of Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12

End point title	Achievement of Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12

End point description:

HiSCR is defined as at least a 50% reduction in the total abscess and inflammatory nodule (AN) count with no increase in abscess count and no increase in draining fistula count relative to baseline. Proportion of patients with achievement of Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12 is reported. Proportion of patients with achievement of HiSCR at Week 12 was calculated as: number of patients with achievement of HiSCR at Week 12/number of patients analyzed. Proportions were rounded up to three decimal places.

End point type	Secondary

End point timeframe:

At baseline (Week 0) and at Week 12.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[5]	35[6]		
Units: proportion of patients				
number (not applicable)	0.176	0.314		

Notes:

[5] - Safety Analysis Set (SAF)

[6] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in the proportion of patients with a response between Spesolimab and placebo was analysed using a logistic regression model. The model included treatment and stratification factor (tumor necrosis factor inhibitor (TNFi)-naive population versus TNFi-failure population) as two categorical variables.

Comparison groups	Placebo v Spesolimab

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.138
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.129
upper limit	0.339

Secondary: Absolute change from baseline in International Hidradenitis Suppurativa Severity Score System (IHS4) value at Week 12

End point title	Absolute change from baseline in International Hidradenitis Suppurativa Severity Score System (IHS4) value at Week 12

End point description:

The IHS4 assesses the hidradenitis suppurativa (HS) severity and the resulting IHS4 score is arrived at by= number of nodules * 1 + number of abscesses * 2 + number of draining fistula * 4.
A total score of 3 or less signifies mild, 4-10 signifies moderate and 11 or higher signifies severe disease.

Absolute change from baseline in IHS4 value at Week 12 was modelled using mixed effects model for repeated measures (MMRM) accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to tumor necrosis factor inhibitor (TNFi)-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit (Weeks 1, 2, 4, 6, 8, 10, and 12). The Least Squares Mean (Standard Error) at Week 12 is reported.

End point type	Secondary

End point timeframe:

At baseline (Week 0) and at Weeks 1, 2, 4, 6, 8, 10, and 12 after first drug administration.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[7]	30[8]		
Units: units on a scale				
least squares mean (standard error)	4.9 (± 4.7)	-9.0 (± 3.2)		

Notes:

[7] - Safety Analysis Set (SAF)

[8] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.6
upper limit	-2.3

Secondary: Absolute change from baseline in Hidradenitis Suppurativa Area and Severity Index (HASI) score at Week 12

End point title	Absolute change from baseline in Hidradenitis Suppurativa Area and Severity Index (HASI) score at Week 12

End point description:

HASI includes four domains to assess the severity of HS disease activity, which are erythema, induration, open ulcer and draining fistula and scored on a Likert scale 0 (none) to 3 (severe/extensive) for each predetermined body region.
For body surface area (BSA) assessment, the number of palms (one palm indicates 1% of the patient's BSA) involved for each body region (head, right axilla, left axilla, anterior chest, back, anterior bathing trunk, posterior bathing trunk, other) is assessed and converted to a percentage of that region. An area score was assigned to each region using the approach (0 = none, 1 = 1–9%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89%, 6 = 90– 100%). Scores for the four domains of HS are summed and adjusted for the area affected, and the score of each area are summed to calculate the total HASI score, which ranges from 0 (no disease) to 72 (severe disease).
The Least Squares Mean (Standard Error (SE)) derive from MMRM.

End point type	Secondary

End point timeframe:

MMRM included measurements at baseline (Week 0) and at Weeks 1, 2, 4, 6, 8, 10, and 12 after first drug administration. MMRM estimates of absolute change from baseline in HASI score at Week 12 is reported in the table below..

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[9]	30[10]		
Units: units on a scale				
least squares mean (standard error)	-3.8 (± 6.9)	-23.6 (± 4.7)		

Notes:

[9] - Safety Analysis Set (SAF)

[10] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-19.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.9
upper limit	-2.7

Secondary: Achievement of Hidradenitis Suppurativa Physician Global Assessment (HS-PGA) score of 0 or 1 at Week 12

End point title	Achievement of Hidradenitis Suppurativa Physician Global Assessment (HS-PGA) score of 0 or 1 at Week 12

End point description:

HS-PGA documents the physician's assessment of the patient's HS at a given timepoint. The HS-PGA score ranges from 0 to 5, where: 0=clear - no abscesses, draining fistula, inflammatory nodules or noninflammatory nodules); 1=minimal - no abscesses, draining fistula or inflammatory nodules and the presence of noninflammatory nodules); 2=mild - no abscesses or draining fistula and 1-4 inflammatory nodules, or 1 abscess or draining tunnel and no inflammatory nodules); 3=moderate - no abscesses or draining fistula and ≥5 inflammatory nodules, or 1 abscess or draining fistula and ≥1 inflammatory nodule, or 2-5 abscesses or draining fistula and <10 inflammatory nodules); 4=severe - 2-5 abscesses or draining fistula and ≥10 inflammatory nodules); 5=very severe - >5 abscesses or draining fistula). Proportion of patients with achievement of HS-PGA score of 0 or 1 at Week 12 was calculated as: number of patients with achievement of HS-PGA score of 0 or 1 at Week 12/number of patients analyzed.

End point type	Secondary

End point timeframe:

At Week 12.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[11]	35[12]		
Units: proportion of patients				
number (not applicable)	0.000	0.057		

Notes:

[11] - Safety Analysis Set (SAF)

[12] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in the proportion of patients with a response between Spesolimab and placebo was analysed using a logistic regression model. The model included treatment and stratification factor (tumor necrosis factor inhibitor (TNFi)-naive population versus TNFi-failure population) as two categorical variables.

Comparison groups	Placebo v Spesolimab

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.132
upper limit	0.186

Secondary: Achievement of at least 30% reduction from baseline in Numerical Rating Scale (NRS30) in Patient's Global Assessment of HS Pain at Week 12

End point title	Achievement of at least 30% reduction from baseline in Numerical Rating Scale (NRS30) in Patient's Global Assessment of HS Pain at Week 12

End point description:

The HS Pain Numerical Rating Scale (NRS) is an endpoint for the assessment of HS-related pain severity. Recall period is 24 hours and response is given by an 11-point scale ranging from 0 (no pain) to 10 (worst possible pain).
For the analysis of pain, weekly average of daily assessment was calculated for each visit based on values prior to the visit. Missing daily values within a week were ignored if there are at least 4 reported values.
Proportion of patients with achievement of at least 30% reduction from baseline in NRS30 in Patient's Global Assessment of HS Pain at Week 12. Proportion of patients with achievement of at least 30% reduction from baseline in NRS30 in Patient's Global Assessment of HS Pain at Week 12 was calculated as: number of patients with achievement of at least 30% reduction from baseline in NRS30 in Patient's Global Assessment of HS Pain at Week 12/number of patients analyzed. Proportions were rounded up to three decimal places.

End point type	Secondary

End point timeframe:

At baseline (Week 0) and at Week 12.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[13]	35[14]		
Units: proportion of patients				
number (not applicable)	0.059	0.229		

Notes:

[13] - Safety Analysis Set (SAF)

[14] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in the proportion of patients with a response between Spesolimab and placebo was analysed using a logistic regression model. The model included treatment and stratification factor (tumor necrosis factor inhibitor (TNFi)-naive population versus TNFi-failure population) as two categorical variables.

Comparison groups	Placebo v Spesolimab

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.067
upper limit	0.338

Secondary: Occurrence of complete elimination of draining fistulas at Week 12

End point title	Occurrence of complete elimination of draining fistulas at Week 12

End point description:

Proportion of patients with occurrence of complete elimination of draining fistulas at Week 12 is reported. Proportion of patients with occurrence of complete elimination of draining fistulas at Week 12 was calculated as: number of patients with occurrence of complete elimination of draining fistulas at Week 12/number of patients analyzed. Proportions were rounded up to three decimal places.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and at Week 12.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[15]	28[16]		
Units: proportion of patients				
number (not applicable)	0.067	0.250		

Notes:

[15] - Safety Analysis Set (SAF)

[16] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in the proportion of patients with a response between Spesolimab and placebo was analysed using a logistic regression model. The model included treatment and stratification factor (tumor necrosis factor inhibitor (TNFi)-naive population versus TNFi-failure population) as two categorical variables.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.183

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.079
upper limit	0.375

Secondary: Occurrence of at least one flare at Week 12

End point title	Occurrence of at least one flare at Week 12

End point description:

Proportion of patients with occurrence of at least one flare at Week 12. Flare was defined as at least 25 % increase in abscess and inflammatory nodule count with a minimum increase of 2 relative to baseline. Proportion of patients with occurrence of at least one flare at Week 12 was calculated as: number of patients with occurrence of at least one flare at Week 12/number of patients analyzed. Proportions were rounded up to three decimal places.

End point type	Secondary

End point timeframe:

At Week 12.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[17]	35[18]		
Units: proportion of patients				
number (not applicable)	0.176	0.086		

Notes:

[17] - Safety Analysis Set (SAF)

[18] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in the proportion of patients with a response between Spesolimab and placebo was analysed using a logistic regression model. The model included treatment and stratification factor (tumor necrosis factor inhibitor (TNFi)-naive population versus TNFi-failure population) as two categorical variables.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-0.091
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.331
upper limit	0.089

Secondary: Absolute change from baseline in hidradenitis Suppurativa Quality of Life (HiS-QoL) total score at Week 12

End point title	Absolute change from baseline in hidradenitis Suppurativa Quality of Life (HiS-QoL) total score at Week 12

End point description:

HiS-QoL is a patient-administered, 17-item instrument to measure HS-specific quality of life in clinical trials with a 7-day recall period. The 17-item HiS-QoL included four symptom items, eight activity-adaptation items and five psychosocial items. The item scores are summed to create a total ranging from 0 to 68, with higher scores indicating more severe impact on health-related quality of life. Absolute change from baseline in HiS-QoL total score at Week 12 was modelled using MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to tumor necrosis factor inhibitor (TNFi)-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit (Weeks 1, 4, 8, and 12).

End point type	Secondary

End point timeframe:

At baseline (Week 0) and at Weeks 1, 4, 8, and 12 after first drug administration.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[19]	25[20]		
Units: units on a scale				
least squares mean (standard error)	-4.5 (± 3.2)	-5.8 (± 2.4)		

Notes:

[19] - Safety Analysis Set (SAF)

[20] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	6.9

Secondary: Absolute change from baseline in Dermatology Life Quality Index (DLQI) score at Week 12

End point title	Absolute change from baseline in Dermatology Life Quality Index (DLQI) score at Week 12

End point description:

The DLQI is a patient-administered, ten-question, quality of life questionnaire that covers six domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment. Response categories include "not relevant" (score of 0), "not at all" (score of 0), "a little" (score of 1), "a lot" (score of 2) and "very much" (score of 3). DLQI total score is calculated by summing the scores of each question resulting in a range of 0 to 30 with higher scores indicating greater health-related quality of life impairment. Absolute change from baseline in DLQI score at Week 12 was modelled using MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to tumor necrosis factor inhibitor (TNFi)-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit (Weeks 1, 4, 8, and 12).

End point type	Secondary

End point timeframe:

At baseline (Week 0) and at Weeks 1, 4, 8, and 12 after first drug administration.

End point values	Placebo	Spesolimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[21]	30[22]		
Units: units on a scale				
least squares mean (standard error)	-2.8 (± 1.8)	-2.8 (± 1.2)		

Notes:

[21] - Safety Analysis Set (SAF)

[22] - Safety Analysis Set (SAF)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM accounting for the following sources of variation: fixed, categorical effects of treatment at each visit, the effect of stratum (stratification according to TNFi-naive population vs. TNFi-failure population) and the fixed continuous effects of baseline at each visit. The unstructured covariance structure was used to model the within patient measurements. To estimate denominator degrees of freedom the Kenward-Roger approximation was used.

Comparison groups	Placebo v Spesolimab
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	4.3

Secondary: The occurrence of Treatment Emergent Adverse Events

End point title	The occurrence of Treatment Emergent Adverse Events

End point description:

Percentage of patients with occurrence of Treatment Emergent Adverse Events (TEAEs) is reported. Percentage of patients with occurrence of Treatment Emergent Adverse Events (TEAEs) was calculated as: number of patients with occurrence of TEAEs / number of patients analyzed. Percentages were rounded to one decimal place.
Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug. One patient randomised to receive placebo took spesolimab during the study, therefore was considered in spesolimab arm instead for safety reporting.

End point type	Secondary

End point timeframe:

Up to 12 weeks for patients who did roll-over to the open-label extension (OLE) trial (trial number 1368-0067 (EudraCT number: 2020-005587-55) and up to 28 weeks who did not roll-over to the OLE trial.

End point values	Placebo	Spesolimab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	36		
Units: percentage of patients				
number (not applicable)	87.5	77.8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks for patients who did roll-over to the open-label extension (OLE) trial (trial number 1368-0067 (EudraCT number: 2020-005587-55) and up to 28 weeks who did not roll-over to the OLE trial.

Adverse event reporting additional description:

Safety Analysis Set (SAF): This patient set included all patients who were randomized and received at least one dose of study drug. One patient randomised to receive placebo took spesolimab during the study, therefore was considered in spesolimab arm instead for safety reporting.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Spesolimab

Reporting group description:

Patients received 1200 mg of spesolimab administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.

Reporting group title	Placebo

Reporting group description:

Patients received placebo administered intravenously (i.v.) at Weeks 0, 1, and 2, and subcutaneously injection at Weeks 4, 6, 8, and 10.

Serious adverse events	Spesolimab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Suicidal behaviour			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Spesolimab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 36 (72.22%)	14 / 16 (87.50%)	
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Injection site erythema			
subjects affected / exposed	4 / 36 (11.11%)	0 / 16 (0.00%)	
occurrences (all)	7	0	
Fatigue			
subjects affected / exposed	4 / 36 (11.11%)	0 / 16 (0.00%)	
occurrences (all)	5	0	
Injection site pain			
subjects affected / exposed	3 / 36 (8.33%)	1 / 16 (6.25%)	
occurrences (all)	4	1	
Injection site papule			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Injection site nodule			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Menstrual disorder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Intermenstrual bleeding			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Breast discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dyspnoea			

subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 36 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Investigations			
Platelet count increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Bacterial test positive			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Animal bite			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Arrhythmia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Headache			

subjects affected / exposed	4 / 36 (11.11%)	3 / 16 (18.75%)	
occurrences (all)	7	5	
Dizziness			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Sciatica			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Angular cheilitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	4 / 36 (11.11%)	0 / 16 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 36 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	3	2	
Intertrigo			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Hidradenitis			

subjects affected / exposed	1 / 36 (2.78%)	2 / 16 (12.50%)	
occurrences (all)	1	3	
Acne			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Hand dermatitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Back pain			
subjects affected / exposed	2 / 36 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	3 / 36 (8.33%)	3 / 16 (18.75%)	
occurrences (all)	3	3	
Folliculitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Pilonidal cyst			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Rhinitis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2021	The wording for HS severity was updated. For Visit 2, the flexibility of timing in some assessments and collection of safety lab samples were increased. Based on Health Authority recommendation, the wording of some secondary efficacy endpoints was rephrased, and treatment-emergent adverse events (TEAEs)-related secondary safety endpoint was added. The wording of some further efficacy endpoints was rephrased. The acceptable equivalent scoring to international hidradenitis suppurativa severity score system (IHS4) scoring in inclusion criteria #3 was clarified. Exclusion criteria #2 regarding the use of systemic non-biologic immunomodulatory and immunosuppressive agents was added. The wording in Exclusion criteria #2 was updated and, the restricted lesion of topical corticosteroids was clarified. The wording in exclusion criteria #3 was updated. Exclusion criteria #4 regarding prior exposure to Interleukin 36 receptor (IL-36R) inhibitors was added. Based on Health Authority recommendation, exclusion criteria #14 regarding hepatic disease was updated. Some scenarios for discontinuation of trial treatment were added. Based on Health Authority recommendation, some examples of reason for temporary interruption of trial treatment were added. Signals of suicidal ideation and suicidal behavior were clarified, and the actions of the concerned patients were updated. Based on Health Authority recommendation, the description regarding handling the trial treatment on a patient treated with rescue treatment was deleted. Restriction of immunosuppressive biologics was clarified for handling rescue treatment. For the adverse event of special interest (AESI) "hepatic injury", the alternative utilizable samples was added to the definition. The flexibility of study visit procedures within the corresponding visit window was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported