Clinical trial results:
An open label, long term safety trial of spesolimab treatment in patients with fistulising Crohn's disease who have completed previous spesolimab trials

Summary

EudraCT number	2019-001673-93
Trial protocol	AT DE HU BE ES DK
Global end of trial date	23 September 2022

Results information

Result version number	v1 (current)
This version publication date	30 September 2023
First version publication date	30 September 2023

Trial information

Trial identification

Sponsor protocol code	1368-0007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04362254
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	21 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2022
Global end of trial reached?	Yes
Global end of trial date	23 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial were to evaluate the long-term safety and the long-term efficacy of spesolimab in patients with perianal fistulising Crohn’s disease who had completed treatment in preceding parent trials.

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	25 May 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Netherlands: 1
Worldwide total number of subjects	12
EEA total number of subjects	11

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label, single group, long-term extension trial of approximately 89 weeks duration, which investigated the long-term safety and efficacy of spesolimab in patients with perianal fistulas due to Crohn's disease (CD) who had completed treatment in a parent spesolimab trial.

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	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open label, single arm trial; therefore, no blinding was necessary.

Arms

Arm title	Spesolimab

Arm description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

Arm type	Experimental
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:

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab.

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:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

Number of subjects in period 1	Spesolimab
Started	12
Completed	0
Not completed	12
Due to early termination of the trial	10
Adverse event, non-fatal	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Spesolimab

Reporting group description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

Reporting group values	Spesolimab	Total	
Number of subjects	12	12	
Age categorical			
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.			
Units: years			
arithmetic mean	37.1		
standard deviation	± 10.2	-	
Sex: Female, Male			
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.			
Units: Participants			
Female	3	3	
Male	9	9	
Race (NIH/OMB)			
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	10	10	
More than one race	0	0	
Unknown or Not Reported	0	0	

Ethnicity (NIH/OMB)			
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	12	12	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Spesolimab

Reporting group description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

Primary: Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment

End point title	Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment[1]

End point description:

Exposure adjusted rate of patients reporting a treatment emergent adverse event (TEAE) during maintenance treatment. The incidence rate was calculated as Incidence rate = 100 * number of patients with TEAE / Total TEAE-specific time at risk. Where the Time at risk (for patients who experienced a TEAE) was calculated as Time at Risk (in subject years) = ((date of onset of AE - study drug start date) +1 day) / 365.25 and Time at risk (for patients who did not experience a TEAE) Time at Risk (in subject years) = ((date of the end of time at risk - study drug start date) +1 day) / 365.25.
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.

End point type	Primary

End point timeframe:

First dose of Spesolimab in this trial through to the last dose of spesolimab + 16 weeks, up to 105 weeks.

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 statistical comparison between groups was planned for this endpoint.

End point values	Spesolimab			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Patients with TEAE per 100 patient years				
number (not applicable)	816.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with perianal fistula remission

End point title	Proportion of patients with perianal fistula remission

End point description:

Proportion of patients with perianal fistula remission at weeks 48 and 96.
Perianal fistula remission was defined as closure of all external openings, i.e. no drainage and discharge

despite gentle finger compression, that were open and draining at baseline of the parent trial and closure of all external openings that were newly emerged during the parent trial or this trial.

End point type	Secondary

End point timeframe:

Baseline, week 48 and 96 of treatment.

End point values	Spesolimab			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Participants				
number (not applicable)				

Notes:

[2] - No data could be calculated for any subject.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with perianal fistula response

End point title	Proportion of patients with perianal fistula response

End point description:

Proportion of patients with perianal fistula response at weeks 48 and 96.
Perianal fistula response was defined as closure and no drainage and discharge despite gentle finger compression of at least 50% in number of external openings regardless of the onset time, compared with the number of open and drainage fistulas at baseline of the parent trial.

End point type	Secondary

End point timeframe:

Baseline, week 48 and 96 of treatment.

End point values	Spesolimab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Participants				
number (not applicable)				

Notes:

[3] - No data could be calculated for any subject.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose of Spesolimab through to the last dose of Spesolimab + 16 weeks, up to 105 weeks.	
Adverse event reporting additional description:	
The safety set (SAF) included all patients who received at least one dose of trial drug in the overall maintenance period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Spesolimab

Reporting group description:

During the maintenance treatment period 300 milligram (mg) Spesolimab was given by subcutaneous injection at Week 0 and then every 4 weeks for a total duration of 89 weeks.

Patient with a confirmed fistula relapse received a single intravenous infusion of 1200 mg Spesolimab followed by an intensified subcutaneous spesolimab maintenance dosing of 600 mg Spesolimab every 4 weeks.

Serious adverse events	Spesolimab		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Spesolimab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Investigations			
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Seroma			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	5		
Injection site reaction			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Injection site swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Anal polyp subjects affected / exposed occurrences (all) Rectal stenosis subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2		
Psychiatric disorders Panic attack subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Fistula			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Fistula discharge			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	6		
Fungal infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pustule			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2020	- Endpoints of endoscopic remission (secondary endpoint) and endoscopic response (further endpoint) were removed as no ileocolonscopy was to be performed. The endoscopic score SES-CD was explored as further endpoint - Endpoint of clinical remission removed from secondary endpoints. The Crohn's Disease Activity Index (CDAI) score was explored as further endpoint as the patient population was expected to have low CDAI scores as per eligibility criteria (CDAI ≤250) - The criteria for treatment discontinuation in case of flare/fistula relapse were changed to allow the investigator to decide whether there was clinical benefit for the patient instead of restricting the chance to continue to those who meet restricted definition of clinical response and to take a more global approach to clinical improvement of patients, as these patients may have had no other options.
21 January 2021	- Luminal inflammatory flare was differentiated from fistula relapse as patients who presented a luminal inflammatory flare without fistula relapse could receive antiinflammatory therapy as per Standard of Care (SOC) to treat luminal flare based on clinician judgement while continuing the same spesolimab maintenance dose - In case of restricted physical visits to the site during the COVID-19 pandemic the investigator could discuss with Boehringer Ingelheim to continue the trial treatment and trial medication could be shipped to the patient's home if acceptable according to local law and regulations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This trial was terminated early due to BI's decision to terminate the development of spesolimab in fistulising and fibrostenotic Crohn's disease.

Notes: