Clinical trial results:
An open-label, single arm, long term trial of Spesolimab treatment in patients with Palmoplantar Pustulosis (PPP) who have completed previous BI Spesolimab trials

Summary

EudraCT number	2020-000189-41
Trial protocol	HU BE FR PL CZ GB DE
Global end of trial date	15 May 2023

Results information

Result version number	v1 (current)
This version publication date	30 May 2024
First version publication date	30 May 2024

Trial information

Trial identification

Sponsor protocol code	1368-0024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04493424
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	27 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2023
Global end of trial reached?	Yes
Global end of trial date	15 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the trial were to evaluate the long-term safety and efficacy of spesolimab in patients with PPP, who have completed
previous spesolimab trials and are qualified for entry in this trial.

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Japan: 35
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	112
EEA total number of subjects	39

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)	93
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was a phase II, open-label, single arm, to test the safety and efficacy of long-term treatment with Spesolimab in patients with Palmoplantar Pustulosis (PPP) who took part in previous studies with Spesolimab

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:

No blinding

Arms

Arm title	Spesolimab (BI 655130)

Arm description:

The patients were administered 600 milligram (mg) Spesolimab (BI 655130) prefilled syringes subcutaneously in thighs or abdomen every 4 weeks for up to 5 years (260 weeks). Patients were to continue the treatment until they no longer benefited, either under patient opinion or investigator assessment, or withdrawal of consent, whichever occurred first.

Arm type	Single arm, interventional
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:

600 mg of spesolimab was administered subcutaneously as a solution for injection.

Number of subjects in period 1[1]	Spesolimab (BI 655130)
Started	108
Completed	0
Not completed	108
Consent withdrawn by subject	9
Termination of the trial by the sponsor	89
Adverse event, non-fatal	5
Lost to follow-up	2
Lack of efficacy	3

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: Originally, 112 patients were enrolled in the parent trial (1368-0016), however 4 patients did not meet the entry/eligibility criteria for this extension trial and were therefore excluded.

Baseline characteristics

Reporting groups	
Reporting group title	Spesolimab (BI 655130)
Reporting group description:	
The patients were administered 600 milligram (mg) Spesolimab (BI 655130) prefilled syringes subcutaneously in thighs or abdomen every 4 weeks for up to 5 years (260 weeks). Patients were to continue the treatment until they no longer benefited, either under patient opinion or investigator assessment, or withdrawal of consent, whichever occurred first.	

Reporting group values	Spesolimab (BI 655130)	Total	
Number of subjects	108	108	
Age categorical			
The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130).			
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)	89	89	
From 65-84 years	19	19	
85 years and over	0	0	
Age Continuous			
The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130).			
Units: years			
arithmetic mean	55.2		
standard deviation	± 10.3	-	
Sex: Female, Male			
The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130).			
Units: Participants			
Female	75	75	
Male	33	33	
Race (NIH/OMB)			
The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	39	39	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	69	69	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			

The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130).			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	108	108	
Unknown or Not Reported	0	0	
Palmoplantar Pustulosis Area and Severity Index (PPP ASI)			
The PPP ASI is an investigator assessment of the extent and severity of pustular and plaque lesions on the palms and soles. The index is a linear combination of the percent of surface area of skin affected on the palms and soles of the body and the severity of erythema (E), pustules (P) and scaling / desquamation (D), providing a numeric score for the overall PPP disease state, ranging from 0 (best outcome) to 72 (worst outcome). The safety analysis set for maintenance treatment (SAF-MT): Included all patients who received at least one dose of the maintenance treatment Spesolimab (BI 655130).			
Units: Score in a scale			
arithmetic mean	24.97		
standard deviation	± 10.93	-	

End points

End points reporting groups

Reporting group title	Spesolimab (BI 655130)

Reporting group description:

The patients were administered 600 milligram (mg) Spesolimab (BI 655130) prefilled syringes subcutaneously in thighs or abdomen every 4 weeks for up to 5 years (260 weeks). Patients were to continue the treatment until they no longer benefited, either under patient opinion or investigator assessment, or withdrawal of consent, whichever occurred first.

Primary: Number of subjects with treatment-emergent adverse events (TEAEs)

End point title	Number of subjects with treatment-emergent adverse events (TEAEs)[1]

End point description:

TEAEs were defined as all AEs occurring between start of treatment in this extension trial and the end of its residual effect period. Adverse events that started before first intake of trial medication in the extension trial and deteriorated under treatment during the extension trial were also considered as 'treatment-emergent'.
Safety analysis set for maintenance treatment (SAF-MT) included those receiving at least one dose of maintenance treatment.

End point type	Primary

End point timeframe:

From first administration of study drug until last administration of study drug + 112 days, up to 869 days.

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: This endpoint was analyzed descriptively. Thus, no statistical hypotheses were tested.

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Participants				
Number of subjects with TEAEs	96			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Palmoplantar Pustulosis Area and Severity Index (PPP ASI) from baseline in parent trial (NCT04015518) at Week 48

End point title	Percent change in Palmoplantar Pustulosis Area and Severity Index (PPP ASI) from baseline in parent trial (NCT04015518) at Week 48

End point description:

Percent change in PPP ASI from baseline in parent trial is reported, derived from a linear combination of the percent of surface area of skin affected on the palms and soles, and severity of erythema (E), pustules (P) and scaling/desquamation (D), providing a numeric score for the overall PPP disease state, ranging from 0 (best outcome) to 72 (worst outcome), calculated as: PPP ASI = [(E+P+D) Area x 0.2 (right palm)] + [(E+P+D) Area x 0.2 (left palm)] + [(E+P+D) Area x 0.3 (right sole)] + [(E+P+D) Area

x 0.3 (left sole)]. The weighted sum of the scores obtained for Erythema (E), Pustules (P), desquamation (D) was based on a score range from 0: None to 4: Very severe, and the area affected on a range from 0 (0%) to 6 (90-100%). Percent change was calculated as: (PPP ASI at Week X - PPP ASI at baseline in parent trial)/PPP ASI at baseline in parent trial * 100%. Safety analysis set for maintenance treatment (SAF-MT) included those receiving at least one dose of maintenance treatment.

End point type	Secondary

End point timeframe:

Week 0 (baseline) and Week 48

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: Percent change				
arithmetic mean (standard deviation)				
Week 48	-76.85 (± 22.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with PPP ASI50 compared to baseline in parent trial (NCT04015518) at Week 96

End point title	Proportion of patients with PPP ASI50 compared to baseline in parent trial (NCT04015518) at Week 96

End point description:

Proportion of patients achieving a 50% decrease in PPP ASI compared to baseline in the parent trial is reported, calculated as a linear combination of the percent of surface area of skin affected on the palms and soles, and severity of erythema, pustules and scaling/desquamation, providing a numeric score for the overall PPP disease state, ranging from 0 (best outcome) to 72 (worst outcome), calculated as: PPP ASI = [(E+P+D) Area x 0.2 (right palm)] + [(E+P+D) Area x 0.2 (left palm)] + [(E+P+D) Area x 0.3 (right sole)] + [(E+P+D) Area x 0.3 (left sole)]. The weighted sum of the scores obtained for Erythema (E), Pustules (P), desquamation (D) were based on a range from 0: None to 4: Very severe, and the area affected from 0 (0%) to 6 (90-100%). Proportion was calculated as: Patients with PPP ASI50 at Week X/number of evaluable patients at Week X. Non-response imputation was used for missing data. SAF-MT included patients who received at least one dose of maintenance treatment.

End point type	Secondary

End point timeframe:

Week 0 (baseline) and Week 96

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Proportion of participants				
number (confidence interval 95%)	0.683 (0.530 to 0.804)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) at Week 48

End point title	Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) at Week 48

End point description:

Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) is reported. The Palmoplantar Pustulosis Physician Global Assessment (PPP PGA) was used to assess the patient's skin presentation on the palms and soles. The investigator scored the individual components (erythema, pustules and scaling/crusting) from 0 to 4 as clear, almost clear, mild, moderate or severe. The PPP PGA was analyzed as PPP PGA total score including erythema, pustules and scaling, and as PPP PGA pustules score for pustules only. Number of patients with PPP PGA of 0/1 at Week X/number of evaluable patients at Week X was calculated. NRI approach was used for missing data imputation. SAF-MT included patients who received at least one dose of maintenance treatment.
The PPP PGA total score was derived as the mean of all individual components:
0 = If mean=0, for all three components:
1 = If 0 < mean <1.5
2 = If 1.5 <= mean <2.5
3 = If 2.5 <= mean <3.5
4 = If mean >=3.5

End point type	Secondary

End point timeframe:

Week 48

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Proportion				
number (confidence interval 95%)				
Week 48	0.720 (0.625 to 0.799)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) at week 96

End point title	Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) at week 96

End point description:

Proportion of patients with PPP PGA of 0 (clear) or 1 (almost clear) is reported. The Palmoplantar Pustulosis Physician Global Assessment (PPP PGA) was used to assess the patient's skin presentation on the palms and soles. The investigator scored the individual components (erythema, pustules and scaling/crusting) from 0 to 4 as clear, almost clear, mild, moderate or severe. The PPP PGA was analyzed as PPP PGA total score including erythema, pustules and scaling, and as PPP PGA pustules score for pustules only. Number of patients with PPP PGA of 0/1 at Week X/number of evaluable patients at Week X was calculated. NRI approach was used for missing data imputation. SAF-MT included patients who received at least one dose of maintenance treatment.
The PPP PGA total score was derived as the mean of all individual components:
0 = If mean=0, for all three components:
1 = If 0 < mean <1.5
2 = If 1.5 <= mean <2.5
3 = If 2.5 <= mean <3.5
4 = If mean >=3.5

End point type	Secondary

End point timeframe:

Week 96

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Proportion				
number (confidence interval 95%)	0.707 (0.555 to 0.824)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Palmoplantar Pustulosis Area and Severity Index (PPP ASI) from baseline in parent trial (NCT04015518) at Week 96

End point title	Percent change in Palmoplantar Pustulosis Area and Severity Index (PPP ASI) from baseline in parent trial (NCT04015518) at Week 96

End point description:

Percent change in PPP ASI from baseline in parent trial is reported, derived from a linear combination of the percent of surface area of skin affected on the palms and soles, and severity of erythema (E), pustules (P) and scaling/desquamation (D), providing a numeric score for the overall PPP disease state, ranging from 0 (best outcome) to 72 (worst outcome), calculated as: PPP ASI = [(E+P+D) Area x 0.2 (right palm)] + [(E+P+D) Area x 0.2 (left palm)] + [(E+P+D) Area x 0.3 (right sole)] + [(E+P+D) Area x 0.3 (left sole)]. The weighted sum of the scores obtained for Erythema (E), Pustules (P), desquamation (D) was based on a score range from 0: None to 4: Very severe, and the area affected on a range from 0 (0%) to 6 (90-100%). Percent change was calculated as: (PPP ASI at Week X - PPP ASI at baseline in parent trial)/PPP ASI at baseline in parent trial * 100%. Safety analysis set for maintenance treatment (SAF-MT) included those receiving at least one dose of maintenance treatment.

End point type	Secondary

End point timeframe:

Week 0 (baseline) and Week 96

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Percent change				
arithmetic mean (standard deviation)				
Week 96	-77.58 (± 18.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with PPP ASI50 compared to baseline in parent trial (NCT04015518) at Week 48

End point title	Proportion of patients with PPP ASI50 compared to baseline in parent trial (NCT04015518) at Week 48

End point description:

Proportion of patients achieving a 50% decrease in PPP ASI compared to baseline in the parent trial is reported, calculated as a linear combination of the percent of surface area of skin affected on the palms and soles, and severity of erythema, pustules and scaling/desquamation, providing a numeric score for the overall PPP disease state, ranging from 0 (best outcome) to 72 (worst outcome), calculated as: PPP ASI = [(E+P+D) Area x 0.2 (right palm)] + [(E+P+D) Area x 0.2 (left palm)] + [(E+P+D) Area x 0.3 (right sole)] + [(E+P+D) Area x 0.3 (left sole)]. The weighted sum of the scores obtained for Erythema (E), Pustules (P), desquamation (D) were based on a range from 0: None to 4: Very severe, and the area affected from 0 (0%) to 6 (90-100%). Proportion was calculated as: Patients with PPP ASI50 at Week X/number of evaluable patients at Week X. Non-response imputation was used for missing data. SAF-MT included patients who received at least one dose of maintenance treatment.

End point type	Secondary

End point timeframe:

Week 0 (baseline) and Week 48

End point values	Spesolimab (BI 655130)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Proportion of participants				
number (confidence interval 95%)				
Week 48	0.770 (0.678 to 0.842)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of study drug until last administration of study drug + 112 days, up to 869 days.

Adverse event reporting additional description:

Safety analysis set for maintenance treatment (SAF-MT): This patient set includes all patients who received at least one dose of the maintenance treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Spesolimab (BI 655130)

Reporting group description:

Patients were administered 600 milligram (mg) Spesolimab (BI 655130) prefilled syringes subcutaneously in thighs or abdomen every 4 weeks for up to 5 years (260 weeks). Patients were to continue the treatment until they no longer benefited, either under patient opinion or investigator assessment, or withdrawal of consent, whichever occurred first.

Serious adverse events	Spesolimab (BI 655130)		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 108 (17.59%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fall				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Hypertrophic cardiomyopathy				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure chronic				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tricuspid valve incompetence				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Epilepsy				

subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial aneurysm			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Guillain-Barre syndrome			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine polyp			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertension			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Scleroderma			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chondropathy			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gangrene			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraspinal abscess			

subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxic shock syndrome			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	1 / 108 (0.93%)		
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 (BI 655130)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 108 (71.30%)		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	9		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	20 / 108 (18.52%)		
occurrences (all)	171		

Injection site induration subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Injection site warmth subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Injection site pruritus subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all)	6 / 108 (5.56%) 22 14 / 108 (12.96%) 21 6 / 108 (5.56%) 47 9 / 108 (8.33%) 44 6 / 108 (5.56%) 38 12 / 108 (11.11%) 54		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Palmoplantar pustulosis subjects affected / exposed occurrences (all)	 9 / 108 (8.33%) 9 7 / 108 (6.48%) 9 8 / 108 (7.41%) 9		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 11 / 108 (10.19%) 11 12 / 108 (11.11%) 16		
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 108 (5.56%) 8		
Nasopharyngitis subjects affected / exposed occurrences (all)	16 / 108 (14.81%) 22		
COVID-19 subjects affected / exposed occurrences (all)	30 / 108 (27.78%) 33		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2020	With global amendment 1, exclusion criterion no. 7 was aligned with the parent trial 1368-0016: The timeframe for the history of malignancy was changed from "at screening" to "within 5 years prior to screening in parent trial" to avoid losing patients with an older history of malignancy from the parent trial. Restrictions on previous and concomitant medications were aligned with the parent trial 1368-0016: the use of non-steroidal anti-inflammatory drugs and acetaminophen/paracetamol was changed from "not allowed/restricted use" to "allowed but recommended to be maintained at stable dose and not to change medication". Phototherapy, previously not allowed, was now allowed if palms and soles were exempted. The benefit-risk assessment of spesolimab in the context of the COVID 19 pandemic was added, with the administration of spesolimab still considered favourable. To mitigate potential risks regarding the COVID-19 pandemic, every patient was to be assessed thoroughly, and individual benefit-risk assessments were made prior to trial entry and during the trial by the investigator in respect of SARSCoV- 2 infection. A suspected or diagnosed COVID-19 infection was to be treated according to the standard of care and trial treatment could be interrupted. In case of a confirmed infection, trial treatment was to be discontinued immediately and appropriate measures for monitoring, treatment and quarantine were to be implemented. A patient could resume trial treatment following recovery from a SARS-CoV-2 infection if he/she was expected to derive clinical benefit, as agreed between the investigator and sponsor.
22 October 2021	With global amendment 2, the description of adverse events (AE) collection was corrected so that after the first administration of trial drug in the extension trial 1368-0024 no further AE updates should be done in the parent trial. The rationale for this change was that the first administration of trial drug in the extension trial was defined as end of study (EoS) for the parent trial and after EoS no further updates were to be made for the parent trial. Regarding the assessment of local tolerability, it was added that any observed local tolerability reaction, e.g. "swelling", "induration", "heat", "redness", "pain", and other findings were to be reported as an AE.

23 June 2022	Global amendment 3, Part 2: Restrictions on previous and concomitant medications were updated: o To align with the parent trial, other systemic immunomodulating treatment was no longer prohibited for other conditions than palmoplantar pustulosis (PPP) o Topical treatment for PPP was now prohibited on all areas affected by PPP (even extended beyond palms/soles) to cover also cases where the topical treatment for PPP extended beyond palms/soles o Topical corticosteroids for other conditions than PPP were now prohibited on all regions affected by PPP to cover cases where topical corticosteroids were applied to regions other than palms/soles and where PPP could have extended to o Topical treatments (other than topical corticosteroids) for other conditions than PPP were now allowed if they did not affect the PPP assessment. This was added to prohibit topical treatments only to regions that could have affected PPP assessment. The terms 'suspected or diagnosed' and 'confirmed' COVID-19 infection were further differentiated to 'suspected or diagnosed, non-severe and non-serious' and 'confirmed severe (according to Rheumatology Common Toxicity Criteria, RCTC grading) and/or serious' COVID-19 infection.
23 June 2022	Global amendment 3, Part 1: With global amendment 3, the exclusion of patients with acute demyelinating neuropathy (exclusion criterion no. 18) was added as mitigation strategy to account for the newly added potential risk "peripheral neuropathy" which was derived from the three cases reported as Guillain-Barré syndrome by the investigator in spesolimab trials. The cases were considered as peripheral neuropathy by an independent external neurologist expert panel. In addition, "peripheral neuropathy" was added to the table including risks, summary of data, and mitigation strategies, described under implications of specific events, and added as adverse event of special interest. With regard to patients who met the trial treatment discontinuation criteria, it was updated that these patients could not only be discontinued from trial treatment but had to be discontinued if discontinuation criteria were met at 2 consecutive visits. This was to ensure that patients who no longer benefit from the trial drug discontinued the trial and received treatment according to local standard of care. It was clarified that patients who needed to take rescue medication or who took prohibited medication had to be discontinued from the trial.

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.

The trial was prematurely discontinued due to the sponsor's (Boehringer Ingelheim) decision to terminate the clinical program studying spesolimab in patients with PPP. This decision was not based on any safety finding in the clinical trials.

Notes: