Clinical trial results:
A pilot, open-label, single arm, multicenter study to evaluate safety, tolerability, pharmacokinetics and efficacy of intravenous administrations of emapalumab, an anti-interferon gamma (anti-IFN) monoclonal antibody, in patients with systemic Juvenile Idiopathic Arthritis (sJIA) or Adult-onset Still's Disease (AOSD) developing Macrophage Activation Syndrome/secondary HLH (MAS/sHLH)

Summary

EudraCT number	2016-004223-23
Trial protocol	IT FR GB ES NL
Global end of trial date	19 May 2020

Results information

Result version number	v1 (current)
This version publication date	23 December 2021
First version publication date	23 December 2021
Summary attachment (see zip file)	Long-term follow-up additional information (Summary attachment_long-term follow-up additional information.pdf)

Trial information

Trial identification

Sponsor protocol code	NI-0501-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03311854
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum AG
Sponsor organisation address	Messeplatz 10, Basel, Switzerland, 4058
Public contact	Veronica Asnaghi, MD, Swedish Orphan Biovitrum AG, 41 61 508 72 13, veronica.asnaghi@sobi.com
Scientific contact	Veronica Asnaghi, MD, Swedish Orphan Biovitrum AG, 41 61 508 72 13, veronica.asnaghi@sobi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002031-PIP01-16
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	29 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 May 2020
Global end of trial reached?	Yes
Global end of trial date	19 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To describe the pharmacokinetic profile of emapalumab
- To confirm the proposed dosing regimen of emapalumab
- To evaluate the safety and tolerability profile of intravenous administrations of emapalumab
- To assess the efficacy of emapalumab
- To assess the levels of relevant pharmacodynamic markers
- To assess other potential disease markers
- To assess the immunogenicity of emapalumab

Protection of trial subjects:

Written informed consent/assent was obtained from all subjects or their parents/legal guardian prior to enrolment into the study, as dictated by the Declaration of Helsinki. Of note, one subject (aged 14 years at study entry) was unable to provide assent because their clinical condition required admission to the intensive care unit; in this case, the parents provided informed consent before enrolment in the study, and assent from the subject was acquired retrospectively.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	14
EEA total number of subjects	9

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)	8
Adolescents (12-17 years)	5
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 16 subjects were screened for this study. Fourteen subjects were enrolled and all completed the study; no subject was withdrawn from the study after the start of treatment with emapalumab.

Pre-assignment

Screening details:

The study population could comprise subjects of both genders with MAS in confirmed sJIA/adult-onset Still's disease (AOSD) or high presumption of sJIA and having shown an inadequate response to high dose intravenous (i.v.) glucocorticoid treatment.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study; no blinding occurred.
Note regarding baseline period:
Data for the baseline demographic characteristics were obtained prior to the start of the treatment period.

Arms

Arm title	All treated population

Arm description:

The all treated population included all subjects who received any part of an infusion of emapalumab.

Arm type	Experimental
Investigational medicinal product name	Emapalumab
Investigational medicinal product code	
Other name	NI-0501
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Infusion

Dosage and administration details:

Emapalumab was administered at an initial dose of 6 mg/kg by intravenous infusion. Emapalumab treatment continued at a dose of 3 mg/kg, every 3 days until study day 15, and then twice-a-week for an additional 2 weeks, i.e., until study day 28. The emapalumab regimen could be adapted (the frequency between infusions shortened, the dose increased, or the treatment prolonged beyond 4 weeks) upon assessment of a favourable benefit-risk profile. The treatment period was followed by a 4-week off-drug follow-up period (up to at least Week 8).

Number of subjects in period 1	All treated population
Started	14
Completed	14

Period 2	
Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study; no blinding occurred.

Arms

Arm title	All treated population

Arm description:

The all treated population included all subjects who received any part of an infusion of emapalumab.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	All treated population
Started	14
Completed	14

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period

Reporting group description:

All subjects who received any part of an infusion of emapalumab.
Note that data for the baseline demographic characteristics were obtained prior to the start of the treatment period.

Reporting group values	Treatment period	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
Children (2-11 years)	8	8	
Adolescents (12-17 years)	5	5	
Adults (18-64 years)	1	1	
Age continuous Units: years			
arithmetic mean	9.9		
standard deviation	± 6.6	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	4	4	
Race Units: Subjects			
Black or African American	2	2	
White	11	11	
Unknown or not reported	1	1	

End points

End points reporting groups

Reporting group title	All treated population
Reporting group description:	
The all treated population included all subjects who received any part of an infusion of emapalumab.	
Reporting group title	All treated population
Reporting group description:	
The all treated population included all subjects who received any part of an infusion of emapalumab.	
Subject analysis set title	All treated population
Subject analysis set type	Full analysis
Subject analysis set description:	
The all treated population included all subjects who received any part of an infusion of emapalumab.	
Subject analysis set title	All treated population: Study Day 0 (pre-dose)
Subject analysis set type	Full analysis
Subject analysis set description:	
Levels measured pre-dose on Study Day 0 in subjects. Study Day 0 corresponds to the first treatment date.	
Subject analysis set title	All treated population: 4-week Follow-up Visit/EoS
Subject analysis set type	Full analysis
Subject analysis set description:	
Levels measured at the 4-week follow-up visit/EoS in subjects.	

Primary: Incidence, Severity, Causality, and Outcomes of AEs (Serious and Non-serious)

End point title	Incidence, Severity, Causality, and Outcomes of AEs (Serious and Non-serious)[1]
End point description:	
End point type	Primary
End point timeframe:	
Up to end of study	

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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects				
Subjects with a TEAE	13			
Subjects with a serious TEAE	6			
Subjects with a severe TEAE	2			
Subjects with a moderate TEAE	10			
Subjects with a mild TEAE	13			
Subjects with a TEAE related to emapalumab	4			
Subjects with a TEAE unrelated to emapalumab	13			

Subjects with a recovered/resolved TEAE	13			
Subjects with a not recovered or resolved TEAE	3			
Subjects with a recovering/resolving TEAE	1			
Subjects with a TEAE with an unknown outcome	1			

Statistical analyses

No statistical analyses for this end point

Primary: Evolution of Laboratory Parameters

End point title	Evolution of Laboratory Parameters[2]

End point description:

Shifts from baseline in the following MAS-relevant laboratory parameters are reported:
- Leukocytes
- Platelets
- Lactate dehydrogenase (LDH)
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Ferritin
- C-reactive protein (CRP)
- Activated partial thromboplastin time (aPTT)
- Prothrombin time (PT)
- D-dimer
- Fibrinogen

Laboratory parameters are described as:
- Low, within the reference range, or high at baseline
- Low, within the reference range, or high at 4th Week Follow-Up/EOS

In the categories below, the first description given is the level at baseline; the second is the level at 4th Week Follow-Up/EOS (i.e., shift from baseline to 4th Week Follow-Up/EOS).

End point type	Primary

End point timeframe:

Up to 4th Week Follow-Up/EOS

Notes:

[2] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects				
Leukocytes: high to within	2			
Leukocytes: low to within	4			
Leukocytes: low to high	2			
Platelets: high to within	1			
Platelets: low to within	6			
Platelets: low to high	3			
LDH: high to within	6			
ALT: high to within	10			

ALT: high to low	1			
AST: high to within	11			
Ferritin: high to within	11			
Ferritin: high to low	2			
CRP: high to within	9			
aPTT: high to within	1			
aPTT: high to low	1			
aPTT: within to low	3			
aPTT: low to within	1			
aPTT: low to high	1			
PT: high to within	5			
PT: high to low	1			
PT: within to low	3			
PT: low to within	1			
D-dimer: high to within	8			
Fibrinogen: high to within	1			
Fibrinogen: within to high	1			
Fibrinogen: low to within	5			
Fibrinogen: low to high	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Withdrawn Due to Safety Reasons

End point title	Number of Subjects Withdrawn Due to Safety Reasons[3]

End point description:

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[3] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Achieving MAS Remission at Week 8 After Initiation of

Emapalumab Treatment

End point title	Number of Subjects Achieving MAS Remission at Week 8 After Initiation of Emapalumab Treatment[4]

End point description:

Remission from MAS was evaluated according to the following criteria:
Resolution of clinical signs and symptoms according to the investigator (MAS clinical signs and symptoms activity score ≤ 1)
and
Normalization of laboratory parameters relevant to MAS, as follows:

- WBC count and platelet count above the LLN.
- LDH below 1.5 × the ULN.
- ALT and AST both below 1.5 × the ULN.
- Fibrinogen higher than 100 mg/dL.
- Ferritin levels decreased by at least 80 % from values at screening or baseline (whichever was higher) or below 2000 ng/mL, whichever was lower.

Out of the 14 patients in the all treated population, 11 patients (78.6%) met the MAS remission criteria at Week 8 (95% CI: 49.2 to 95.3%).

End point type	Primary

End point timeframe:

Up to Week 8

Notes:

[4] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	11			

Statistical analyses

No statistical analyses for this end point

Primary: Time to First MAS Remission

End point title	Time to First MAS Remission[5]

End point description:

Time to the first MAS remission is calculated from the date of first emapalumab infusion until the date of first MAS remission.

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[5] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Days				
median (confidence interval 95%)	25 (19 to 56)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects for Whom Glucocorticoids Could be Permanently Tapered at Any Time During the Study

End point title	Number of Subjects for Whom Glucocorticoids Could be Permanently Tapered at Any Time During the Study[6]

End point description:

Permanently tapering by at least 50% of the equivalent dose of prednisone. This was defined as achieving reduction of 50% of the baseline dose [SD0] and maintaining the reduction until the end of study.
A total of 12 patients (85.7%) permanently tapered glucocorticoids at any time during the study (95% CI: 57.2 to 98.2%).

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[6] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	12			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Achievement of Permanent Glucocorticoids Tapering

End point title	Time to Achievement of Permanent Glucocorticoids Tapering[7]

End point description:

Time to first achievement of permanent glucocorticoid tapering by at least 50% of the equivalent dose of prednisone administered at emapalumab treatment start (SD0).

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[7] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Days				
median (confidence interval 95%)	14.5 (4 to 28)			

Statistical analyses

No statistical analyses for this end point

Primary: Survival at End of Study

End point title	Survival at End of Study[8]

End point description:

Number of subjects alive at the end of the study

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[8] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	14			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Withdrawn From the Study Due to Lack of Efficacy

End point title	Number of Subjects Withdrawn From the Study Due to Lack of Efficacy[9]

End point description:

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[9] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Levels of Emapalumab Concentration

End point title	Levels of Emapalumab Concentration[10]

End point description:

Levels of emapalumab concentration are provided for the following time points:
- Study Day 0 (pre-dose)
- Study Day 0 (post-dose)
- Week 4 Visit 2 (pre-dose)
- Week 4 visit 2 (post-dose)
- 4-week follow-up visit/EoS

Note: Emapalumab concentrations were below the detection limit for all subjects at SD0, except for one subject in whom the emapalumab concentration (pre-dose) was 62108.4 µg/L. It should be noted that on SD1, the measurement results of emapalumab were below the detection limit for that subject; it could not be ruled out that the samples from SD0 and SD1 for this subject were interchanged.

End point type	Primary

End point timeframe:

Up to Week 8

Notes:

[10] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14[11]			
Units: ug/L				
arithmetic mean (standard deviation)				
Study Day 0 (pre-dose)	5455.444 (± 19985.0660)			
Study Day 0 (post-dose)	104740.254 (± 20994.1054)			
Week 4 Visit 2 (pre-dose)	115472.076 (± 58676.7953)			
Week 4 Visit 2 (post-dose)	212900.657 (± 87466.3031)			
4-week follow-up Visit/EoS	46447.462 (± 33657.0174)			

Notes:

[11] - Note: the Week 4 Visit 2 (post-dose) emapalumab concentration levels were based on 7 subjects.

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacodynamic Parameters

End point title	Pharmacodynamic Parameters[12]

End point description:

Levels of total interferon-gamma (free interferon-gamma and interferon-gamma bound to emapalumab), CXCL9 and CXCL10

End point type	Primary

End point timeframe:

Up to Week 8

Notes:

[12] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population: Study Day 0 (pre-dose)	All treated population: 4-week Follow-up Visit/EoS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: ng/L				
arithmetic mean (standard deviation)				
Total interferon-gamma	425.528 (± 1191.8391)	2132.656 (± 2967.4920)		
CXCL9	21986.010 (± 29405.8787)	255.654 (± 596.4149)		
CXCL10	7935.418 (± 9115.2857)	639.102 (± 1058.9589)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Demonstrated a Presence of Circulating Antibodies Against Emapalumab to Determine Immunogenicity

End point title	Number of Subjects Who Demonstrated a Presence of Circulating Antibodies Against Emapalumab to Determine Immunogenicity[13]

End point description:

The presence of circulating antibodies against emapalumab was inferred by positive results for anti-drug antibodies (ADAs).

End point type	Primary

End point timeframe:

Up to end of study

Notes:

[13] - 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: All endpoint variables in the study are analyzed descriptively considering the nature of this pilot study.

End point values	All treated population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All TEAEs reported by the subjects or their relatives or observed by the Investigator or their staff during the clinical study from the first emapalumab administration up to and including the end-of-study visit were recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	All treated population

Reporting group description:

The all treated population included all subjects who received any part of an infusion of emapalumab.

Serious adverse events	All treated population		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 14 (42.86%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiopulmonary failure			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericarditis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Juvenile myoclonic epilepsy			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pneumatosis intestinalis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Still's disease			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All treated population		
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 14 (92.86%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
Thrombophlebitis superficial subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
General disorders and administration site conditions Catheter site thrombosis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Chest pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Condition aggravated subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Injection site reaction subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Pyrexia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 4		
Secretion discharge subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Respiratory, thoracic and mediastinal disorders Cough			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	3		
Pharyngeal erythema			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Tachypnoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Investigations			
Adenovirus test positive			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
BK polyomavirus test positive			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cytomegalovirus test positive			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Respirovirus test positive			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Axonal neuropathy			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	4		
Lethargy			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Seizure			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tympanic membrane hyperaemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye disorders			
Eye oedema			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye pruritus			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hepatobiliary disorders			

Cholelithiasis subjects affected / exposed occurrences (all) Hepatic steatosis subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		
Skin and subcutaneous tissue disorders Acanthosis nigricans subjects affected / exposed occurrences (all) Dermatitis diaper subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash erythematous subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) Rash pruritic subjects affected / exposed occurrences (all) Skin ulcer subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 3 / 14 (21.43%) 3 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		
Musculoskeletal and connective tissue disorders Tenosynovitis subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Infections and infestations			

Cytomegalovirus infection subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Cytomegalovirus infection reactivation subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Viral infection subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 January 2020	Protocol V2.0: • The sponsor changed from Novimmune to Swedish Orphan Biovitrum AG (Sobi AG). • The protocol was updated to reflect NI-0501 being assigned the international nonproprietary name "emapalumab". • The amendment allowed the inclusion of MAS patients with AOSD and description of Yamaguchi disease criteria added in Appendix E. • The study, running according to twin protocols in North America and Europe, was updated to enroll approximately 12 patients across these areas, with a minimum of 10 patients diagnosed with sJIA. • The maximum patient age was removed. • An objective list of clinical symptoms for response evaluation was implemented, in addition to laboratory parameters. • It was added that emapalumab treatment could be initiated upon discontinuation of tocilizumab, canakinumab, and TNF inhibitors. • Continuation of anakinra was allowed if started at least 3 days before initiation of emapalumab, and methotrexate was permitted to be continued if ongoing as treatment for the underlying disease. Introduction of concomitant medication during the study was updated and specified. • Additional modifications were implemented to ensure clearer instructions were provided to the investigators (e.g., for AE reporting) and to correct obvious mistakes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported