Clinical trial results:
A multicentre study for the long-term follow-up of HLH patients who received treatment with NI-0501, an anti-interferon gamma monoclonal antibody

Summary

EudraCT number	2012-005753-23
Trial protocol	IT CZ DE ES AT SE GB FR NL
Global end of trial date	18 May 2021

Results information

Result version number	v1 (current)
This version publication date	21 July 2022
First version publication date	21 July 2022

Trial information

Trial identification

Sponsor protocol code	NI-0501-05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02069899
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 111015

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum
Sponsor organisation address	12 Chemin des Aulx, Plan les Ouates, Switzerland, 1228
Public contact	Radmila Kanceva/Senior Medical Director Immunology, Sobi AG , +46 8697 2000, Radmila.Kanceva@sobi.com
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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	09 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 May 2021
Global end of trial reached?	Yes
Global end of trial date	18 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To monitor the long-term safety profile of NI-0501, hereafter referred to as emapalumab
• To assess hemophagocytic lymphohistiocytosis (HLH) participants' survival after emapalumab treatment
• To assess duration of response to emapalumab treatment (i.e., maintenance of HLH control)
• To assess post-hematopoietic stem cell transplantation (HSCT) outcome measures, if applicable
• To assess background disease activity in participants with secondary forms of HLH
• To study the elimination profile of emapalumab
• To evaluate the pharmacodynamic effects (levels of circulating total interferon gamma [IFNγ])
• To assess the immunogenicity of emapalumab

Protection of trial subjects:

The informed consent form had to be signed by the participant (as required by local law) or by the participant's parents or legally authorized representative prior to any study-related procedures, with the assent of participants who were deemed suitable to provide it, as applicable.
Written informed consent/assent was obtained from all participants or their parents/legally authorized representative prior to enrolment into the study, as dictated by the Declaration of Helsinki.
The method of obtaining and documenting informed consent and the contents of the consent complied with International Conference on Harmonisation-Good Clinical Practice and all applicable regulatory requirement(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	58
EEA total number of subjects	30

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)	28
Children (2-11 years)	24
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:

The Enrolled-04 cohort comprised 37 patients treated in Study NI-0501-04, and the Enrolled-06 cohort comprised 14 patients treated in Study NI-0501-06. The Enrolled-CU cohort comprised 7 patients who had previously been treated through a compassionate use (CU) request and were not treated in either Study NI-0501-04 or NI-0501-06.

Pre-assignment

Screening details:

Participants with HLH who had received at least 1 dose of emapalumab in the context of a previous emapalumab clinical study (NI-0501-04 or NI-0501-06) in which no long-term follow-up was planned, and participants who received emapalumab through CU were enrolled in the current study (NI-0501-05).

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Enrolled-04 Cohort

Arm description:

Participants enrolled in Study NI-0501-04 were invited to participate in long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
In Study NI-0501-04, participants received emapalumab for 4 to 8 weeks. After the treatment period, participants could have undergone HSCT.
Participants for whom an appropriate donor was not identified by Week 8, or in cases where HSCT was delayed for reasons unrelated to the administration of emapalumab, could continue receiving treatment with emapalumab beyond the foreseen 8 weeks in Study NI-0501-05 at the request of the investigator, providing a favorable benefit/risk assessment of treatment was established.
Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study, or an adjusted dose was administered.

Arm type	Interventional for selected participants
Investigational medicinal product name	Emapalumab
Investigational medicinal product code	
Other name	NI-0501
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in the context of Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study in which the participant was enrolled, or an adjusted dose was administered, if necessary.

Arm title	Enrolled-06 Cohort

Arm description:

All participants who received at least 1 dose of emapalumab and were monitored for at least 4 weeks after the last drug administration in Study NI-0501-06 were invited to participate for long-term follow-up for 1 year after the last administration of emapalumab.
Participants did not receive emapalumab in the current study (NI-0501-05).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Enrolled-CU Cohort

Arm description:

In exceptional cases, at the spontaneous request of a treating physician, compassionate use (CU) treatment with emapalumab was granted to participants who had exhausted all possible treatment options and who could not be enrolled in a clinical study. All participants who received at least 1 dose of emapalumab under these circumstances were invited to participate for long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
Participants could have continued treatment with emapalumab in the context of the current Study (NI-0501-05) while stem cell donor search was ongoing, or if the investigator assessed that continuation of treatment was beneficial.

Arm type	Interventional for selected participants
Investigational medicinal product name	Emapalumab
Investigational medicinal product code	
Other name	NI-0501
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in the context of Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study in which the participant was enrolled, or an adjusted dose was administered, if necessary.

Number of subjects in period 1	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort
Started	37	14	7
Treated with emapalumab in current study	22 [1]	0 [2]	5
Completed	24	13	4
Not completed	13	1	3
Consent withdrawn by subject	2	-	-
Adverse event, non-fatal	6	-	1
Serious adverse event, fatal	1	-	-
No matching reasons found	-	1	-
Withdrew to receive emapalumab in Study NI-0501-CU	-	-	1
Lost to follow-up	1	-	1
Patient transferred to receive transplant	1	-	-
Early termination	1	-	-
Patient death	1	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 22 participants in the Enrolled-04 Cohort were treated with emapalumab in the current study; being treated with emapalumab was not a criterion for study completion.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: No participants in the Enrolled-06 Cohort were treated with emapalumab in the current study; being treated with emapalumab was not a criterion for study completion.

Baseline characteristics

Reporting groups	
Reporting group title	Enrolled-04 Cohort

Reporting group description:

Participants enrolled in Study NI-0501-04 were invited to participate in long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
In Study NI-0501-04, participants received emapalumab for 4 to 8 weeks. After the treatment period, participants could have undergone HSCT.
Participants for whom an appropriate donor was not identified by Week 8, or in cases where HSCT was delayed for reasons unrelated to the administration of emapalumab, could continue receiving treatment with emapalumab beyond the foreseen 8 weeks in Study NI-0501-05 at the request of the investigator, providing a favorable benefit/risk assessment of treatment was established.
Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study, or an adjusted dose was administered.

Reporting group title	Enrolled-06 Cohort

Reporting group description:

All participants who received at least 1 dose of emapalumab and were monitored for at least 4 weeks after the last drug administration in Study NI-0501-06 were invited to participate for long-term follow-up for 1 year after the last administration of emapalumab.
Participants did not receive emapalumab in the current study (NI-0501-05).

Reporting group title	Enrolled-CU Cohort

Reporting group description:

In exceptional cases, at the spontaneous request of a treating physician, compassionate use (CU) treatment with emapalumab was granted to participants who had exhausted all possible treatment options and who could not be enrolled in a clinical study. All participants who received at least 1 dose of emapalumab under these circumstances were invited to participate for long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
Participants could have continued treatment with emapalumab in the context of the current Study (NI-0501-05) while stem cell donor search was ongoing, or if the investigator assessed that continuation of treatment was beneficial.

Reporting group values	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort
Number of subjects	37	14	7
Age categorical 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)	24	0	4
Children (2-11 years)	13	8	3
Adolescents (12-17 years)	0	5	0
Adults (18-64 years)	0	1	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	1	12	1.7
full range (min-max)	0.2 to 10.2	2.2 to 25.5	0.6 to 10.6

Gender categorical Units: Subjects			
Female	19	10	4
Male	18	4	3
Race Units: Subjects			
White/Caucasian	27	11	5
Asian	4	0	1
Black/African descent	3	2	1
Other	3	0	0
Not collected/missing	0	1	0

Reporting group values	Total		
Number of subjects	58		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	28		
Children (2-11 years)	24		
Adolescents (12-17 years)	5		
Adults (18-64 years)	1		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	33		
Male	25		
Race Units: Subjects			
White/Caucasian	43		
Asian	5		
Black/African descent	6		
Other	3		
Not collected/missing	1		

End points

End points reporting groups

Reporting group title	Enrolled-04 Cohort

Reporting group description:

Participants enrolled in Study NI-0501-04 were invited to participate in long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
In Study NI-0501-04, participants received emapalumab for 4 to 8 weeks. After the treatment period, participants could have undergone HSCT.
Participants for whom an appropriate donor was not identified by Week 8, or in cases where HSCT was delayed for reasons unrelated to the administration of emapalumab, could continue receiving treatment with emapalumab beyond the foreseen 8 weeks in Study NI-0501-05 at the request of the investigator, providing a favorable benefit/risk assessment of treatment was established.
Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study, or an adjusted dose was administered.

Reporting group title	Enrolled-06 Cohort

Reporting group description:

All participants who received at least 1 dose of emapalumab and were monitored for at least 4 weeks after the last drug administration in Study NI-0501-06 were invited to participate for long-term follow-up for 1 year after the last administration of emapalumab.
Participants did not receive emapalumab in the current study (NI-0501-05).

Reporting group title	Enrolled-CU Cohort

Reporting group description:

In exceptional cases, at the spontaneous request of a treating physician, compassionate use (CU) treatment with emapalumab was granted to participants who had exhausted all possible treatment options and who could not be enrolled in a clinical study. All participants who received at least 1 dose of emapalumab under these circumstances were invited to participate for long-term follow-up for 1 year after either HSCT or the last administration of emapalumab.
Participants could have continued treatment with emapalumab in the context of the current Study (NI-0501-05) while stem cell donor search was ongoing, or if the investigator assessed that continuation of treatment was beneficial.

Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events[1]

End point description:

Adverse events were defined as any undesirable experience occurring in a participant during the study, whether or not considered related to emapalumab.

End point type	Primary

End point timeframe:

From the date of enrollment in this study up to 1 year after either HSCT or the last administration of emapalumab (maximum duration: 639 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: No statistical analysis was carried out; this end point was the number of participants with an adverse event during the study.

End point values	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	14	7	
Units: Participants	37	12	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Duration of Response

End point title	Cumulative Duration of Response[2]

End point description:

Cumulative duration of response: total number of days in response from 1st achievement of overall response until HSCT or last treatment date if the participant did not undergo HSCT.
Overall response: achievement of either Complete (CR) or Partial Response (PR), or HLH Improvement (HI).
CR: no fever, normal spleen size, no cytopenia (absolute neutrophil count [ANC] ≥1.0 x 10^9/L and platelet count ≥100 x 10^9/L), no hyperferritinemia (serum ferritin <2000 µg/L), no coagulopathy (normal D-dimer and/or fibrinogen >150 mg/dL), no neurological and cerebrospinal fluid [CSF] abnormalities attributed to HLH, no sustained worsening of soluble cluster of differentiation (CD) 25.
PR: at least 3 HLH clinical and laboratory criteria (including central nervous system [CNS] abnormalities) met the CR criteria, no progression of other aspects of HLH disease pathology.
HI: improvement (>50% change from baseline) of at least 3 HLH clinical and laboratory abnormalities (including CNS involvement).

End point type	Secondary

End point timeframe:

From 1st achievement of overall response until HSCT or last treatment date if participant did not undergo HSCT (maximum duration: 250 days)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data were available only for participants in the Enrolled-04 Cohort.

End point values	Enrolled-04 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: day				
arithmetic mean (standard deviation)	70.7 (± 56.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of First Response

End point title	Duration of First Response[3]

End point description:

Duration of first response was defined as the number of days between first date of response and first date of loss of response or death. Response was defined as macrophage activation syndrome (MAS) remission, which was resolution of clinical signs and symptoms according to the investigator (MAS

clinical signs and symptoms score ≤1) and normalization of laboratory parameters relevant to MAS as follows: white blood cells (WBC) and platelet count above the lower limit of normal (LLN), lactate dehydrogenase <1.5 × upper limit of normal (ULN), aspartate aminotransferase/alanine aminotransferase <1.5 × ULN, fibrinogen >100 mg/dL, ferritin level decreased by at least 80% from values at screening or baseline (whichever was higher) or <2000 ng/mL, whichever was lower.

End point type	Secondary

End point timeframe:

From first date of response and first date of loss of response or death (maximum duration: 416 days)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data from Enrolled-06 Cohort were available.

End point values	Enrolled-06 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: day				
median (inter-quartile range (Q1-Q3))	61 (9.00 to 358.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival: Number of Participants Alive

End point title	Overall Survival: Number of Participants Alive

End point description:

Overall survival was defined as time from the date of last emapalumab dose to the date of death. Participants without an event were censored at the time of last contact or 12 months after last dose (whichever came first). As some participants had their last emapalumab dose in the parent study, data from NI-0501-04, NI-0501-05 and NI-0501-06 studies were considered for the assessment of overall survival.
Kaplan-Meier methodology was used for estimation.
Median overall survival was not reached in any of the groups as 28 of the 37 participants (75.7%) in the Enrolled-04 Cohort, all 14 participants (100.0%) in the Enrolled-06 Cohort, and 5 participants (71.4%) were alive at last observation or 12 months post last dose, whichever came first.

End point type	Secondary

End point timeframe:

From the date of last of emapalumab dose to the date of death or last contact or 12 months after last dose, whichever came first (maximum 366 days)

End point values	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	14	7	
Units: Participants	28	14	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Post-HSCT outcome indices

End point title	Post-HSCT outcome indices[4]

End point description:

Engraftment failure rate was based on the number of participants experiencing primary or secondary graft failure (blood stem cell transplant failure, engraft failure, or transplant dysfunction), as reported as an adverse event.
Achievement of donor chimerism was considered based on donor chimerism in peripheral blood completed, that is, donor cells >95%.
The number of participants who reported graft-versus-host-disease as an AE in Study NI-0501-05 provided the occurrence of graft-versus-host-disease.

End point type	Secondary

End point timeframe:

From HSCT to 12 months post-HSCT

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants in the Enrolled-04 and Enrolled-CU cohorts underwent HSCT.

End point values	Enrolled-04 Cohort	Enrolled-CU Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[5]	2[6]		
Units: Participants				
number (not applicable)				
Engraftment failure rate	6	1		
Achievement of donor chimerism	22	0		
Occurrence of graft-versus-host-disease	7	2		

Notes:

[5] - Of the 37 participants, 29 (78.4%) underwent HSCT

[6] - Of the 7 participants, 2 (28.6%) underwent HSCT

Statistical analyses

No statistical analyses for this end point

Secondary: Background Disease Activity: Macrophage Activation Syndrome in sHLH participants

End point title	Background Disease Activity: Macrophage Activation Syndrome in sHLH participants[7]

End point description:

MAS activity was monitored using a visual analog scale (VAS) ranging from 0 to 10 with a higher score indicating higher disease activity.

End point type	Secondary

End point timeframe:

Baseline (first NI-0501-05 visit), Day 100, Month 12/End of Study

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is relevant only to participants in the Enrolled-06 Cohort.

End point values	Enrolled-06 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	14[8]			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0 (± 0)			
Day 100	0 (± 0)			
Month 12/End of Study	0.2 (± 0.48)			

Notes:

[8] - Baseline: 13 participants
Day 100: 12 participants
Month 12/End of Study: 13 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Circulating Emapalumab Levels: Enrolled-04 Cohort

End point title	Circulating Emapalumab Levels: Enrolled-04 Cohort[9]

End point description:

Circulating emapalumab levels in participants who continued to receive treatment with emapalumab in the current study (NI-0501-05). Samples were not taken once it had been determined that emapalumab was below the measurable level of of 62.5 µg/L.

End point type	Secondary

End point timeframe:

First infusion day (infusion duration: 1-2 hours) in Study NI-0501-05, last infusion day (infusion Day 188), 12 months post-transplant

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is relevant only to participants in the Enrolled-04 Cohort.

End point values	Enrolled-04 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	37[10]			
Units: µg/L				
arithmetic mean (standard deviation)				
First infusion day (Infusion Day 1)	165148.4 (± 175057.98)			
Last infusion day (Infusion Day 188)	157849.0 (± 66180.28)			
12 months post-transplant	80.5 (± 43.52)			

Notes:

[10] - Day 1: 22 participants
Day 188: 2 participants
12 months post-transplant: 12 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Circulating Emapalumab Levels: Enrolled-06 Cohort

End point title	Circulating Emapalumab Levels: Enrolled-06 Cohort[11]

End point description:

Circulating emapalumab levels in the Enrolled-06 Cohort who did not continue to receive treatment with emapalumab in the current study (NI-0501-05). Samples were not taken once it had been determined that emapalumab was below the measurable level of 62.5 µg/L.

End point type	Secondary

End point timeframe:

Baseline (first NI-0501-05 visit), Day 100, Month 6

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is relevant only to participants in the Enrolled-06 Cohort.

End point values	Enrolled-06 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	14[12]			
Units: µg/L				
arithmetic mean (standard deviation)				
Baseline (first NI-0501-05 visit)	20968.0 (± 18226.14)			
Day 100	8515.3 (± 6814.50)			
Month 6	1628.5 (± 1427.46)			

Notes:

[12] - Baseline: 12 participants
Day 100: 10 participants
Month 6: 8 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Total Human Interferon Gamma Levels: Enrolled-04 Cohort

End point title	Total Human Interferon Gamma Levels: Enrolled-04 Cohort[13]

End point description:

Concentrations of human interferon gamma (IFNγ) levels for participants in the Enrolled-04 Cohort. IFNγ concentrations post-dose are the sum of free and bound IFNγ. It should be noted that participants had already been treated with emapalumab at the time of enrollment into Study NI-0501-05. In addition, the number of observations and median values fluctuated, as the duration and the timing of the PD samples varied between participants.

End point type	Secondary

End point timeframe:

First infusion day (infusion duration: 1-2 hours) in Study NI-0501-05, Day 100 post-transplant, 12 months post-transplant

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is relevant only to participants in the Enrolled-04 Cohort.

End point values	Enrolled-04 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	37[14]			
Units: ng/L				
arithmetic mean (standard deviation)				
First infusion day (Infusion Day 1)	5290.4 (± 4992.27)			
Day 100 post-transplant	3613.6 (± 6052.31)			
12 months post-transplant	447.4 (± 1096.99)			

Notes:

[14] - Infusion Day 1: 11 participants
Day 100 post-transplant: 23 participants
12 months:24 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Total Human Interferon Gamma Levels: Enrolled-06 Cohort

End point title	Total Human Interferon Gamma Levels: Enrolled-06 Cohort[15]

End point description:

Concentrations of IFNγ levels for participants in the Enrolled-06 Cohort. IFNγ concentrations post-dose are the sum of free and bound IFNγ. It should be noted that participants had already been treated with emapalumab at the time of enrollment into Study NI-0501-05.

End point type	Secondary

End point timeframe:

Baseline (first NI-0501-05 visit), Day 100, Month 12/End of Study

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is relevant only to participants in the Enrolled-06 Cohort.

End point values	Enrolled-06 Cohort			
Subject group type	Reporting group			
Number of subjects analysed	13[16]			
Units: ng/L				
arithmetic mean (standard deviation)				
Baseline	5544.3 (± 8285.12)			
Day 100	2958.7 (± 6762.6)			
Month 12/End of Study	1111.0 (± 1311.04)			

Notes:

[16] - Baseline: 13 participants
Day 100: 12 participants
Month 12/End of Study: 9 participants

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Antidrug Antibodies

End point title	Number of Participants with Antidrug Antibodies

End point description:

The number of participants in which antidrug antibodies (ADA)-confirmed positive samples were noted.

End point type	Secondary

End point timeframe:

From enrolment up to 12 months post-transplant or last emapalumab infusion (maximum 639 days)

End point values	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	14	7	
Units: Participants	1	3	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of enrollment in this study up to 1 year after either HSCT or the last administration of emapalumab (maximum duration: 639 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Enrolled-04 Cohort

Reporting group description:

Participants enrolled in Study NI-0501-04 were invited to participate in long-term follow-up for 1 year either after HSCT or the last administration of emapalumab.
In Study NI-0501-04, participants received emapalumab for 4 to 8 weeks. After the treatment period, participants could have undergone HSCT.
For participants for whom an appropriate donor was not identified by Week 8, or in cases where HSCT was delayed for reasons unrelated to the administration of emapalumab, they could continue receiving treatment with emapalumab beyond the foreseen 8 weeks in Study NI-0501-05 at the request of the investigator, providing a favorable benefit/risk assessment of treatment was established.
Treatment with emapalumab was not planned for all enrolled participants. For participants who continued receiving emapalumab in Study NI-0501-05, the dose and timing was either carried forward from the last administered emapalumab dose as part of the parent study, or an adjusted dose was administered.

Reporting group title	Enrolled-06 Cohort

Reporting group description:

All participants who received at least 1 dose of emapalumab and were monitored for at least 4 weeks after the last drug administration in Study NI-0501-06 were invited to participate for long-term follow-up for 1 year after the last administration of emapalumab.
Participants did not receive emapalumab in the current study (NI-0501-05).

Reporting group title	Enrolled-CU Cohort

Reporting group description:

In exceptional cases, at the spontaneous request of a treating physician, compassionate use (CU) treatment with emapalumab was granted to the participants who had exhausted all possible treatment options and who could not be enrolled in a clinical study. All participants who received at least 1 dose of emapalumab under these circumstances were invited to participate for long-term follow-up for 1 year either after HSCT or after the last administration of emapalumab.
Participants could have continued treatment with emapalumab in the context of the current Study (NI-0501-05) while stem cell donor search was ongoing, or if the investigator assessed that continuation of treatment was beneficial.

Serious adverse events	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 37 (75.68%)	3 / 14 (21.43%)	6 / 7 (85.71%)
number of deaths (all causes)	9	0	2
number of deaths resulting from adverse events	9	0	2
Vascular disorders			
Circulatory collapse			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	5 / 37 (13.51%)	1 / 14 (7.14%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	6 / 37 (16.22%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Acute graft versus host disease in intestine			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Engraftment syndrome			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1

Pulmonary oedema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Blood stem cell transplant failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Engraft failure			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular dysfunction			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Neurological decompensation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subdural hygroma			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Coombs positive haemolytic anaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye movement disorder			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myositis			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Still's disease			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus infection			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gianotti-Crosti syndrome			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia pseudomonal			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			

subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Enrolled-04 Cohort	Enrolled-06 Cohort	Enrolled-CU Cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 37 (100.00%)	12 / 14 (85.71%)	7 / 7 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hyperaemia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hypertension			
subjects affected / exposed	9 / 37 (24.32%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	9	0	1
Hypotension			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	5	0	1
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Complication associated with device			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Complication of device insertion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Condition aggravated			
subjects affected / exposed	5 / 37 (13.51%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	6	0	2
Face oedema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Fibrosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	7 / 37 (18.92%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	7	0	0
Oedema			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	17 / 37 (45.95%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	26	1	2
Swelling face			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Visceral pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Xerosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Allergy to immunoglobulin therapy			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Bacille Calmette-Guerin scar reactivation			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Engraftment syndrome			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Food allergy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Graft versus host disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Graft versus host disease in liver			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Graft versus host disease in skin			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	4	0	1
Reproductive system and breast disorders			
Scrotal swelling			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Cough			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Dysphonia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Haemothorax			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Lung infiltration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nasal flaring			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Pleural effusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pneumothorax			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pulmonary haemorrhage			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Pulmonary hypertension			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Respiratory distress			

subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Respiratory failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Sneezing			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	6	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Irritability			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	7	0	0
Major depression			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Separation anxiety disorder			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Investigations			
Acinetobacter test positive			

subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Adenovirus test positive			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Atypical mycobacterium test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
BK polyomavirus test positive			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Blood albumin decreased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood electrolytes abnormal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood immunoglobulin G decreased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	5	0	0
Campylobacter test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Candida test positive			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Clostridium test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Herpes simplex test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Human rhinovirus test positive			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Klebsiella test positive			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Mycobacterium test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	8	0	0
Norovirus test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oxygen saturation decreased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pseudomonas test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Respirovirus test positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Roseolovirus test positive			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Transaminases increased			
subjects affected / exposed	4 / 37 (10.81%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	5	0	0
Ubiquinone decreased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Urine output increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Adverse event following immunisation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Allergic transfusion reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood stem cell transplant failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Burns first degree			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Engraft failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Femoral neck fracture			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Subdural haematoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Torus fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Transfusion reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Transplant dysfunction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Unintentional medical device removal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vascular access complication			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Sickle cell trait			

subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Cyanosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Left ventricular hypertrophy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pericardial effusion			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Right ventricular dysfunction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	6 / 37 (16.22%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	9	0	0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 37 (5.41%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Hydrocephalus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypotonia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Neuralgia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nystagmus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Opisthotonus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pleocytosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Subdural effusion			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Haemolytic anaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Increased tendency to bruise			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0

Lymphocytosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Macrocytosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Thrombotic microangiopathy			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye movement disorder			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Maculopathy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Retinal disorder			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Retinal ischaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	8 / 37 (21.62%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	9	0	0
Ascites			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 37 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	11 / 37 (29.73%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	17	0	0
Diverticulum			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Duodenal ulcer			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Enterocolitis haemorrhagic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Gastric mucosa erythema			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Lip ulceration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 37 (8.11%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	4	1	0
Oral mucosal discolouration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Pancreatitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Rectal prolapse			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Stomatitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0

Tongue ulceration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Umbilical hernia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	9 / 37 (24.32%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	17	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Drug-induced liver injury			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperplastic cholecystopathy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
Dermatitis allergic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Drug eruption			

subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ingrowing nail			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Panniculitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Papule			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	5	0	0
Pruritus			
subjects affected / exposed	5 / 37 (13.51%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	5	0	0
Rash			
subjects affected / exposed	7 / 37 (18.92%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	11	0	1
Rash erythematous			
subjects affected / exposed	5 / 37 (13.51%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	6	1	0

Rash macular			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Rash maculo-papular			
subjects affected / exposed	5 / 37 (13.51%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	9	0	0
Rash papular			
subjects affected / exposed	2 / 37 (5.41%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
Rash pruritic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin disorder			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Skin exfoliation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
Urticaria			
subjects affected / exposed	1 / 37 (2.70%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Anuria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			

subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Oliguria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pelvi-ureteric obstruction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hypothyroidism			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 37 (5.41%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Arthritis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Bone pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Flank pain			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Growth failure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypertrophic osteoarthropathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Osteonecrosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Osteopenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Still's disease			
subjects affected / exposed	0 / 37 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	1
BK virus infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Bacillus bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Candida infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Cestode infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile infection			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Croup infectious			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus chorioretinitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus infection reactivation			
subjects affected / exposed	5 / 37 (13.51%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	6	0	0
Enterobacter sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Enterococcal bacteraemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Enterovirus infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Epstein-Barr viraemia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Epstein-Barr virus infection			
subjects affected / exposed	1 / 37 (2.70%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Escherichia bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis adenovirus			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis salmonella			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Herpes simplex gastritis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Human herpesvirus 6 infection reactivation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Klebsiella bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Meningitis enterococcal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Oesophageal candidiasis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Parainfluenzae virus infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Periorbital cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pneumonia bacterial			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pseudomonal sepsis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	2 / 7 (28.57%)
occurrences (all)	3	0	3
Rhinovirus infection			
subjects affected / exposed	1 / 37 (2.70%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Serratia bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Sinusitis bacterial			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin bacterial infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	8	0	0
Staphylococcal infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tracheitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tracheobronchitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection bacterial			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection viral			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Viral haemorrhagic cystitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0

Viral upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	4 / 14 (28.57%)	1 / 7 (14.29%)
occurrences (all)	1	5	2
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Fluid overload			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Fluid retention			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Hypercreatininaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Hypokalaemia			

subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	2 / 7 (28.57%)
occurrences (all)	4	0	2
Hypomagnesaemia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 14 (0.00%)	2 / 7 (28.57%)
occurrences (all)	4	0	3
Hypophagia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Malnutrition			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Milk soy protein intolerance			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Poor feeding infant			
subjects affected / exposed	1 / 37 (2.70%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 December 2013	United States, Version 2.0 - Modification to reflect increased frequency of visits pre- and post-HSCT; visits initially performed monthly basis were to be performed weekly - Addition of flexibility added to the visits to be performed - Addition of clarification regarding patients who, in the context of Study NI-0501-05, could continue receiving emapalumab beyond the 8 weeks foreseen in the Study NI-0501-04 protocol or in the NI-0501-CU protocol, including additional flexibility to be given in the assessment to be performed - Clarification that vaccinations were to be avoided until emapalumab was detected in serum and of what was not considered a protocol deviation - Addition of assessment of clinical response 1 month post-HSCT - Addition of consistency of visit description overall design section with explanations on how to adapt the SOA in the event conditioning and possibly the HSCT were performed before patient inclusion in Study NI-0501-05 - Addition of assessments to be performed, most of which were noninvasive - Addition of laboratory parameters of d-Dimers, gamma-glutamyl transferase, and lactate dehydrogenase and removal of proteinemia from safety laboratory assessments - Addition of evaluation for viral pathogens every 2 weeks as long as emapalumab was detectable in the serum - Addition of chest X-rays to detect tuberculosis at least every 3 weeks until 30 days post-HSCT and potentially at Day 60 post-HSCT, as long as emapalumab was detectable in the serum - Addition of text to Section 9.2, clarifying the potential risks linked to treatment applied only to patients receiving emapalumab during Study NI-0501-05 - Modification of Appendix A for patients still receiving NI-0501, to ensure transition from the on-drug to off-drug part of protocol was clear and accounted for variations in timing for conditioning and HSCT among patients - Modification of Appendix B, to clarify dosing regimen was responsibility of sponsor based on PK results

16 December 2013	Europe, Version 2.0 - Implementation of consistency with the US "twin" protocol to ensure patients in Europe had the same long-term follow-up monitoring as patients in the US and to allow for a combined analysis of the data generated by patients in Europe and the US - Implementation of recommendations made by the NI-0501-04 Scientific Steering Committee and Data Monitoring Committee based on the preliminary data assessment of the first patient enrolled - Modification of study design to increase the frequency of pre- and post-HSCT visits and implement flexibility to ensure assessments were adapted to patients' condition and emapalumab concentrations detected - Modification of study design to account for patients whose conditioning and HSCT occurred during the short-term follow-up period for Study NI-0501-04 - Provide flexibility for the efficacy and safety assessments of patients who continued to receive emapalumab beyond Study NI-0501-04 - Clarification: that vaccinations were to be avoided until emapalumab concentration was detectable; surrounding what was not considered a protocol deviation; that stopping rules applied only to patients who continued receiving emapalumab - Addition of assessment of clinical response 1 month post-HSCT - Addition of a 1-week time-window for follow-up visits to be performed beyond 30 days post-HSCT - Specification that unplanned visits might occur to allow for additional assessments or treatment required - Modification of schedule of assessments (SOA) to ensure consistency with text of the protocol - Modification to risk analysis text to clarify potential risks linked to treatment applied only to patients still on treatment during Study NI-0501-05 - Modification of Appendix A, SOA for patients still receiving NI-0501, to be consistent with that in Study NI-0501-04 (version 3.0) - Modification of Appendix B, Investigational medicinal produce preparation and handling - Removal of Appendix E, NI-0501-04 protocol
16 January 2015	Europe, Version 2.1 - Update to Appendix A, SOA for patients still receiving NI-0501, to ensure consistency with text of protocol regarding recording of physical examination findings and vital sign measurements at each visit
11 February 2015	United States, Version 2.2 - Refer to the changes made under Europe amendment version 2.1, as the same modifications were made

26 October 2017	Europe, Version 3.0 - Addition of information regarding MAS to study rationale and update of studies included in clinical development program - Update of study objectives to include assessment of duration of response, post-HSCT outcome measures, background of disease activity, PD effects and the profile of relevant HLH biomarkers - Update to study design to expand the patient population to include subjects who participated in a previous emapalumab clinical study in which no long-term follow up was already planned and to state that patients having received emapalumab under the NI-0501-CU protocol could also be considered for enrollment whenever appropriate - Modification of the study design to remove details on the last visit performed and to remove the visits foreseen at the time of HSCT - Addition of details to study design for patients who underwent or were to undergo HSCT and for patients who whom HSCT was not planned - Update to inclusion criteria to include males with partner(s) of childbearing age must have agreed to take appropriate precautions to avoid pregnancy until 6 months after receipt of the last dose of emapalumab - Update to patient background and treatment care to clarify any treatment ongoing at the time of study entry was to be continued as deemed necessary by the Investigator and that patients receiving prophylactic treatments for infections at study entry were to continue therapy as long as emapalumab concentrations are detectable in serum - Clarification there was no restriction in the use of medications, except for live or attenuated-live vaccinations that were to be avoided as long as emapalumab concentrations were detectable in serum - Revision of study endpoints to clarify safety, efficacy, PK, PD, and immunogenicity assessments and to remove clinical response and survival from the monitoring of background disease activity - Removal of select laboratory parameters - Addition of serious criteria to AE assessment and clarification
31 October 2017	United States, Version 3.0 - Refer to the changes made under Europe amendment version 3.0, as the same modifications were made

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported