Clinical trial results:
An Open-label, Single Arm, Multicenter Study to Broaden Access to Emapalumab, an Anti-Interferon Gamma (Anti-IFN) Monoclonal Antibody, and to Assess its Efficacy, Safety, Impact on Quality of Life, and Long-term Outcome in Pediatric Patients with Primary Hemophagocytic Lymphohistiocytosis

Summary

EudraCT number	2017-003114-10
Trial protocol	DE ES GB IT SE
Global end of trial date	14 September 2022

Results information

Result version number	v1 (current)
This version publication date	17 September 2023
First version publication date	17 September 2023
Summary attachment (see zip file)	Global substantial amendments to the protocol (Protocol amendments.pdf)

Trial information

Trial identification

Sponsor protocol code	NI-0501-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01818492
WHO universal trial number (UTN)	-
Other trial identifiers	US IND number: 111015

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum AG
Sponsor organisation address	10 Messeplatz, Basel, Switzerland, 4058
Public contact	Radmila Kanceva, MD, Swedish Orphan Biovitrum AG, +41 793048899, Radmila.Kanceva@sobi.com
Scientific contact	Radmila Kanceva, MD , Swedish Orphan Biovitrum AG, +41 793048899, Radmila.Kanceva@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 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 August 2021
Global end of trial reached?	Yes
Global end of trial date	14 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to expand the knowledge on the efficacy and safety of emapalumab (previously known as NI-0501) in children, as a treatment for primary haemophagocytic lymphohistiocytosis (HLH) patients, including long-term outcomes and quality of life assessments. Emapalumab can be administered as the first-line therapy to patients not previously treated with the current standard of care, or can be given to patients who have either failed or were unable to tolerate the available standard of care.

Emapalumab is to be administered until the start of conditioning for hematopoietic stem cell transplantation (HSCT), with an anticipated duration ranging from a minimum of 4 weeks to approximately 12 weeks and not exceeding 6 months.

After treatment completion, patients will continue in the study for long-term follow-up (in the follow-up period [FUP]) until 1 year after either HSCT or last emapalumab infusion (if HSCT is not performed).

Protection of trial subjects:

Written informed consent/assent was obtained from all patients or their parents/legal guardian 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 ICH-GCP and all applicable regulatory requirement(s). If an amended protocol impacted the content of the informed consent document, the consent/assent document had to be revised. Patients already participating in the study when the amended protocol was implemented had to be reconsented/re-assented with the revised version of the informed consent/assent document.
From Protocol V2.0 for North America (dated 18 July 2018), an Independent Data Monitoring Committee (iDMC) was appointed in place of the safety management team to regularly assess the benefit/risk profile of emapalumab treatment.

Background therapy:

Dexamethasone from Study Day -1.

Evidence for comparator: -

Actual start date of recruitment	06 February 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Switzerland: 1
Worldwide total number of subjects	35
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	5
Infants and toddlers (28 days-23 months)	22
Children (2-11 years)	6
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was open to enrollment of pediatric patients with pHLH who were treatment-naïve, failed conventional HLH therapy, or showed signs of intolerance to it.

Pre-assignment

Screening details:

Screening was carried out within 2 weeks prior to first administration of emapalumab (SD0) to enable confirmation of patient eligibility, and following the completion of the Informed Consent Form (and Informed Assent Form, when applicable). A total of 41 patients were screened for this study, with 6 patients failing screening (due to not meeting th

Period 1

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

Arms

Arm title	All patients (emapalumab)

Arm description:

Emapalumab was administered by intravenous infusion, twice weekly to all patients during the treatment period. The duration of treatment was foreseen until the start of conditioning for HSCT but was not to exceed 6 months. The minimum treatment duration was 4 weeks if the patient's condition and donor availability allowed HSCT to be performed. After treatment completion or treatment discontinuation (for any reason), patients could continue in the study for long-term follow-up until 1 year after either HSCT or the last emapalumab infusion (if HSCT was not performed).

Arm type	Experimental
Investigational medicinal product name	emapalumab
Investigational medicinal product code	NI-0501
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Emapalumab was administered by IV infusion over 1 to 2 hours, at a dose of 3 mg/kg, twice weekly (not >4 days apart), except the second infusion was to be administered on SD3. The 3 mg/kg-dose was maintained unless the Investigator deemed a dose increase appropriate. At any time during the study the dose could be increased to 6 mg/kg. A further dose increase to 10 mg/kg could be considered based on the patient's clinical and laboratory response.
If a patient experienced HLH reactivation during the follow up, they could be retreated upon discussion with the Sponsor. Retreated patients followed the same schedule of assessments as applicable during initial treatment (i.e., starting from Visit 1) and re-entered the follow up after completion of retreatment.
Upon achievement of a complete response the dose of emapalumab was to be lowered to achieve 1 mg/kg twice a week and maintained until conditioning for transplant. Decrease of the emapalumab dose was to occur in a stepwise fashion.

Number of subjects in period 1	All patients (emapalumab)
Started	35
Completed	18
Not completed	17
Death	16
Other	1

Baseline characteristics

Reporting groups	
Reporting group title	All patients (emapalumab)

Reporting group description:

Emapalumab was administered by intravenous infusion, twice weekly to all patients during the treatment period. The duration of treatment was foreseen until the start of conditioning for HSCT but was not to exceed 6 months. The minimum treatment duration was 4 weeks if the patient's condition and donor availability allowed HSCT to be performed. After treatment completion or treatment discontinuation (for any reason), patients could continue in the study for long-term follow-up until 1 year after either HSCT or the last emapalumab infusion (if HSCT was not performed).

Reporting group values	All patients (emapalumab)	Total	
Number of subjects	35	35	
Age categorical Units: Subjects			
Newborns (0-27 days)	5	5	
Infants and toddlers (28 days-23 months)	22	22	
Children (2-11 years)	6	6	
Adolescents (12-17 years)	2	2	
Gender categorical Units: Subjects			
Female	14	14	
Male	21	21	

Subject analysis sets	
Subject analysis set title	All-treated analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The All-treated analysis set included all patients who received any part of an infusion of study drug. The All-treated analysis set was the primary analysis set for efficacy endpoints and was used for safety and PK/PD endpoints.

Subject analysis set title	All-treated analysis set - treatment naïve
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the All-treated analysis set who were naïve to HLH treatment.

Subject analysis set title	All-treated analysis set - treatment experienced
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the All-treated analysis set who have received conventional HLH therapy (as per site standard of care), without having obtained a satisfactory response according to the Investigator or having shown signs of intolerance to previous HLH therapy.

Subject analysis set title	Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set was entered only to allow the addition of the statistical analyses for the primary endpoint which uses a comparison within each group to the null hypothesis.

Reporting group values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced
Number of subjects	35	16	19
Age categorical Units: Subjects			
Newborns (0-27 days)	5	4	1
Infants and toddlers (28 days-23 months)	22	10	12
Children (2-11 years)	6	2	4
Adolescents (12-17 years)	2	0	2
Gender categorical Units: Subjects			
Female	14	3	11
Male	21	13	8

Reporting group values	Baseline		
Number of subjects	35		
Age categorical Units: Subjects			
Newborns (0-27 days)	5		
Infants and toddlers (28 days-23 months)	22		
Children (2-11 years)	6		
Adolescents (12-17 years)	2		
Gender categorical Units: Subjects			
Female	14		
Male	21		

End points

End points reporting groups

Reporting group title	All patients (emapalumab)

Reporting group description:

Emapalumab was administered by intravenous infusion, twice weekly to all patients during the treatment period. The duration of treatment was foreseen until the start of conditioning for HSCT but was not to exceed 6 months. The minimum treatment duration was 4 weeks if the patient's condition and donor availability allowed HSCT to be performed. After treatment completion or treatment discontinuation (for any reason), patients could continue in the study for long-term follow-up until 1 year after either HSCT or the last emapalumab infusion (if HSCT was not performed).

Subject analysis set title	All-treated analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The All-treated analysis set included all patients who received any part of an infusion of study drug. The All-treated analysis set was the primary analysis set for efficacy endpoints and was used for safety and PK/PD endpoints.

Subject analysis set title	All-treated analysis set - treatment naïve
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the All-treated analysis set who were naïve to HLH treatment.

Subject analysis set title	All-treated analysis set - treatment experienced
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the All-treated analysis set who have received conventional HLH therapy (as per site standard of care), without having obtained a satisfactory response according to the Investigator or having shown signs of intolerance to previous HLH therapy.

Subject analysis set title	Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set was entered only to allow the addition of the statistical analyses for the primary endpoint which uses a comparison within each group to the null hypothesis.

Primary: Overall Response at Week 8 or End of Treatment (if earlier)

End point title	Overall Response at Week 8 or End of Treatment (if earlier)

End point description:

The overall response rate (ORR) of patients achieving either Complete or Partial Response or HLH Improvement, at Week 8 or EOT (whichever occurs earlier).
ORR comprised complete response, partial response, or HLH improvement. The 1-sided p-value was based on a 1-sided exact binomial test comparing proportion of patients with overall response to hypothesized null hypothesis of at most 40%.
The ORR for the all-treated analysis set was 62.9% (95% CI [exact]: 44.9% to 78.5%), with a statistically significant difference from the pre-set null hypothesis of 40% (p-value = 0.0053). The number of patients with a compete response was 5; there were 16 patients with a partial response, 1 patient with HLH improvement, and 13 patients with no response.

End point type	Primary

End point timeframe:

Up to Week 8.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	Baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	16	19	35
Units: Overall response rate				
number (confidence interval 95%)				
Overall response rate	62.9 (44.9 to 78.5)	50.0 (24.7 to 75.3)	73.7 (48.8 to 90.9)	0 (0 to 0)

Statistical analyses

Statistical analysis title	Exact binomial test - all-treated analysis set

Statistical analysis description:

The analysis of the primary endpoint utilized an exact binomial test to evaluate the null hypotheses that the overall response rate (ORR) was, at most, 40%. The test was undertaken at the 1-sided 0.025 level. Due to the inability of presenting the statistical analysis for single arm studies within EudraCT, it is presented here as a comparison to baseline. The number of subjects analyzed was 35, as the comparison was within a single group.

Comparison groups	Baseline v All-treated analysis set
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0053 [2]
Method	Exact binomial

Notes:

[1] - The pre-specified null hypothesis was that the ORR was, at most, 40%.

[2] - This test was undertaken at the one-sided 0.025 significance level.

Statistical analysis title	Exact binomial test - treatment-naïve

Statistical analysis description:

The analysis of the primary endpoint utilized an exact binomial test to evaluate the null hypotheses that the overall response rate (ORR) was, at most, 40%. The test was undertaken at the 1-sided 0.025 level. Due to the inability of presenting the statistical analysis for single arm studies within EudraCT, it is presented here as a comparison to baseline. The number of subjects analyzed was 16, as the comparison was within a single group.

Comparison groups	Baseline v All-treated analysis set - treatment naïve
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.2839 [4]
Method	Exact binomial

Notes:

[3] - The pre-specified null hypothesis was that the ORR was, at most, 40%.

[4] - This test was undertaken at the one-sided 0.025 significance level.

Statistical analysis title	Exact binomial test - treatment-experienced

Statistical analysis description:

The analysis of the primary endpoint utilized an exact binomial test to evaluate the null hypotheses that the overall response rate (ORR) was, at most, 40%. The test was undertaken at the 1-sided 0.025 level. Due to the inability of presenting the statistical analysis for single arm studies within EudraCT, it is presented here as a comparison to baseline. The number of subjects analyzed was 19, as the comparison was within a single group.

Comparison groups	Baseline v All-treated analysis set - treatment experienced
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0031 [6]
Method	Exact binomial

Notes:

[5] - The pre-specified null hypothesis was that the ORR was, at most, 40%.

[6] - This test was undertaken at the one-sided 0.025 significance level.

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Number of patients surviving, including survival to HSCT and survival after either HSCT or last emapalumab infusion (if HSCT was not performed).
25 patients (71.4 %) overall in the All-treated analysis set received HSCT or were alive at end of study if HSCT was not deemed as indicated by the Investigators (treatment naïve: 12 patients [75.0 %] and treatment-experienced: 13 patients [68.4 %]).
Among the 23 patients who underwent HSCT, 17 patients (73.9 %) overall were alive at the end of the study (8 treatment-naïve patients [72.7 %] and 9 treatment-experienced patients [75.0 %]). Six patients died after HSCT (3 treatment-naïve and 3 treatment-experienced).

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	25[7]	12[8]	13[9]	
Units: Patients				
Alive without having received HSCT	2	1	1	
Alive at end of the study having undergone HSCT	17	8	9	
Died after receiving HSCT	6	3	3	

Notes:

[7] - 25 patients received HSCT or were alive at end of study

[8] - 12 patients received HSCT or were alive at end of study

[9] - 13 patients received HSCT or were alive at end of study

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival

End point title	Event-free Survival

End point description:

The duration of event-free survival was defined as time from HSCT to date of (whichever occurs first): death from any cause, graft failure, or HLH reactivation.
23 patients (65.7%) underwent HSCT, with a similar number of treatment-naïve patients (11 patients [68.8%]) and treatment-experienced patients (12 patients [63.2%]).
One treatment-experienced patient experienced graft failure, and 6 patients overall died (3 treatment-naïve and 3 treatment-experienced patients) post-HSCT. There were no patients with HLH reactivation

post-HSCT.

End point type	Secondary

End point timeframe:

Up to 18 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Event-free at the end of the study	16	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response at Start of Conditioning

End point title	Overall Response at Start of Conditioning

End point description:

Number of patients achieving either a Complete or Partial Response or HLH Improvement, at start of conditioning (or at last emapalumab infusion if HSCT is not performed).
Overall response in the All-treated analysis set at the start of conditioning for HSCT (or at last emapalumab infusion, if HSCT was not performed) showed an ORR of 45.7% (95% CI: 28.8% to 63.4%); the responses comprised 4 complete responses, 11 partial responses, and 1 HLH improvement.

End point type	Secondary

End point timeframe:

Up to 6 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Complete response	4	3	1	
Partial response	11	5	6	
HLH improvement	1	0	1	
No response	19	8	11	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of response, i.e., maintenance of the response achieved at any time during the study (with censoring time at start of conditioning for patients with no event) calculated only for patients showing confirmed overall response.
28 patients in the All-treated analysis set (80.0%) experienced at least 1 response that was maintained for at least 4 days, at some point during the study (in contrast with the primary efficacy analysis, responses included here were not necessarily observed at EOT or Week 8). Patients who never had a response were not included in the analysis.
Median time to loss of response was 40 days (95% CI: 19.0 to not calculable [NC]) in the treatment-naïve group and 61 days (95% CI: 21.0 to NC). In the All-treated analysis set, median time to loss of response was 61 days (95% CI: 21.0 to NC).

End point type	Secondary

End point timeframe:

Up to 18 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28[10]	12[11]	16[12]	
Units: Patients				
In response at EOT	11	4	7	
Treatment discontinued due to AE	1	0	1	
Treatment discontinued due to physician’s decision	2	1	1	

Notes:

[10] - Only patients with a response were included

[11] - Only patients with a response were included

[12] - Only patients with a response were included

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

Time to first response at any time during the study.
7 patients (20.0%) did not experience a response at any time during the study and were censored in the analysis at the date of last contact (time of their death in all of them). In the All-treated analysis set, 28 patients (80%) achieved a response (maintained for at least 4 days) at some point during the study.

End point type	Secondary

End point timeframe:

Up to 18 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28[13]	12[14]	16[15]	
Units: Days				
median (confidence interval 95%)	4 (4.0 to 13.0)	5 (4.0 to 21.0)	4 (4.0 to 30.0)	

Notes:

[13] - Only patients with a response were included

[14] - Only patients with a response were included

[15] - Only patients with a response were included

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Able to Reduce Glucocorticoids by 50% or More of the Baseline Dose During Emapalumab Treatment

End point title	Number of Patients Able to Reduce Glucocorticoids by 50% or More of the Baseline Dose During Emapalumab Treatment

End point description:

Number of patients able to reduce glucocorticoids by 50% or more of the baseline dose during emapalumab treatment.
In the All-treated analysis set, 15 patients (42.9%) were able to reduce their glucocorticoid dose by 50% of the baseline dose or more until EOT; these included 8 treatment-naïve patients (50.0%) and 7 treatment-experienced patients (36.8%).

End point type	Secondary

End point timeframe:

Up to 6 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Able to reduce glucocorticoids by 50 % or more	15	8	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Proceeding to HSCT

End point title	Number of Patients Proceeding to HSCT

End point description:

Number of patients able to proceed to HSCT when deemed indicated.
A total of 23 patients (65.7%) in the All-treated analysis set were able to proceed to HSCT, including 11 treatment-naïve patients (68.8%) and 12 treatment-experienced patients (63.2%).

End point type	Secondary
End point timeframe: Up to 18 months.	

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Patients proceeding to HSCT	23	11	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessed Through PedsQL™, Pediatric Quality of Life Inventory™

End point title	Quality of Life Assessed Through PedsQL™, Pediatric Quality of Life Inventory™
End point description: Assessment of the quality of life using the PedsQL "Pediatric Quality of Life Inventory". The PedsQL uses a 100-point scale ranging from 0 to 100 with higher values indicating better quality of life. Mean change from baseline for each age group is provided. There were no treatment-naïve patients available in the 13-24 months, 2-4 years, and 13-18 years age groups; no treatment experienced patients were available in the 8-12 years age group. No patients were available in the 5-7 years age group. Mean (SD) values for these categories are presented as "0" where no patients are available.	
End point type	Secondary
End point timeframe: Up to Week 8.	

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: scale score				
arithmetic mean (standard deviation)				
Change from Baseline at EOT/Week 8 - 1-12 months	0.208 (± 18.0737)	-6.514 (± 14.8977)	5.810 (± 19.8220)	
Change from Baseline at EOT/Week 8 - 13-24 months	0.794 (± 4.8152)	0 (± 0)	0.794 (± 4.8152)	
Change from Baseline at EOT/Week 8 - 2-4 years	8.469 (± 9.6897)	0 (± 0)	8.469 (± 9.6897)	
Change from Baseline at EOT/Week 8 - 8-12 years	15.978 (± 0)	15.978 (± 0)	0 (± 0)	

Change from Baseline at EOT/Week 8 - 13-18 years	-7.862 (± 13.4760)	0 (± 0)	-7.862 (± 13.4760)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessed Through Behavioral, Affective and Somatic Experiences Scales (BASES)

End point title	Quality of Life Assessed Through Behavioral, Affective and Somatic Experiences Scales (BASES)

End point description:

Assessment of the quality of life using the BASES questionnaires, a validated 38-item questionnaire; a reduced non-validated 22-item version of the questionnaire was used in an exploratory nature for the secondary endpoint. BASES subscale scores were calculated using a 5-point Likert scale from 1 to 5 for all items and they were weighted equally to calculate subscale scores for the following domains:
- Physical Discomfort (5 items – 1 is considered best response)
- Cooperation/Compliance (5 items – 1 is considered best response)
- Mood/Behavior (7 items – 5 is considered best response)
- Quality of Interactions (3 items – 1 is considered best response)
- Activity/Sleep (2 items – 5 is considered best response for patient's activity level and 1 is considered best response for patient's sleeping)

Only patients with HSCT performed were analyzed. The BASES scores showed comparable mean values between treatment-naïve and treatment-experienced patients at the end of treatment.

End point type	Secondary

End point timeframe:

Up to 6 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15[16]	7[17]	8[18]	
Units: Scale score				
arithmetic mean (standard deviation)				
Physical discomfort	10.0 (± 3.57)	9.4 (± 2.99)	10.5 (± 4.14)	
Cooperation/compliance	9.3 (± 3.02)	9.6 (± 2.76)	9.1 (± 3.4)	
Mood/behavior	20.4 (± 8.82)	15.1 (± 8.88)	25.0 (± 6.02)	
Quality of interactions	5.8 (± 2.34)	6.1 (± 2.48)	5.5 (± 2.33)	
Activity	3.1 (± 1.22)	2.7 (± 0.95)	3.4 (± 1.41)	
Sleep	2.1 (± 1.04)	1.8 (± 1.10)	2.3 (± 1.03)	

Notes:

[16] - For all categories but sleep, n = 15
For sleep, n = 11
[17] - For all categories but sleep, n = 7
For sleep, n = 5
[18] - For all categories but sleep, n = 8
For sleep, n = 6

Statistical analyses

No statistical analyses for this end point

Secondary: 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)

End point description:

All 35 patients (100%) experienced at least 1 TEAE, with 9 patients (25.7%) experiencing 30 TEAEs assessed as related to the study drug. Related TEAEs were reported in 3 of 16 treatment-naïve patients and in 6 of 19 treatment-experienced patients. 129 serious TEAEs were reported in 32 patients (91.4%), in all of the treatment-naïve patients (100%) and in 84.2% of the treatment-experienced patients. Six of these events were assessed as related to the study drug in 4 patients (11.4%). No patient withdrew from the study due to an AE. There were 21 SAEs with an outcome of death in 16 patients (45.7%). None were assessed as related to the study drug. The incidence of related serious TEAEs and serious TEAEs with an outcome of death was similar in treatment-naïve and treatment-experienced patients.

End point type	Secondary

End point timeframe:

Up to 18 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Non-TEAEs	15	5	10	
TEAEs	35	16	19	
TEAEs related to study drug	9	3	6	
Mild TEAEs	30	12	18	
Moderate TEAEs	27	12	15	
Severe TEAEs	31	15	16	
TEAEs leading to discontinuation of study drug	7	3	4	
TEAEs with an outcome of death	16	7	9	
Serious TEAEs	32	16	16	
Treatment-emergent SAEs related to study drug	4	2	2	
TEAEs with infections	29	14	15	
Mild infections	21	10	11	
Moderate infections	15	8	7	
Severe infections	16	7	9	
TEAEs with infusion-related reactions	7	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of Laboratory Parameters

End point title	Evolution of Laboratory Parameters

End point description:

Number of patients experiencing shifts from baseline in the following relevant laboratory parameters are reported:
- Biochemistry: glucose ferritin, C-reactive protein (CRP), liver function (alkaline phosphatase [ALP], alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma glutamyl transferase [γGT], lactate dehydrogenase [LDH], bilirubin, renal function (albumin, creatinine, urea, urea nitrogen), triglycerides
- Complete blood count: basophils, basophils/leukocytes, eosinophils, eosinophils/leukocytes, hematocrit, hemoglobin, large unstained cells, lymphocytes, lymphocytes/leukocytes, monocytes, monocytes/leukocytes, neutrophils band form, neutrophils band form/leukocytes, platelets, erythrocytes, leukocytes
- Coagulation tests (activated partial thromboplastin time [aPTT], aPTT ratio, prothrombin time, prothrombin international normalized ratio [INR]), D-dimer, fibrinogen

End point type	Secondary

End point timeframe:

Up to 6 months.

End point values	All-treated analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: Patients				
Albumin: low to within	6			
Albumin: within to low	2			
Alkaline phosphatase: low to within	5			
Alkaline phosphatase: within to low	8			
Alkaline phosphatase: high to within	2			
Alanine aminotransferase: within to high	3			
Alanine aminotransferase: high to within	8			
Aspartate aminotransferase: within to high	3			
Aspartate aminotransferase: high to low	1			
Aspartate aminotransferase: high to within	8			
Bilirubin: within to low	1			
Bilirubin: within to high	1			
Bilirubin: high to within	4			
Creatinine: low to within	1			
Creatinine: within to low	5			
Creatinine: within to high	1			
Creatinine: high to within	2			
C-reactive protein: within to high	6			
C-reactive protein: high to within	4			
Ferritin: high to low	1			
Ferritin: high to within	5			
γGT: within to high	3			
γGT: high to within	4			
Glucose: within to high	2			
Glucose: high to within	8			
Lactate dehydrogenase: low to within	1			
Lactate dehydrogenase: within to high	4			
Lactate dehydrogenase: high to within	8			
Triglycerides: within to high	1			

Triglycerides: high to within	5			
Urea: within to low	5			
Urea: within to high	4			
Urea: high to within	4			
Urea nitrogen: low to within	1			
Urea nitrogen: within to low	1			
Urea nitrogen: within to high	1			
Basophils: low to within	1			
Basophils: within to high	1			
Basophils: high to within	1			
Basophils/leukocytes: high to within	1			
Eosinophils: low to within	3			
Eosinophils: within to low	1			
Eosinophils/leukocytes: within to high	2			
Hematocrit: low to within	9			
Hematocrit: within to low	5			
Hemoglobin: low to within	9			
Hemoglobin: low to high	1			
Hemoglobin: within to low	5			
Large unstained cells: high to within	1			
Lymphocytes: low to within	4			
Lymphocytes: within to low	6			
Lymphocytes: within to high	1			
Lymphocytes: high to within	1			
Lymphocytes/leukocytes: within to low	4			
Lymphocytes/leukocytes: within to high	1			
Lymphocytes/leukocytes: high to within	2			
Monocytes: low to within	6			
Monocytes: low to high	3			
Monocytes: within to low	2			
Monocytes: within to high	2			
Monocytes: high to within	2			
Monocytes/leukocytes: within to high	3			
Monocytes/leukocytes: high to within	1			
Neutrophils band form: low to within	9			
Neutrophils band form: within to low	2			
Neutrophils band form: within to high	2			
Neutrophils band form: high to within	1			
Neutrophils band form/leukocytes: low to within	2			
Neutrophils band form/leukocytes: within to low	1			
Neutrophils band form/leukocytes: within to high	1			
Platelets: low to within	5			
Platelets: low to high	2			
Platelets: within to low	3			
Platelets: within to high	1			
Platelets: high to within	1			
Erythrocytes: low to within	8			
Erythrocytes: within to low	4			
Erythrocytes: within to high	1			
Leukocytes: low to within	9			

Leukocytes: low to high	1			
Leukocytes: within to low	4			
Leukocytes: high to within	1			
aPTT: low to within	2			
aPTT: within to low	4			
aPTT: within to high	3			
aPTT: high to within	4			
aPTT ratio: low to within	2			
aPTT ratio: within to low	1			
aPTT ratio: within to high	2			
aPTT ratio: high to within	2			
D-dimer: within to high	4			
D-dimer: high to within	6			
Fibrinogen: low to within	13			
Fibrinogen: low to high	1			
Fibrinogen: within to low	2			
Fibrinogen: within to high	2			
Fibrinogen: high to within	3			
Prothrombin time: within to high	3			
Prothrombin time: high to within	6			
Prothrombin INR: within to high	1			
Prothrombin INR: high to low	1			
Prothrombin INR: high to within	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients who Discontinued Emapalumab Treatment

End point title	Number of Patients who Discontinued Emapalumab Treatment

End point description:

Number of patients who discontinued emapalumab treatment for safety reasons.
The study drug was discontinued due to 10 TEAEs in 7 patients overall (20.0%); 3 of 16 treatment-naïve patients and 4 of 19 treatment-experienced patients. In 5 patients (14.2%), emapalumab was discontinued in connection to worsening of the disease under study. In 1 patient (2.9%) emapalumab was discontinued due to pulmonary hypertension. In 1 patient (2.9%), the TEAE of acute respiratory failure leading to discontinuation of study drug was the only TEAE assessed as related to the study drug; the outcome was reported as resolved.

End point type	Secondary

End point timeframe:

Up to 6 months.

End point values	All-treated analysis set	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	35	16	19	
Units: Patients				
Treatment discontinuation due to AE	7	3	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Signing of ICF until end of follow-up period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	All-treated analysis set - treatment naïve
Reporting group description: Patients naïve to HLH treatment.	
Reporting group title	All-treated analysis set - treatment experienced
Reporting group description: Patients could have received conventional HLH therapy without having obtained a satisfactory response according to the Investigator or having shown signs of intolerance to previous HLH therapy.	
Reporting group title	All-treated analysis set
Reporting group description: -	

Serious adverse events	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	All-treated analysis set
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	16 / 19 (84.21%)	32 / 35 (91.43%)
number of deaths (all causes)	7	9	16
number of deaths resulting from adverse events	7	9	16
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Epstein-Barr virus associated lymphoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	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	4 / 16 (25.00%)	8 / 19 (42.11%)	12 / 35 (34.29%)
occurrences causally related to treatment / all	0 / 4	0 / 8	0 / 12
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 16 (6.25%)	4 / 19 (21.05%)	5 / 35 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 4
Pyrexia			
subjects affected / exposed	2 / 16 (12.50%)	3 / 19 (15.79%)	5 / 35 (14.29%)
occurrences causally related to treatment / all	1 / 2	0 / 3	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Engraftment syndrome			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Acute graft versus host disease			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences causally related to treatment / all	1 / 2	0 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Acute respiratory failure			
subjects affected / exposed	3 / 16 (18.75%)	0 / 19 (0.00%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pulmonary haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

Asthma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung consolidation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Respiratory disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Klebsiella test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Graft loss			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Fanconi syndrome			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiac arrest			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiac failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 16 (0.00%)	3 / 19 (15.79%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			

subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Nervous system disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Neurological decompensation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 19 (15.79%)	4 / 35 (11.43%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulopathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual field defect			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumatosis intestinalis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive liver disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia viral			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Septic shock			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Bacterial sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site cellulitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection reactivation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus infection reactivation			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex viraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypervolaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	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	All-treated analysis set - treatment naïve	All-treated analysis set - treatment experienced	All-treated analysis set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	19 / 19 (100.00%)	35 / 35 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 16 (37.50%)	5 / 19 (26.32%)	11 / 35 (31.43%)
occurrences (all)	6	5	11
Hypotension			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	2	4
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Superficial vein thrombosis			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Venoocclusive disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Pain management			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Vitamin supplementation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Pregnancy, puerperium and perinatal conditions			
Umbilical granuloma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 16 (37.50%)	8 / 19 (42.11%)	14 / 35 (40.00%)
occurrences (all)	11	17	28
Pain			
subjects affected / exposed	3 / 16 (18.75%)	6 / 19 (31.58%)	9 / 35 (25.71%)
occurrences (all)	7	9	16
Mucosal inflammation			
subjects affected / exposed	1 / 16 (6.25%)	4 / 19 (21.05%)	5 / 35 (14.29%)
occurrences (all)	1	4	5
Oedema peripheral			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences (all)	2	5	7
Condition aggravated			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Hypothermia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Catheter site rash			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Crying			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	2
Generalised oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Vascular device occlusion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Acute graft versus host disease in intestine			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Acute graft versus host disease in skin			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Cell-mediated immune deficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Chronic graft versus host disease in skin			

subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Cytokine release syndrome			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Drug hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Graft versus host disease in liver			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Graft versus host disease in skin			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Immune system disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 16 (12.50%)	3 / 19 (15.79%)	5 / 35 (14.29%)
occurrences (all)	3	3	6
Pleural effusion			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Stridor			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Tachypnoea			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Dyspnoea			

subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	2	3
Epistaxis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	2	2	4
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	3	3
Rhinorrhoea			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Interstitial lung abnormality			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Lung consolidation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Lung disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Nasal dryness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Pneumothorax			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Pulmonary haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Pulmonary hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Respiratory distress			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Delirium			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Irritability			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Restlessness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Investigations			
Adenovirus test positive			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	3	4
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	3 / 19 (15.79%)	3 / 35 (8.57%)
occurrences (all)	0	3	3
C-reactive protein increased			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	2	3
Platelet count decreased			
subjects affected / exposed	0 / 16 (0.00%)	3 / 19 (15.79%)	3 / 35 (8.57%)
occurrences (all)	0	3	3
Weight increased			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	2	3
Blood creatinine increased			

subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Fibrin D dimer increased			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Gram stain positive			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Haemoglobin decreased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	8	8
Human rhinovirus test positive			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Respirovirus test positive			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Bacterial test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Blood creatinine decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Blood glucose decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Blood magnesium decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1

Candida test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Culture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Cytomegalovirus test positive			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Enterobacter test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Epstein-Barr virus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
General physical condition abnormal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Glycocholic acid increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Klebsiella test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Oxygen saturation decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Pseudomonas test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Sapovirus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Staphylococcus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Ultrasound abdomen abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Ultrasound kidney abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Ultrasound liver abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Urine output decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Vitamin D increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	2	4
Perineal injury			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Genital injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Scratch			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Subcutaneous haematoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 16 (18.75%)	4 / 19 (21.05%)	7 / 35 (20.00%)
occurrences (all)	3	4	7
Sinus tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 19 (15.79%)	4 / 35 (11.43%)
occurrences (all)	1	5	6
Bradycardia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Left ventricular hypertrophy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Sinus bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Nervous system disorders			
Cerebral atrophy			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Hypotonia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Cerebral ventricle dilatation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Depressed level of consciousness			

subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Dyskinesia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hyperaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Leukoencephalopathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Myoclonus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Nervous system disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Seizure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	3	1	4
Thrombotic microangiopathy			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Iron deficiency anaemia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2

Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Coagulopathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hypofibrinogenaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Pancytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Middle ear effusion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Blepharitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Eye swelling			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	2
Glaucoma			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Lagophthalmos			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Ocular hyperaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Periorbital oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Swelling of eyelid			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	7 / 16 (43.75%)	10 / 19 (52.63%)	17 / 35 (48.57%)
occurrences (all)	10	15	25
Diarrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	5 / 16 (31.25%)	10 / 19 (52.63%)	15 / 35 (42.86%)
occurrences (all)	7	16	23
Abdominal pain			
subjects affected / exposed	2 / 16 (12.50%)	5 / 19 (26.32%)	7 / 35 (20.00%)
occurrences (all)	5	6	11
Stomatitis			
subjects affected / exposed	2 / 16 (12.50%)	4 / 19 (21.05%)	6 / 35 (17.14%)
occurrences (all)	2	7	9
Constipation			
subjects affected / exposed	2 / 16 (12.50%)	3 / 19 (15.79%)	5 / 35 (14.29%)
occurrences (all)	2	3	5
Nausea			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences (all)	2	3	5
Pneumatosis intestinalis			

subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	2	3
Abdominal distension			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Anal erythema			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Proctalgia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Anal blister			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Ascites			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Colitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Dyschezia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gastrointestinal wall thickening			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Mouth haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Mouth swelling			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Rectal prolapse			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Small intestinal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Hypertransaminasaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Drug-induced liver injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gallbladder disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gallbladder enlargement			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gallbladder oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Hepatobiliary disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hepatomegaly			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1

Hepatosplenomegaly			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Liver disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Liver injury			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 16 (25.00%)	4 / 19 (21.05%)	8 / 35 (22.86%)
occurrences (all)	6	7	13
Dermatitis diaper			
subjects affected / exposed	3 / 16 (18.75%)	2 / 19 (10.53%)	5 / 35 (14.29%)
occurrences (all)	4	2	6
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	4 / 19 (21.05%)	5 / 35 (14.29%)
occurrences (all)	1	5	6
Erythema			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences (all)	3	2	5
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	4 / 19 (21.05%)	4 / 35 (11.43%)
occurrences (all)	0	7	7
Blister			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Dry skin			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Erythema multiforme			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	3
Petechiae			

subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Rash erythematous			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Skin lesion			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Livedo reticularis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Macule			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Papule			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Skin disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Skin irritation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Skin mass			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Urticaria			

subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 16 (18.75%)	1 / 19 (5.26%)	4 / 35 (11.43%)
occurrences (all)	3	1	4
Nephrocalcinosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Azotaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Cystitis haemorrhagic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Glycosuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Kidney enlargement			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Nephrolithiasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Proteinuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences (all)	2	2	4
Adrenal suppression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Cushingoid			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Arthritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Spinal deformity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Infections and infestations			
Cytomegalovirus infection reactivation			
subjects affected / exposed	3 / 16 (18.75%)	1 / 19 (5.26%)	4 / 35 (11.43%)
occurrences (all)	4	2	6
Epstein-Barr virus infection			
subjects affected / exposed	1 / 16 (6.25%)	3 / 19 (15.79%)	4 / 35 (11.43%)
occurrences (all)	1	4	5
Bacteraemia			

subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	3	4
Candida infection			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Urinary tract infection			
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	3 / 35 (8.57%)
occurrences (all)	2	2	4
Adenovirus reactivation			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Cytomegalovirus infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Epstein-Barr virus infection reactivation			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Fungal infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Oral fungal infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Paronychia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Rhinitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	2
Skin infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Adenovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2

Bacterial disease carrier			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	4	4
Bacterial sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	2
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Clostridium difficile infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Enterocolitis viral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	2
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gastroenteritis norovirus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Lymph gland infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Norovirus infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1

Oral candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Pneumonia fungal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Sepsis neonatal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Systemic candida			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	3	0	3
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 16 (18.75%)	4 / 19 (21.05%)	7 / 35 (20.00%)
occurrences (all)	3	6	9
Hypomagnesaemia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 19 (10.53%)	4 / 35 (11.43%)
occurrences (all)	2	2	4
Hypervolaemia			

subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	3 / 35 (8.57%)
occurrences (all)	1	3	4
Acidosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Decreased appetite			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Hyponatraemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Malnutrition			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	2 / 35 (5.71%)
occurrences (all)	1	1	2
Fluid retention			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Hyperchloraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hyperglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	2
Hyperphosphataemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hyperuricaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Hypophagia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Hypovolaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Iron overload			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Metabolic acidosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2020	There was 1 global protocol amendment (version 4.0, global, dated 31-Mar-2020). Full details of the changes introduced in that amendment are included in the uploaded PDF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported