Clinical trial results:
Phase 2/3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of Posoleucel (ALVR105, Viralym-M) Compared to Placebo for the Prevention of AdV, BKV, CMV, EBV, HHV-6, and JCV Infection and/or Disease, in High-Risk Patients After Allogeneic Hematopoietic Cell Transplant

Summary

EudraCT number	2021-005105-27
Trial protocol	IT FR ES BE
Global end of trial date	30 January 2024

Results information

Result version number	v1 (current)
This version publication date	05 May 2024
First version publication date	05 May 2024

Trial information

Trial identification

Sponsor protocol code	P-105-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05305040
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AlloVir, Inc
Sponsor organisation address	1100 Winter Street, Waltham, United States, MA 02451
Public contact	Clinical Trials Information Line, AlloVir, Inc., +1 833 409-2281, clinicaltrials@allovir.com
Scientific contact	Clinical Trials Information Line, AlloVir, Inc., +1 833 409-2281, clinicaltrials@allovir.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002908-PIP01-20
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 January 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of posoleucel (ALVR105) to placebo by the number of clinically significant infections or episodes of end-organ disease per patient due to Adenovirus (AdV), BK virus (BKV), Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Human herpes virus 6 (HHV-6), or JC virus (JCV) as determined by an independent, blinded Clinical Adjudication Committee (CAC) through Week 14.

Protection of trial subjects:

This study was performed in accordance with Good Clinical Practice, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Belgium: 23
Country: Number of subjects enrolled	France: 44
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 34
Country: Number of subjects enrolled	Türkiye: 47
Country: Number of subjects enrolled	United States: 233
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Canada: 9
Worldwide total number of subjects	451
EEA total number of subjects	111

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)	4
Children (2-11 years)	45
Adolescents (12-17 years)	22
Adults (18-64 years)	271
From 65 to 84 years	109
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants at high risk for viral infection after allogeneic Hematopoietic Cell Transplant were enrolled in the Phase 3 portion of study P-105-202 between Mar 2022 and Jan 2024. The Phase 3 study was discontinued in Dec 2023 after futility analysis of the Primary Outcome Measure. No safety concerns were identified.

Pre-assignment

Screening details:

A total of 451 participants were enrolled in this Phase 3 study. Due to the early termination of this study, 74 were not dosed. The 377 randomized participants that were dosed comprise the Safety Population and are presented in the participant flow.

Pre-assignment period milestones

Number of subjects started	451
Number of subjects completed	377

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Randomized but not dosed: 74

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Posoleucel (ALVR105)

Arm description:

Participants received posoleucel administered as 2-4 mL intravenous (IV) infusion once every 14 days for 7 doses.

Arm type	Experimental
Investigational medicinal product name	Posoleucel
Investigational medicinal product code	ALVR105
Other name	Viralym-M
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2×10^7 cells or 4 × 10^7cells administered as a 2-4 mL IV infusion once every 14 days for 7 doses.

Arm title	Placebo

Arm description:

Participants received placebo administered as 2-4 mL IV infusion once every 14 days for 7 doses.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered as a 2-4 mL IV infusion once every 14 days for 7 doses.

Number of subjects in period 1[1]	Posoleucel (ALVR105)	Placebo
Started	188	189
Completed	100	101
Not completed	88	88
Adverse event, serious fatal	14	13
Consent withdrawn by subject	15	10
Investigator's Decision	1	1
Study Closure	34	46
Adverse event, non-fatal	3	3
Not Specified	13	10
Graft versus host disease	2	-
Lost to follow-up	2	1
Primary Malignancy Relapse	3	4
COVID-19 Reasons	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the participants that were randomized, 74 were not dosed and are not included in the baseline population. The baseline period represents the safety population which included all participants who received at least one dose of posoleucel or placebo.

Baseline characteristics

Reporting groups	
Reporting group title	Posoleucel (ALVR105)
Reporting group description:	
Participants received posoleucel administered as 2-4 mL intravenous (IV) infusion once every 14 days for 7 doses.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered as 2-4 mL IV infusion once every 14 days for 7 doses.	

Reporting group values	Posoleucel (ALVR105)	Placebo	Total
Number of subjects	188	189	377
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)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	55.0	53.0	
full range (min-max)	1 to 77	0 to 75	-
Gender categorical Units: Subjects			
Female	78	66	144
Male	110	123	233
Ethnicity Units: Subjects			
Hispanic or Latino	13	24	37
Not Hispanic or Latino	143	144	287
Unknown or Not Reported	32	21	53
Race Units: Subjects			
American Indian or Alaskan Native	1	1	2
Asian	25	21	46
Black or African American	7	5	12
Native Hawaiian or Other Pacific Islander	1	1	2
White	118	131	249
Other	9	8	17
Unknown	27	22	49

End points

End points reporting groups

Reporting group title	Posoleucel (ALVR105)
Reporting group description: Participants received posoleucel administered as 2-4 mL intravenous (IV) infusion once every 14 days for 7 doses.	
Reporting group title	Placebo
Reporting group description: Participants received placebo administered as 2-4 mL IV infusion once every 14 days for 7 doses.	

Primary: Average Number of Clinically Significant Infections or Episodes of End-Organ Disease Through Week 14

End point title	Average Number of Clinically Significant Infections or Episodes of End-Organ Disease Through Week 14
End point description: The number of clinically significant infections or episodes of end-organ disease per participant due to AdV, BKV, CMV, EBV, HHV-6, or JCV. Analysis Population Description: Includes modified Intent-to-Treat (mITT) Population comprised of all randomized participants who received study drug and completed through Week 14 visit.	
End point type	Primary
End point timeframe: Through Week 14	

End point values	Posoleucel (ALVR105)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	155		
Units: Infections/Episodes per participant				
arithmetic mean (standard deviation)	0.2 (± 0.44)	0.2 (± 0.42)		

Statistical analyses

Statistical analysis title	ANCOVA Analysis
Comparison groups	Placebo v Posoleucel (ALVR105)
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5603 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.049

Notes:

[1] - 1-sided p-value

Secondary: Average Number of Clinically Significant Infections or Episodes of End-Organ Disease Through Week 26

End point title	Average Number of Clinically Significant Infections or Episodes of End-Organ Disease Through Week 26

End point description:

The number of clinically significant infections or episodes of end-organ disease per participant due to AdV, BKV, CMV, EBV, HHV-6, or JCV.

End point type	Secondary

End point timeframe:

Through Week 26

End point values	Posoleucel (ALVR105)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Infections/Episodes per participant				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Data not collected due to early termination of the study.

[3] - Data not collected due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Infections or Episodes of End-Organ Disease Due to Each Virus

End point title	Number of Participants With Clinically Significant Infections or Episodes of End-Organ Disease Due to Each Virus

End point description:

The number of participants with clinically significant infections or episodes of end-organ disease due to each of the following viruses: AdV, BKV, CMV, EBV, HHV-6, or JCV.
Analysis Population Description: Includes mITT Population comprised of all randomized participants who received study drug and completed through Week 14 visit.

End point type	Secondary

End point timeframe:

Through Week 14

End point values	Posoleucel (ALVR105)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	155		
Units: participants				
AdV	3	2		
BKV	2	2		
CMV	16	19		
EBV	10	6		
HHV-6	0	0		
JCV	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Week 26

Adverse event reporting additional description:

Adverse events are reported for the Safety Population which included all participants who received at least one dose of posoleucel or placebo. Non-serious AEs can be calculated by subtracting the number of events from the serious AE table from the corresponding events in the combined table.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Posoleucel (ALVR105)

Reporting group description:

Participants received posoleucel (2×10^7 cells [if <40 kg body weight at screening] or 4 × 10^7cells [if ≥40 kg body weight at screening]), administered as a 2-4 mL intravenous (IV) infusion once every 14 days for 7 doses.

Reporting group title	Placebo

Reporting group description:

Participants received placebo administered as a 2-4 mL IV infusion once every 14 days for 7 doses.

Serious adverse events	Posoleucel (ALVR105)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 188 (46.81%)	86 / 189 (45.50%)	
number of deaths (all causes)	18	19	
number of deaths resulting from adverse events	18	19	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myeloid leukaemia recurrent			

subjects affected / exposed	1 / 188 (0.53%)	6 / 189 (3.17%)	
occurrences causally related to treatment / all	0 / 1	1 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukaemia recurrent			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelodysplastic syndrome			
subjects affected / exposed	2 / 188 (1.06%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Myelofibrosis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Post transplant lymphoproliferative disorder			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Precursor T-lymphoblastic lymphoma/leukaemia recurrent			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Hypertensive crisis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	3 / 188 (1.60%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 1	
Fatigue			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fever and rigors			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Positive cultures from indwelling CVAD			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 188 (2.13%)	12 / 189 (6.35%)	
occurrences causally related to treatment / all	1 / 4	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Acute graft versus host disease			
subjects affected / exposed	1 / 188 (0.53%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute graft versus host disease in intestine			
subjects affected / exposed	1 / 188 (0.53%)	3 / 189 (1.59%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute graft versus host disease in liver			
subjects affected / exposed	2 / 188 (1.06%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute graft versus host disease in skin			
subjects affected / exposed	4 / 188 (2.13%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune disorder			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in liver			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in skin			

subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytokine release syndrome			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease			
subjects affected / exposed	1 / 188 (0.53%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	7 / 188 (3.72%)	7 / 189 (3.70%)	
occurrences causally related to treatment / all	1 / 7	1 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Graft versus host disease in liver			
subjects affected / exposed	2 / 188 (1.06%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in skin			
subjects affected / exposed	1 / 188 (0.53%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Dyspnoea			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 188 (0.00%)	3 / 189 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	4 / 188 (2.13%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Enterobacter test positive			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epstein-Barr virus antigen positive			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus test positive			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex test positive			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Human rhinovirus test positive			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus test positive			

subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	3 / 188 (1.60%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Aplasia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 188 (0.00%)	3 / 189 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac failure			
subjects affected / exposed	2 / 188 (1.06%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest with sepsis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 188 (1.06%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haematoma			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Cerebral haemorrhage			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Headache			
subjects affected / exposed	3 / 188 (1.60%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient aphasia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytopenia			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			

subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	4 / 188 (2.13%)	6 / 189 (3.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukocytosis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Warm autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strabismus			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 188 (3.19%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	1 / 6	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalization for nausea and vomiting			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 188 (0.00%)	3 / 189 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic necrosis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertransaminasaemia			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 188 (2.13%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			

subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Chondrocalcinosis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenoviral haemorrhagic cystitis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	1 / 188 (0.53%)	3 / 189 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus reactivation			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal infection			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 188 (1.06%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	

Bacterial sepsis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	5 / 188 (2.66%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial sepsis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis viral			

subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	3 / 188 (1.60%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 188 (0.53%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus viraemia			
subjects affected / exposed	2 / 188 (1.06%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related bacteraemia			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter bacteraemia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis bacterial			

subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr viraemia			
subjects affected / exposed	2 / 188 (1.06%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection reactivation			
subjects affected / exposed	2 / 188 (1.06%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 188 (1.06%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human bocavirus infection			

subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human herpesvirus 6 infection reactivation			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Norovirus infection			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			

subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 188 (2.13%)	4 / 189 (2.12%)	
occurrences causally related to treatment / all	0 / 4	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory tract infection viral			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	5 / 188 (2.66%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Sepsis with fever and rigor			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis with multiple organ failure			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinusitis			

subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	0 / 188 (0.00%)	2 / 189 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral haemorrhagic cystitis			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 188 (0.53%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 188 (0.53%)	0 / 189 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 188 (0.00%)	1 / 189 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Posoleucel (ALVR105)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	180 / 188 (95.74%)	184 / 189 (97.35%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 188 (8.51%)	7 / 189 (3.70%)	
occurrences (all)	16	7	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	11 / 188 (5.85%)	8 / 189 (4.23%)	
occurrences (all)	11	8	
Fatigue			
subjects affected / exposed	22 / 188 (11.70%)	17 / 189 (8.99%)	
occurrences (all)	22	17	
Oedema peripheral			
subjects affected / exposed	17 / 188 (9.04%)	20 / 189 (10.58%)	
occurrences (all)	17	20	
Pyrexia			
subjects affected / exposed	33 / 188 (17.55%)	36 / 189 (19.05%)	
occurrences (all)	33	36	
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	11 / 188 (5.85%)	7 / 189 (3.70%)	
occurrences (all)	11	7	
Acute graft versus host disease in skin			
subjects affected / exposed	36 / 188 (19.15%)	27 / 189 (14.29%)	
occurrences (all)	36	27	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	24 / 188 (12.77%)	16 / 189 (8.47%)	
occurrences (all)	24	16	
Graft versus host disease in skin			
subjects affected / exposed	15 / 188 (7.98%)	15 / 189 (7.94%)	
occurrences (all)	15	15	
Hypogammaglobulinaemia			
subjects affected / exposed	6 / 188 (3.19%)	12 / 189 (6.35%)	
occurrences (all)	6	12	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	30 / 188 (15.96%)	20 / 189 (10.58%)	
occurrences (all)	30	20	
Dyspnoea			

subjects affected / exposed	14 / 188 (7.45%)	22 / 189 (11.64%)	
occurrences (all)	14	22	
Oropharyngeal pain			
subjects affected / exposed	9 / 188 (4.79%)	14 / 189 (7.41%)	
occurrences (all)	9	14	
Rhinorrhoea			
subjects affected / exposed	10 / 188 (5.32%)	5 / 189 (2.65%)	
occurrences (all)	10	5	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 188 (5.85%)	7 / 189 (3.70%)	
occurrences (all)	11	7	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	14 / 188 (7.45%)	16 / 189 (8.47%)	
occurrences (all)	14	16	
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 188 (4.79%)	11 / 189 (5.82%)	
occurrences (all)	9	11	
Blood creatinine increased			
subjects affected / exposed	30 / 188 (15.96%)	22 / 189 (11.64%)	
occurrences (all)	30	22	
Neutrophil count decreased			
subjects affected / exposed	10 / 188 (5.32%)	8 / 189 (4.23%)	
occurrences (all)	10	8	
Platelet count decreased			
subjects affected / exposed	22 / 188 (11.70%)	15 / 189 (7.94%)	
occurrences (all)	22	15	
White blood cell count decreased			
subjects affected / exposed	12 / 188 (6.38%)	8 / 189 (4.23%)	
occurrences (all)	12	8	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 188 (4.26%)	10 / 189 (5.29%)	
occurrences (all)	8	10	
Nervous system disorders			

Dizziness			
subjects affected / exposed	10 / 188 (5.32%)	12 / 189 (6.35%)	
occurrences (all)	10	12	
Headache			
subjects affected / exposed	22 / 188 (11.70%)	22 / 189 (11.64%)	
occurrences (all)	22	22	
Tremor			
subjects affected / exposed	14 / 188 (7.45%)	11 / 189 (5.82%)	
occurrences (all)	14	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	26 / 188 (13.83%)	24 / 189 (12.70%)	
occurrences (all)	26	24	
Febrile neutropenia			
subjects affected / exposed	10 / 188 (5.32%)	9 / 189 (4.76%)	
occurrences (all)	10	9	
Neutropenia			
subjects affected / exposed	12 / 188 (6.38%)	7 / 189 (3.70%)	
occurrences (all)	12	7	
Thrombocytopenia			
subjects affected / exposed	6 / 188 (3.19%)	14 / 189 (7.41%)	
occurrences (all)	6	14	
Eye disorders			
Dry eye			
subjects affected / exposed	5 / 188 (2.66%)	13 / 189 (6.88%)	
occurrences (all)	5	13	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	25 / 188 (13.30%)	16 / 189 (8.47%)	
occurrences (all)	25	16	
Constipation			
subjects affected / exposed	12 / 188 (6.38%)	10 / 189 (5.29%)	
occurrences (all)	12	10	
Diarrhoea			
subjects affected / exposed	46 / 188 (24.47%)	37 / 189 (19.58%)	
occurrences (all)	46	37	
Nausea			

subjects affected / exposed	36 / 188 (19.15%)	22 / 189 (11.64%)	
occurrences (all)	36	22	
Vomiting			
subjects affected / exposed	29 / 188 (15.43%)	21 / 189 (11.11%)	
occurrences (all)	29	21	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	10 / 188 (5.32%)	9 / 189 (4.76%)	
occurrences (all)	10	9	
Erythema			
subjects affected / exposed	11 / 188 (5.85%)	9 / 189 (4.76%)	
occurrences (all)	11	9	
Pruritus			
subjects affected / exposed	17 / 188 (9.04%)	14 / 189 (7.41%)	
occurrences (all)	17	14	
Rash			
subjects affected / exposed	16 / 188 (8.51%)	14 / 189 (7.41%)	
occurrences (all)	16	14	
Rash maculo-papular			
subjects affected / exposed	17 / 188 (9.04%)	12 / 189 (6.35%)	
occurrences (all)	17	12	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	14 / 188 (7.45%)	6 / 189 (3.17%)	
occurrences (all)	14	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 188 (4.26%)	11 / 189 (5.82%)	
occurrences (all)	8	11	
Infections and infestations			
COVID-19			
subjects affected / exposed	13 / 188 (6.91%)	11 / 189 (5.82%)	
occurrences (all)	13	11	
Cytomegalovirus infection			
subjects affected / exposed	13 / 188 (6.91%)	18 / 189 (9.52%)	
occurrences (all)	13	18	

Cytomegalovirus infection reactivation			
subjects affected / exposed	10 / 188 (5.32%)	11 / 189 (5.82%)	
occurrences (all)	10	11	
Pneumonia			
subjects affected / exposed	11 / 188 (5.85%)	14 / 189 (7.41%)	
occurrences (all)	11	14	
Sepsis			
subjects affected / exposed	10 / 188 (5.32%)	3 / 189 (1.59%)	
occurrences (all)	10	3	
Upper respiratory tract infection			
subjects affected / exposed	5 / 188 (2.66%)	14 / 189 (7.41%)	
occurrences (all)	5	14	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	18 / 188 (9.57%)	22 / 189 (11.64%)	
occurrences (all)	18	22	
Hyperglycaemia			
subjects affected / exposed	18 / 188 (9.57%)	11 / 189 (5.82%)	
occurrences (all)	18	11	
Hypokalaemia			
subjects affected / exposed	23 / 188 (12.23%)	12 / 189 (6.35%)	
occurrences (all)	23	12	
Hypomagnesaemia			
subjects affected / exposed	19 / 188 (10.11%)	13 / 189 (6.88%)	
occurrences (all)	19	13	
Hyponatraemia			
subjects affected / exposed	10 / 188 (5.32%)	7 / 189 (3.70%)	
occurrences (all)	10	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2020	Major revisions include: • Clarification on cell line change language • Clarification on retreatment option • Update to blood volume table • Update to Open Label Cohort Inclusion criteria • Clarification to unblinding section direction
07 April 2021	Major revisions include: • Extended the window for dosing post-HCT • Increased cap on percentage of patients receiving letermovir prophylaxis • Changes to inclusion/exclusion criteria • Assessment of viremia prior to randomization • Reduction in plasma samples collected in pediatric patients < 12 years of age • Updates to Schedule of Activities • Updated language regarding adverse events assessments • Treatment of Overdose • Updated Concomitant Therapy and Excluded Medications Sections • Definitions of clinical viremia, disease, and resolution • Infection Assessments • Updated Statistical Analysis Section • Updated Laboratory Tests • Updated Cytokine Release Syndrome Information • Changed references to the study drug from Viralym-M to posoleucel to conform to other company protocols.
28 July 2021	Major revisions include: • Randomized patients are now in one cohort, the Phase 3 study cohort. The open label cohort remains the same. Cohorts A and B were removed. • The study schema was updated to identify the Phase 3 study cohort and to be clearer on the timing of the Open Label cohort. Cohorts A and B were removed. • The inclusion criterion indicates that patients should have no known or suspected clinically significant disease from any of the 6 viruses. Inclusion criteria for viremia levels for Cohorts A and B were removed. • Exclusion criterion #2 regarding having evidence for more than 3 viruses was removed. • Removed optional pre-screening period to assess viral load because it is no longer necessary since patients are not assigned to cohort based on viral load. • A targeted percentage of patients not receiving letermovir is described.
19 October 2021	Major revisions include: • to add stratification factors • revise power and sample size • revise endpoints • remove visits and laboratories at odd numbered weeks for patients <12 years of age to reduce patient burden.
11 January 2023	Major revisions include: • ALVR105 was changed to posoleucel throughout • Clarifications made to language throughout protocol
01 May 2023	Major revisions include: • changes made to inclusion/exclusion criteria to capture the highest risk patients without compromising safety • removed requirement for engraftment for randomization. • engraftment now required prior to dosing with no change to criterion for confirming engraftment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The Phase 3 study was discontinued in Dec 2023 after futility analysis of the Primary Outcome Measure. No safety concerns were identified. The Phase 2 portion of study P-105-202 was not carried out within the EU.

Notes: