Clinical trial results:
Phase I/II Study of CaspaCIDe T Cells (BPX-501; Rivogenlecleucel) From an HLA Partially Matched Family Donor After Negative Selection of TCR+ T Cells in Paediatric Patients Affected by Haematological Disorders.

Summary

EudraCT number	2014-000584-41
Trial protocol	IT GB ES
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	11 February 2023
First version publication date	11 February 2023

Trial information

Trial identification

Sponsor protocol code	BP-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02065869
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bellicum Pharmaceuticals, Inc.
Sponsor organisation address	3730 Kirby Drive, Suite 1200 , Houston, United States, 77098
Public contact	Rivogenlecleucel Study Team, Bellicum Pharmaceuticals, Inc., +1 (832) 384 1100, clinicaltrials@bellicum.com
Scientific contact	Rivogenlecleucel Study Team, Bellicum Pharmaceuticals, Inc., +1 (832) 384 1100, clinicaltrials@bellicum.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001870-PIP01-15, EMEA-001869-PIP01-15
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	Interim
Date of interim/final analysis	07 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 February 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This is a Phase I/II study evaluating the safety and feasibility of BPX-501 T cells infused after partially mismatched, related, TCR alpha beta T cell depleted hematopoietic stem cell transplant (HSCT) in pediatric patients. The purpose of this clinical trial is to determine whether BPX-501 infusion can enhance immune reconstitution in those patients with hematologic disorders, with the potential for reducing the severity and duration severe acute graft versus host disease (GvHD). The trial will also evaluate the treatment of GvHD by the infusion of dimerizer drug (AP1903/rimiducid) in those subjects who present with GVHD who progress or do not respond to standard of care treatment.

Protection of trial subjects:

The study was conducted according to the study protocol, the ethical principles of the declaration of Helsinki, the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines, the EU Clinical Trial Directive (2001/120/EG), the Italian Ministry of Health decree of 15 Jul 1997, the Food and Drug Administration (FDA), and other international regulatory agencies. All investigators agreed to conduct all aspects of this study in accordance with national and local laws and regulations. Before study onset, the original protocol, the informed consent form (ICF) and any other written information regarding this study were reviewed by the relevant Independent Ethics Committee (IEC). Written informed consent was obtained from the patient and/or their parent/legal guardian and donor before the performance of any study-specific procedure.

The patient/donor or legal guardian was given clear explanations about the nature, scope and possible consequences and risks of the clinical study by the investigator. Information was provided both in writing (patient information sheet [PIS]) and verbally with ample opportunity provided to ask questions and decide whether to participate in this study. It was also made clear to patients that they could withdraw from the trial at any time without giving a reason. Patients who turned 18 years of age during the study completed an adult ICF at that time. The ICFs along with a declaration on data privacy were signed and dated by both the informing physician and the donor/patient or their legal guardian before the beginning of the study. A copy of the signed ICF was given to the patient. To ensure medical confidentiality and data protection, the signed ICFs were stored in the investigator's site file and retained within it.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	15 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Italy: 162
Worldwide total number of subjects	184
EEA total number of subjects	162

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)	43
Children (2-11 years)	105
Adolescents (12-17 years)	35
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening activities occurred after consenting. The screening procedures included medical and cancer history, physical and neurological exams, vital signs, scans, bone marrow aspirate, and laboratory tests (chimerism, hematology, chemistry, immune function flow panel, immunoglobulins, infectious disease titers, HLA typing, HAMA, RCR, pregnancy test

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	BPX-501 T Cells and Rimiducid

Arm description:

TCR alpha beta depleted graft infusion with addback of BPX-501 T cells (rivogenlecleucel). Rimiducid/AP1903: Dimerizer drug administered to subjects who develop Grade III-IV acute GVHD, Grade II gut/liver acute GVDH or Grade I/II skin-only acute GvHD which is non-responsive after 7 days of standard of care treatment.BPX-501 T cells: 1x10E6 cells/kg infused on Day 0
Rimiducid: 0.4mg/kg administered IV to treat GVHD

Arm type	Experimental
Investigational medicinal product name	Rivogenlecleucel
Investigational medicinal product code	
Other name	BPX-501
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Phase 1, rivogenlecleucel was administered via intravenous infusion at 3 different escalating doses (0.25×10^6, 0.5×10^6 and 1×10^6 cells/kg recipient total body weight) in all patient populations. Two further escalation doses of 2×10^6 and 4×10^6 cells/kg recipient total body weight were evaluated in patients with malignant disease only. In Phase 2, patients (with either malignant or non-malignant haematological diseases) were infused with rivogenlecleucel at the 1×10^6 cells/kg dose.

Investigational medicinal product name	Rimiducid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.4 mg/kg rimiducid was administered via intravenous infusion to patients who received rivogenlecleucel and developed GvHD which progressed or did not respond within 7 days to standard of care treatment

Number of subjects in period 1	BPX-501 T Cells and Rimiducid
Started	184
Patients Receiving Rivogenlecleucel	171
ITT Population	142 [1]
Patients Receiving ≥ 1 Dose of Rimiducid	16 [2]
Completed	149
Not completed	35
Death	7
No rivogenlecleucel cells infused (non-evaluable)	7
Disease relapse	16
Unknown	1
Lost to follow-up	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 184 subjects were enrolled in the study. 171 subjects received BPX-501 T cells and rimiducid. Of these subjects, 142 were placed in the intent-to-treat population i.e. patients treated with haematopoietic stem cell transplantation (HSCT) and who received a dose of BPX-501 at 1x10^6 cells/kg. 16 subjects received at least 1 dose of rimiducid for the treatment of acute or chronic GvHD refractory to standard of care treatment

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 184 subjects were enrolled in the study. 171 subjects received BPX-501 T cells and rimiducid. Of these subjects, 142 were placed in the intent-to-treat population i.e. patients treated with haematopoietic stem cell transplantation (HSCT) and who received a dose of BPX-501 at 1x10^6 cells/kg. 16 subjects received at least 1 dose of rimiducid for the treatment of acute or chronic GvHD refractory to standard of care treatment

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	184	184	
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	5.8		
full range (min-max)	0.1 to 18.1	-	
Gender categorical Units: Subjects			
Female	83	83	
Male	101	101	

End points

End points reporting groups

Reporting group title	BPX-501 T Cells and Rimiducid

Reporting group description:

TCR alpha beta depleted graft infusion with addback of BPX-501 T cells (rivogenlecleucel).
Rimiducid/AP1903: Dimerizer drug administered to subjects who develop Grade III-IV acute GVHD, Grade II gut/liver acute GVDH or Grade I/II skin-only acute GvHD which is non-responsive after 7 days of standard of care treatment.BPX-501 T cells: 1x10E6 cells/kg infused on Day 0
Rimiducid: 0.4mg/kg administered IV to treat GVHD

Primary: Event-free Survival (EFS) at 180 Days After Transplant

End point title	Event-free Survival (EFS) at 180 Days After Transplant[1]

End point description:

Events included transplant-related mortality (TRM) / non-relapse mortality (NRM), severe GvHD (acute Grades 2-4 organ or extensive chronic GvHD) and life-threatening infections (Grade 4). Time to the first event only is represented in the primary endpoint, if a subsequent event occurred in the same patient this was not captured in this outcome.

End point type	Primary

End point timeframe:

180 days after transplant

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparator in the study so statistical analysis not feasible. Kaplan-Meier technique was used to estimate event free survival at Day 180.

End point values	BPX-501 T Cells and Rimiducid			
Subject group type	Reporting group			
Number of subjects analysed	142			
Units: Kaplan Meier EFS Estimate (%)				
number (confidence interval 95%)	90.8 (84.6 to 94.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within 180 days post BPX-501 or 30 days post Rimiducid

Adverse event reporting additional description:

Analysis of safety, regardless of study treatment and in relation to BPX-501, was conducted with the BPX-501 Safety Population (patients who received HSCT and subsequently received a dose of BPX-501)
Analysis of safety in relation to rimiducid treatment was performed with the Rimiducid Population (patients who received at least 1 dose of rimiducid)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Rivogenlecleucel

Reporting group description:

Analysis of safety, regardless of study treatment and in relation to rivogenlecleucel (BPX-501), was conducted with the rivogenlecleucel Safety Population (patients who received HSCT and subsequently received any dose of rivogenlecleucel)

Reporting group title	Rimiducid

Reporting group description:

Rimiducid/AP1903 (0.4 mg/kg) is a dimerizer drug administered via intravenous infusion to subjects who develop Grade III-IV acute GVHD, Grade II gut/liver acute GVDH or Grade I/II skin-only acute GvHD which is non-responsive after 7 days of standard of care treatment.

Analysis of safety in relation to rimiducid treatment was performed with the Rimiducid Population, (patients who received at least 1 dose of rimiducid)

Serious adverse events	Rivogenlecleucel	Rimiducid	
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 171 (30.41%)	7 / 16 (43.75%)	
number of deaths (all causes)	7	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Juvenile chronic myelomonocytic leukaemia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic venous thrombosis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Device damage			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device complication			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	7 / 171 (4.09%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	4 / 171 (2.34%)	2 / 16 (12.50%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumopericardium			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Miller Fisher syndrome			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytopenia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemolytic anaemia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	

Haematemesis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotid gland enlargement			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	3 / 171 (1.75%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Device related infection			
subjects affected / exposed	3 / 171 (1.75%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	1 / 171 (0.58%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	2 / 171 (1.17%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rivogenlecleucel	Rimiducid	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	140 / 171 (81.87%)	9 / 16 (56.25%)	
Cardiac disorders			
Right ventricular failure			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Central nervous system lesion			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	33 / 171 (19.30%)	0 / 16 (0.00%)	
occurrences (all)	33	0	
Immune system disorders			
Chronic graft versus host disease			
subjects affected / exposed	5 / 171 (2.92%)	1 / 16 (6.25%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 171 (11.70%)	0 / 16 (0.00%)	
occurrences (all)	20	0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	10 / 171 (5.85%)	0 / 16 (0.00%)	
occurrences (all)	10	0	
Parotid gland enlargement			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Vomiting			

subjects affected / exposed	20 / 171 (11.70%)	0 / 16 (0.00%)	
occurrences (all)	20	0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertension			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Respiratory distress			
subjects affected / exposed	2 / 171 (1.17%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	12 / 171 (7.02%)	0 / 16 (0.00%)	
occurrences (all)	12	0	
Rash			
subjects affected / exposed	21 / 171 (12.28%)	0 / 16 (0.00%)	
occurrences (all)	21	0	
Skin discolouration			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Infections and infestations			
Acute graft versus host disease			
subjects affected / exposed	48 / 171 (28.07%)	3 / 16 (18.75%)	
occurrences (all)	48	3	
Adenovirus infection			
subjects affected / exposed	11 / 171 (6.43%)	0 / 16 (0.00%)	
occurrences (all)	11	0	
Cytomegalovirus infection A			
subjects affected / exposed	34 / 171 (19.88%)	0 / 16 (0.00%)	
occurrences (all)	34	0	
Human herpesvirus 6 infection			
subjects affected / exposed	9 / 171 (5.26%)	0 / 16 (0.00%)	
occurrences (all)	9	0	

Sepsis			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Septic shock			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Staphylococcal infection			
subjects affected / exposed	1 / 171 (0.58%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 171 (1.17%)	1 / 16 (6.25%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2014	Version 2.0
17 December 2014	Version 3.0
05 March 2015	Version 4.0
30 October 2015	Version 5.1 (Italy)
15 November 2015	Version 6.0 (Italy)
22 April 2016	Version 7.0 (Italy)
08 November 2016	Version 8.0 (Italy)
10 February 2017	Version 9.0 (Italy)
10 February 2017	Version 5.0 (UK)
02 April 2018	Version 10.0 (Italy)
02 April 2018	Version 6.0 (UK)
29 October 2018	Version 11.0 (Italy)
01 November 2018	Version 7.0 (UK)
30 June 2020	Version 8.0 (UK)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported