Clinical trial results:
An open-label, Phase I/II study to assess the safety and clinical activity of NKR-2 treatment administration after a non-myeloablative preconditioning chemotherapy in relapse/refractory acute myeloid leukemia or myelodysplastic syndrome patients.

Summary

EudraCT number	2018-000205-22
Trial protocol	BE
Global end of trial date	01 February 2021

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	CYAD-N2T-005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Celyad Oncology SA
Sponsor organisation address	Rue Edouard Belin 2, Mont-Saint-Guibert, Belgium, 1435
Public contact	Clinical Trial Information, Celyad Oncology SA, 32 10394100, info@celyad.com
Scientific contact	Clinical Trial Information, Celyad Oncology SA, 32 10394100, info@celyad.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2021
Global end of trial reached?	Yes
Global end of trial date	01 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to document and characterized the safety of the NKR-2 treatment administration in r/r AML/MDS patients after a non-myeloablative preconditioning.

Protection of trial subjects:

This study was conducted in accordance with the protocol, standards of Good Clinical Practice (as defined by the International Council on Harmonisation), ethical principles that have their origin in the Declaration of Helsinki and all applicable national and local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2018
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?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	17
EEA total number of subjects	6

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	7

From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 25 patients were screened in the study of which 17 patients treated.
These patients have been recruited at 7 sites of which 3 in Belgium and 4 in the United States.
The first patient was enrolled on 18 Sep 2018 and the last patient was enrolled on 03 Jun 2020.

Pre-assignment

Screening details:

A total of 25 patients signed Informed Consent and entered the Screening phase.
8 patients were considered screening failures as they did not meet all of the In- and Exclusion criteria at the end of the Screening Phase.

Pre-assignment period milestones

Number of subjects started	17
Number of subjects completed	17

Period 1

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

Arms

Arm title	NKR-2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	NKR-2, Human T-cells transduced with a retrovirus containing the NKG2D-based chimeric antigen receptor (CAR) construct
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

In the first segment (dose escalation) all patients received a preconditioning regimen prior to a single NKR-2 administration. This segment was divided into four sequential cohorts aimed to determine the recommended investigational treatment option (schedule of preconditioning and NKR-2 dose).
Patients without Progression of Disease (PD) could receive a consolidation cycle with three additional NKR-2 administrations.
In the second segment (i.e., extension segment) patients were treated at the recommended NKR 2 dose (1x10^8, 3x10^8 or 1x10^9 NKR-2 cells/injection) and CY-FLU preconditioning.

Number of subjects in period 1	NKR-2
Started	17
Completed	17

Baseline characteristics

Reporting groups	
Reporting group title	Overall study period (overall trial)

Reporting group description: -

Reporting group values	Overall study period (overall trial)	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	10	10	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	64.71		
full range (min-max)	50 to 75	-	
Gender categorical			
sex of patients			
Units: Subjects			
Female	8	8	
Male	9	9	

End points

End points reporting groups

Reporting group title	NKR-2

Reporting group description: -

Primary: DLT occurrence during dose escalation phase

End point title	DLT occurrence during dose escalation phase[1]

End point description:

End point type	Primary

End point timeframe:

study treatment phase

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: Based on 3+3 study design for dose escalation in phase I part of the study, no statistical analysis required in the study protocol.

End point values	NKR-2			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: event	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AE's have been reported from the point of apheresis (after ICF signature) until the end of the Treatment follow up-phase.
All SAE's have been reported from ICF signature until the end of the Long-Term Safety follow up period (=entire study period).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	NKR2

Reporting group description: -

Serious adverse events	NKR2		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 17 (82.35%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events			
Investigations			
Clostridium test positive			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Acute haemolytic transfusion reaction			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Toxic encephalopathy			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
General physical health deterioration			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

Pyrexia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	9 / 11		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fungaemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemophilus infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rectal abscess			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	NKR2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Muscle spasms			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Leukaemia cutis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular disorders			

Embolism			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	9		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	6		
Facial pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	7		
Generalised oedema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Hypothermia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	7		
Pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Peripheral swelling			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	10 / 17 (58.82%)		
occurrences (all)	13		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	10 / 17 (58.82%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Atelectasis			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	8		
Dyspnoea			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	6		
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	8		
Lung consolidation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Non-cardiogenic pulmonary oedema			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pharyngeal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	7		
Pleuritic pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pulmonary mass			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pulmonary oedema			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Rhinitis allergic			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Tachypnoea			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Hallucination			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Nervousness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	6		
Blood antidiuretic hormone abnormal			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood fibrinogen decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Breath sounds abnorma			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Clostridium test positive			

subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Ejection fraction decreased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
International normalised ratio increased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Liver function test abnormal				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	9			
Neutrophil count decreased				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	8			
Oxygen saturation decreased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Platelet count decreased				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	17			
Respiratory syncytial virus test positive				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Troponin T increased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Urine output decreased				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Weight increased				

subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	7		
White blood cell count decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Muscle injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin wound			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pericardial effusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Sinus tachycardia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	5		
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	3		
Neuropathy peripheral			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Taste disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 17 (52.94%)		
occurrences (all)	38		
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Febrile neutropenia			
subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	7		
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	4		
Leukopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Lymphopenia			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	21		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Dry eye			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	8 / 17 (47.06%)		
occurrences (all)	8		
Dry mouth			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gingival bleeding			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Hiatus hernia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Lip dry			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	6		
Proctalgia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Hepatobiliary disorders			
Hepatosplenomegaly			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Ecchymosis			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Petechiae			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Purpura			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Rash maculo-papular			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	5		
Dysuria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Micturition urgency			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Renal cyst			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Joint swelling			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	3		
Pain in extremity			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Soft tissue swelling			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Synovial cyst			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	3		
Clostridium difficile infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Enterocolitis infectious			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Erysipelas			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Rash pustular			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Sepsis syndrome			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	4		
Fluid retention			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Hyperglycaemia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Hyperphosphataemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	6		
Hypokalaemia			
subjects affected / exposed	8 / 17 (47.06%)		
occurrences (all)	17		
Hypomagnesaemia			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	15		
Hyponatraemia			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	5		

Hypophosphataemia subjects affected / exposed occurrences (all)	5 / 17 (29.41%) 8		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2018	The main changes were related to (i) a prolongation of the mandatory period of hospitalization when the NKR-2 treatment is administered after a preconditioning therapy, (ii) an update of criteria to grading both CRS and CRES, (iii) an updated of the DLT definition and (iv) an extension of the age of patient till 75 years old.
08 May 2018	The main changes were related to the reduction of potential risks to the trial subjects and to better manage adverse events, including (i) a simplification of the administration scheme (patients, whatever their clinical response status, will no longer receive a new NKR-2 injection with a prior lymphodepletion preconditioning), (ii) an updated of patient's staggering and (iv) an update of inclusion and exclusion cirtieria.
21 January 2019	The main changes were related to (i) the addition of a 4th cohort, (ii) the addition of a study phase II, (iii) the simplification of the administration phase and (iv) an update of the Object Response Rate (ORR) definition.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported