Clinical trial results:
Phase 1/2 Study of Bempegaldesleukin in Combination With Nivolumab in Children, Adolescents, and Young Adults With Recurrent or Refractory Malignancies (PIVOT IO 020)

Summary

EudraCT number	2020-000854-85
Trial protocol	FR ES DE IT Outside EU/EEA
Global end of trial date	22 June 2022

Results information

Result version number	v1 (current)
This version publication date	06 January 2023
First version publication date	06 January 2023

Trial information

Trial identification

Sponsor protocol code	CA045-020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04730349
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002492-PIP01-18
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	25 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of bempegaldesleukin (bempeg; NKTR-214) in combination with nivolumab (nivo) in pediatric participants with malignant neoplasms that were refractory, or relapsed, or in participants for whom curative treatments are lacking.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2021
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	Australia: 3
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	15
EEA total number of subjects	9

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)	7
Adolescents (12-17 years)	8

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

15 participants were treated in Part A. Study did not progress to Part B; therefore, no participants enrolled in Part B.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)

Arm description:

Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks

Arm type	Experimental
Investigational medicinal product name	Bempegaldesleukin (NKTR-214)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Bempegaldesleukin 0.006 mg/kg administered intravenously every 3 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 4.5 mg/kg administered intravenously every 3 weeks

Arm title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)

Arm description:

Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 360 mg administered intravenously every 3 weeks

Investigational medicinal product name	Bempegaldesleukin (NKTR-214)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection

Routes of administration	Intravenous use

Dosage and administration details:

Bempegaldesleukin 0.006 mg/kg administered intravenously every 3 weeks

Number of subjects in period 1	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)
Started	8	7
Completed	1	2
Not completed	7	5
Disease progression	6	4
Participant withdrew consent	1	-
Study drug toxicity	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)
Reporting group description:	
Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks	
Reporting group title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)
Reporting group description:	
Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks	

Reporting group values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)	Total
Number of subjects	8	7	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	7	0	7
Adolescents (12-17 years)	1	7	8
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	7.5	14.9	
standard deviation	± 3.9	± 1.5	-
Sex: Female, Male Units: Participants			
Female	4	2	6
Male	4	5	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	4	6	10
Unknown or Not Reported	3	1	4
Race/Ethnicity, Customized Units: Subjects			
White	6	5	11
Black or African American	1	0	1
Other	1	2	3

End points

End points reporting groups

Reporting group title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)
Reporting group description:	
Bempegaldesleukin 0.006 mg/kg + Nivolumab 4.5 mg/kg administered intravenously every 3 weeks	
Reporting group title	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)
Reporting group description:	
Bempegaldesleukin 0.006 mg/kg + Nivolumab 360 mg administered intravenously every 3 weeks	

Primary: Number of Participants with Dose-Limiting Toxicities (DLTs) - Part A

End point title	Number of Participants with Dose-Limiting Toxicities (DLTs) - Part A[1]
End point description:	
Number of participants with dose-limiting toxicities (DLTs). DLTs were collected and evaluated for Part A within the DLT evaluation period, which started on Cycle 1 Day 1 (first dose) and ended at Day 42 (42 days after first dose of the study therapy).	
End point type	Primary
End point timeframe:	
From first dose to 42 days after first dose	

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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs) - Part A

End point title	Number of Participants with Adverse Events (AEs) - Part A[2]
End point description:	
Number of participants with adverse events (AEs). An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.	

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[2] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	8	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events (SAEs) - Part A

End point title	Number of Participants with Serious Adverse Events (SAEs) - Part A[3]

End point description:

Number of participants with serious adverse events (SAEs). SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[3] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	6	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Drug-Related Adverse Events - Part A

End point title	Number of Participants with Drug-Related Adverse Events - Part A[4]

End point description:

Number of participants with drug-related adverse events. An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[4] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	6	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events Leading to Discontinuation - Part A

End point title	Number of Participants with Adverse Events Leading to Discontinuation - Part A[5]

End point description:

Number of participants with adverse events leading to discontinuation. An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[5] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Died - Part A

End point title	Number of Participants Who Died - Part A[6]

End point description:

Number of participants who died.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[6] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) - Part A

End point title	Maximum Observed Plasma Concentration (Cmax) - Part A[7]

End point description:

Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[7] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[8] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[9] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Primary: Primary: Trough Observed Concentration (Ctrough) - Part A

End point title	Primary: Trough Observed Concentration (Ctrough) - Part A[10]

End point description:

Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[10] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[11] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[12] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration (AUC) - Part A

End point title	Area Under the Plasma Concentration (AUC) - Part A[13]

End point description:

Pharmacokinetics (PK) of bempegaldesleukin and nivolumab derived from serum concentration versus time data.

End point type	Primary

End point timeframe:

From first dose to 30 days after last dose (up to approximately 6 months)

Notes:

[13] - 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: Only summary statistics planned for this endpoint.

End point values	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	Part A: Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[14] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

[15] - Study terminated. PK samples not shipped for bioanalytical analysis. No PK data generated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants assessed for all-cause mortality from first dose to study completion (up to approximately 13 months). SAEs and NSAEs were assessed from first dose to 150 days after last dose of study therapy (up to approximately 11 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)
Reporting group description: -	
Reporting group title	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)

Reporting group description: -

Serious adverse events	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	8 / 8 (100.00%)	
number of deaths (all causes)	2	7	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 7 (28.57%)	6 / 8 (75.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 6	
Injury, poisoning and procedural complications			
Skin wound			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
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			
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	
occurrences causally related to treatment / all	2 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (360 mg)	Bempegaldesleukin (0.006 mg/kg)+ Nivolumab (4.5 mg/kg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	8 / 8 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 7 (28.57%)	4 / 8 (50.00%)	
occurrences (all)	8	4	
Generalised oedema			

subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	3 / 7 (42.86%)	2 / 8 (25.00%)	
occurrences (all)	6	3	
Pain			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Nasal congestion			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Lung disorder			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Pulmonary embolism			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pneumothorax			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pneumonitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Behaviour disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Alanine aminotransferase increased			
subjects affected / exposed	3 / 7 (42.86%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Lymphocyte count decreased			
subjects affected / exposed	3 / 7 (42.86%)	1 / 8 (12.50%)	
occurrences (all)	8	1	
Neutrophil count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
White blood cell count decreased			
subjects affected / exposed	3 / 7 (42.86%)	0 / 8 (0.00%)	
occurrences (all)	6	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Ligament sprain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Dizziness			

subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Ataxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	2 / 7 (28.57%)	3 / 8 (37.50%)	
occurrences (all)	3	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 7 (42.86%)	1 / 8 (12.50%)	
occurrences (all)	7	1	
Eosinophilia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Photophobia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	3 / 7 (42.86%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
Tooth discolouration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	
occurrences (all)	5	2	
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Rash			

subjects affected / exposed	1 / 7 (14.29%)	3 / 8 (37.50%)	
occurrences (all)	1	4	
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Hyperthyroidism			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Bone pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Infections and infestations			

Lymphangitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hypophosphataemia			

subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 8 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2021	Updated the minimum days from "100" to "150" days following discontinuation of drug for collection of all serious adverse events (SAEs) and Non-Serious Adverse Events (NSAEs).

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.

This study was terminated on 22-Jun-2022. This results disclosure report provides analyses from CA045-020 Part A safety analyses only. Part B of the study (expansion phase) did not enroll any participants.

Notes: