Clinical trial results:
A first-in-human, open-label, dose escalation followed by dose expansion phase I/IIa trial to evaluate the safety, preliminary efficacy and pharmacokinetics of intratumoral CyPep-1 monotherapy and in combination with pembrolizumab in patients with advanced solid cancers.

Summary

EudraCT number	2019-003317-33
Trial protocol	NL FR ES
Global end of trial date	05 July 2024

Results information

Result version number	v1 (current)
This version publication date	02 July 2025
First version publication date	02 July 2025

Trial information

Trial identification

Sponsor protocol code	CyPep-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cytovation ASA
Sponsor organisation address	5058 Bergen, Bergen, Norway,
Public contact	General contact, Cytovation ASA, contact@cytovation.com
Scientific contact	General contact, Cytovation ASA, contact@cytovation.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	05 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2024
Global end of trial reached?	Yes
Global end of trial date	05 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of IT administration of CyPep-1 as monotherapy and in combination with pembrolizumab.
To identify the recommended phase II dose (RP2D) of CyPep-1 as monotherapy and in combination with pembrolizumab.

Protection of trial subjects:

The Dose Escalation Committee (DEC) was comprised of all the Investigators or designees, medical monitor, and representatives of the Sponsor. The decisions on dose escalation and CyPep 1 maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D) were taken by the DEC after reviewing safety data (including dose-limiting toxicities [DLTs] from all patients who entered Phase I of the study and completed the DLT observation period). The DEC was responsible for the review of all data after all patients in the highest dose cohort completed the DLT observation period and before enrolment of patients in the expansion cohort at RP2D in monotherapy and combination with pembrolizumab cohort was initiated. The decision to de escalate the dose of CyPep-1 based on the observed severity and relatedness of safety events (DLT/treatment limiting toxicity [TLT] criteria for CyPep-1) and to what dose (either dose level of the next lowest dose level from Phase I or 50-70% of current dose level), was also made by the DEC after reviewing available safety data (including TLTs). Based on the review of this data, recommendations were made regarding the further conduct and the scientific and ethical integrity of the study. The final decision to act upon these recommendations was the responsibility of the Sponsor

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 42
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	France: 14
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	20
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 7 investigational sites in 3 countries (France, Spain, and The Netherlands). A total of 87 patients were screened for eligibility, with 27 excluded (25 due to screening failures, and 2 not assigned). Of the original 87 patients screened, 60 were eligible and were allocated into corresponding Phase I and II treatment arms

Pre-assignment

Screening details:

The study consisted of 2 phases and 4 arms. For both phases and all study arms, patients signed the ICF and completed the Screening visit to determine eligibility to participate in the study. Patients stayed in the study until end of study or until confirmed disease progression, unacceptable toxicity, death or discontinuation for any other reason.

Period 1

Period 1 title	Phase 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study, blinding not applicable.

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 1

Arm description:

Cohort 1: dose escalation at 0.5 mg/mL, n=3

Arm type	Experimental
Investigational medicinal product name	CyPep-1 0.5 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

0.5 mL via intratumoral administration

Arm title	Cohort 2

Arm description:

Cohort 2: 2 mg/mL, n=5

Arm type	Experimental
Investigational medicinal product name	CyPep-1 2.0 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

CyPep-1 2.0 mg/mL intratumoral

Arm title	Cohort 3

Arm description:

Cohort 3: 5 mg/mL, n=6

Arm type	Experimental

Investigational medicinal product name	CyPep-1 5.0 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

5.0 mg/mL via intratumoral

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	3	5	6
Completed	0	0	0
Not completed	3	5	6
Consent withdrawn by subject	-	1	-
Death	3	4	6

Period 2

Period 2 title	Phase 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study, blinding not applicable.

Arms

Are arms mutually exclusive?	No
Arm title	Arm B

Arm description:

The safety and tolerability of CyPep-1 in combination with pembrolizumab was evaluated in a cohort of 15 patients in total, using a staggered approach. Initially, 3 patients received CyPep-1 at RP2D in combination with pembrolizumab once every 6 weeks

Arm type	Experimental
Investigational medicinal product name	CyPep-1 5.0 mg/mL + IV pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

5.0mg/mL via intratumoral administration

Arm title	Arm C (Cohort 4)

Arm description:

the safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver (Cohort 4: 2 mg/mL, n=6)

Arm type	Experimental

Investigational medicinal product name	CyPep-1 2.0 mg/mL for liver metastases
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

2.0mg/mL via intratumoral administration

Arm title	Arm C (Cohort 5)

Arm description:

The safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver. The RP2D (Cohort 5: 5 mg/mL, n=6)

Arm type	Experimental
Investigational medicinal product name	CyPep-1 5.0 mg/mL for liver metastases
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

5.0mg/mL via intratumoral administration

Arm title	Arm D

Arm description:

The safety and tolerability of CyPep-1 at RP2D was planned to be further evaluated with focus on assessing efficacy signals of CyPep-1 monotherapy in 30 patients with cutaneous melanoma

Arm type	Experimental
Investigational medicinal product name	CyPep-1 5.0 mg/mL for melanoma
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

5.0mg/mL via intratumoral administration

Arm title	Arm A

Arm description:

CyPep-1 5.0mg/mL Monotherapy

Arm type	Experimental
Investigational medicinal product name	CyPep-1 5.0 mg/mL Monotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intratumoral use

Dosage and administration details:

5.0 mg/mL via intratumoral

Number of subjects in period 2	Arm B	Arm C (Cohort 4)	Arm C (Cohort 5)
Started	15	6	6
Completed	1	1	0
Not completed	14	5	6
Consent withdrawn by subject	-	-	-
Death	14	5	5
Termination of the study	-	-	-
Sponsor terminated	-	-	1

Number of subjects in period 2	Arm D	Arm A
Started	1	18
Completed	0	2
Not completed	1	16
Consent withdrawn by subject	1	2
Death	-	13
Termination of the study	-	1
Sponsor terminated	-	-

Baseline characteristics

Reporting groups[1]	
Reporting group title	Cohort 1
Reporting group description:	
Cohort 1: dose escalation at 0.5 mg/mL, n=3	
Reporting group title	Cohort 2
Reporting group description:	
Cohort 2: 2 mg/mL, n=5	
Reporting group title	Cohort 3
Reporting group description:	
Cohort 3: 5 mg/mL, n=6	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects in both the phases are different because the arms are not mutually exclusive. The subjects in Phase 1 (dose escalation) did not roll over into Phase 2 (dose expansion).

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	3	5	6
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	2	2
From 65-84 years	3	3	4
85 years and over	0	0	0
Age continuous Units: years			
median	53	64	57.0
standard deviation	± 11.2	± 10.8	± 5.9
Gender categorical Units: Subjects			
Female	1	2	2
Male	2	3	4

Reporting group values	Total		
Number of subjects	14		
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)	4		
From 65-84 years	10		
85 years and over	0		
Age continuous Units: years			
median			
standard deviation	-		
Gender categorical Units: Subjects			
Female	5		
Male	9		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Cohort 1: dose escalation at 0.5 mg/mL, n=3	
Reporting group title	Cohort 2
Reporting group description:	
Cohort 2: 2 mg/mL, n=5	
Reporting group title	Cohort 3
Reporting group description:	
Cohort 3: 5 mg/mL, n=6	
Reporting group title	Arm B
Reporting group description:	
The safety and tolerability of CyPep-1 in combination with pembrolizumab was evaluated in a cohort of 15 patients in total, using a staggered approach. Initially, 3 patients received CyPep-1 at RP2D in combination with pembrolizumab once every 6 weeks	
Reporting group title	Arm C (Cohort 4)
Reporting group description:	
the safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver (Cohort 4: 2 mg/mL, n=6)	
Reporting group title	Arm C (Cohort 5)
Reporting group description:	
The safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver. The RP2D (Cohort 5: 5 mg/mL, n=6)	
Reporting group title	Arm D
Reporting group description:	
The safety and tolerability of CyPep-1 at RP2D was planned to be further evaluated with focus on assessing efficacy signals of CyPep-1 monotherapy in 30 patients with cutaneous melanoma	
Reporting group title	Arm A
Reporting group description:	
CyPep-1 5.0mg/mL Monotherapy	

Primary: Type and number of adverse events

End point title	Type and number of adverse events[1]
End point description:	
End point type	Primary
End point timeframe:	
From the time of ICF signing until Follow up visit (or until EoT, if it occurred >30 days after the last CyPep-1 administration for Phase I and Arms A, C, and D; for Arm B. After the FU visit, only ongoing AEs or SAEs related to CyPep-1 were collected.	

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: Descriptive statistics was used. The total number/incidence of TEAEs was summarized, including the number of patients with at least one TEAE and the number of TEAEs per cohort and overall. The number of TEAEs per intensity (CTCAE) and relation to study drug was also included and summarized per cohort and overall.

End point values	Cohort 1	Cohort 2	Cohort 3	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	6	15
Units: Number of events				
TEAE	24	37	62	262
TESAE	1	0	0	7
CTCAE Grade ≥3	9	4	5	12
TEAE Leading to Study Treatment Discontinuation	0	0	1	0
Dose-Limiting Toxicity	0	0	0	0
Treatment-Limiting Toxicity	0	0	0	0
Fatal TEAE	0	0	0	0
TEAE Leading to CyPep-1 Interruption	1	1	1	8
TEAE Leading to Pembrolizumab Interruption	0	0	0	5

End point values	Arm C (Cohort 4)	Arm C (Cohort 5)	Arm D	Arm A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	1	18
Units: Number of events				
TEAE	91	91	4	143
TESAE	1	3	0	3
CTCAE Grade ≥3	4	12	0	8
TEAE Leading to Study Treatment Discontinuation	0	0	0	1
Dose-Limiting Toxicity	0	2	0	0
Treatment-Limiting Toxicity	0	0	0	0
Fatal TEAE	0	1	0	0
TEAE Leading to CyPep-1 Interruption	1	2	0	10
TEAE Leading to Pembrolizumab Interruption	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

End point type	Secondary

End point timeframe:

28 days after the date of the initial response

End point values	Cohort 1	Cohort 2	Cohort 3	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	6	15
Units: percentage				
number (not applicable)				
Overall Response Rate	0	0	0	0

End point values	Arm C (Cohort 4)	Arm C (Cohort 5)	Arm D	Arm A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	1	18
Units: percentage				
number (not applicable)				
Overall Response Rate	16.7	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall Survival

End point title	Overall Survival

End point description:

End point type	Other pre-specified

End point timeframe:

from start of study treatment to the date of death

End point values	Cohort 1	Cohort 2	Cohort 3	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	6	15
Units: Months				
median (full range (min-max))	5.2 (2.1 to 21.9)	5.5 (0.6 to 16.6)	13.2 (5.3 to 19.8)	5.8 (1.5 to 26.7)

End point values	Arm C (Cohort 4)	Arm C (Cohort 5)	Arm D	Arm A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	1	18
Units: Months				
median (full range (min-max))	8.3 (3.3 to 26.3)	4.2 (3.3 to 26.3)	0 (0 to 0)	7.7 (1.0 to 26.2)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression free survival

End point title	Progression free survival

End point description:

End point type	Other pre-specified

End point timeframe:

time from treatment start until disease relapse or disease progression (based on all lesions, using iRECIST) or death due to any cause, whichever occurred earliest

End point values	Cohort 1	Cohort 2	Cohort 3	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	6	15
Units: Months				
median (full range (min-max))	1.6 (1.2 to 1.9)	0.9 (0.0 to 9.3)	2.8 (1.6 to 12.3)	1.8 (0.0 to 5.4)

End point values	Arm C (Cohort 4)	Arm C (Cohort 5)	Arm D	Arm A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	1	18
Units: Months				
median (full range (min-max))	2.1 (1.4 to 5.7)	1.9 (1.8 to 16.6)	1.9 (1.8 to 16.6)	1.8 (0.0 to 5.4)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of ICF signing until Follow up visit (or until EoT, if it occurred >30 days after the last CyPep-1 administration for Phase I and Arms A, C, and D; for Arm B. After the FU visit, only ongoing AEs or SAEs related to CyPep-1 were collected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Cohort 1
Reporting group description:	
CyPep-1 5.0 mg/mL Monotherapy	
Reporting group title	Cohort 2
Reporting group description:	
CyPep-1 2.0 mg/mL	
Reporting group title	Cohort 3
Reporting group description:	
CyPep-1 5.0 mg/mL	
Reporting group title	Arm A
Reporting group description:	
CyPep-1 5.0 mg/mL Monotherapy	
Reporting group title	Arm B
Reporting group description:	
CyPep-1 5.0 mg/mL + IV pembrolizumab	
Reporting group title	Arm C (Cohort 4)
Reporting group description:	
CyPep-1 2.0 mg/mL for liver metastases	
Reporting group title	Arm C (Cohort 5)
Reporting group description:	
CyPep-1 5.0 mg/mL for liver metastases	
Reporting group title	Arm D
Reporting group description:	
CyPep-1 5.0 mg/mL for melanoma	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	3	4	6
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Brachiocephalic vein thrombosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Injection site hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			

subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm A	Arm B	Arm C (Cohort 4)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 18 (16.67%)	2 / 15 (13.33%)	1 / 6 (16.67%)

number of deaths (all causes)	13	14	5
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Injection site hypersensitivity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site ulcer			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site inflammation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Dyspnea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm C (Cohort 5)	Arm D	
Total subjects affected by serious adverse events			

subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
number of deaths (all causes)	5	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Injection site hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Dyspnea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 5 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 6 (33.33%)
occurrences (all)	0	4	14
Metastases to bone			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tumour thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	3 / 5 (60.00%)	3 / 6 (50.00%)
occurrences (all)	0	3	5
Pyrexia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	1 / 3 (33.33%)	4 / 5 (80.00%)	6 / 6 (100.00%)
occurrences (all)	2	6	23
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Inflammation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngeal oedema			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Drain site complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural fever			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stoma site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 6 (33.33%)
occurrences (all)	0	2	3
Ear and labyrinth disorders			

Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	3	1	4
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oesophageal obstruction			

subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			

Hepatic pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vitiligo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperthyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Oral fungal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Arm A	Arm B	Arm C (Cohort 4)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	15 / 15 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	5 / 18 (27.78%)	7 / 15 (46.67%)	0 / 6 (0.00%)
occurrences (all)	8	11	0
Metastases to bone			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tumour thrombosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertension			

subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 18 (50.00%)	8 / 15 (53.33%)	2 / 6 (33.33%)
occurrences (all)	13	16	5
Pyrexia			
subjects affected / exposed	2 / 18 (11.11%)	1 / 15 (6.67%)	3 / 6 (50.00%)
occurrences (all)	2	1	4
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	4	1
Pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	15 / 18 (83.33%)	12 / 15 (80.00%)	5 / 6 (83.33%)
occurrences (all)	60	72	15
Malaise			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Chills			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Injection site haematoma			

subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Face oedema			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Inflammation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injection site injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	2 / 6 (33.33%)
occurrences (all)	1	5	2
Hypoxia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Pleural effusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Dyspnoea at rest			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Laryngeal oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pneumothorax			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Depression			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Delirium			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	5	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	5	0
Blood creatinine increased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Amylase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urine output decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	3
Drain site complication			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Post procedural erythema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Post procedural fever			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Stoma site erythema			

subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Aphasia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depressed level of consciousness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 18 (27.78%)	5 / 15 (33.33%)	2 / 6 (33.33%)
occurrences (all)	5	6	2
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 18 (5.56%)	5 / 15 (33.33%)	3 / 6 (50.00%)
occurrences (all)	1	7	6
Nausea			
subjects affected / exposed	2 / 18 (11.11%)	5 / 15 (33.33%)	3 / 6 (50.00%)
occurrences (all)	2	9	8
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	3	1	1
Vomiting			

subjects affected / exposed	1 / 18 (5.56%)	4 / 15 (26.67%)	3 / 6 (50.00%)
occurrences (all)	1	5	8
Rectal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ileus			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oesophageal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 18 (11.11%)	2 / 15 (13.33%)	1 / 6 (16.67%)
occurrences (all)	3	4	1
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Abdominal distension			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Breath odour			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eructation			

subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Inguinal hernia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oedema mouth			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Retching			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitiligo			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Rash			

subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Urticaria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Scar pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin wound			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Hyperthyroidism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flank pain			

subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	6 / 15 (40.00%)	1 / 6 (16.67%)
occurrences (all)	0	6	1
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Bone pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mobility decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain in jaw			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pyelonephritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	3 / 18 (16.67%)	2 / 15 (13.33%)	1 / 6 (16.67%)
occurrences (all)	3	2	1

Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	3 / 15 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 18 (22.22%)	4 / 15 (26.67%)	2 / 6 (33.33%)
occurrences (all)	5	7	4
Hyponatraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	3
Hypercalcaemia			

subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Hypophosphataemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Malnutrition			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Arm C (Cohort 5)	Arm D	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	1 / 1 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Metastases to bone			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Tumour thrombosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)	1 / 1 (100.00%)	
occurrences (all)	6	2	
Pyrexia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Catheter site haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Injection site reaction			
subjects affected / exposed	5 / 6 (83.33%)	1 / 1 (100.00%)	
occurrences (all)	26	2	
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Injection site injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			

Breast tenderness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dyspnoea at rest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Laryngeal oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Productive cough			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Urine output decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Drain site complication			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Post procedural erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Post procedural fever			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Post procedural haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Stoma site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sinus tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Brachial plexopathy			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Depressed level of consciousness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Presyncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Somnolence subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	0 / 1 (0.00%) 0	
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 1 (0.00%) 0	
Hypoacusis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Oesophageal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			

subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Breath odour			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eructation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Inguinal hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Oedema mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vitiligo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Psoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Scar pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin wound			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperthyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Mobility decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Oral fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Malnutrition			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2019	• Removal Day 2 from Schedule of Events • Clarification prophylactic hydration requirement • Update non-clinical data • Clarification of risks and benefits • Clarification SUSAR definition • Clarification safety analysis will be performed for RP2D selection

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 April 2020	Temporary halt of recruitment due to the COVID-19 pandemic Apr2020- May2020	01 June 2020

Notes:

Limitations and caveats

None reported