



Clinical trial results:

A Phase 1-2, Open-Label, Dose-Finding, Proof of Concept, First-in-Human Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of CX-2009 in Adults with Metastatic or Locally Advanced Unresectable Solid Tumors (PROCLAIM-CX-2009)

Summary

EudraCT number	2017-000625-12
Trial protocol	NL ES DE
Global end of trial date	10 September 2020

Results information

Result version number	v1 (current)
This version publication date	17 October 2021
First version publication date	17 October 2021

Trial information

Trial identification

Sponsor protocol code	CTMX-M-2009-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03149549
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CytomX Therapeutics, Inc
Sponsor organisation address	151 Oyster Point Blvd, South San Francisco, United States, 94080
Public contact	Clinical Trial Team, CytomX Therapeutics, Inc, 001 650-763-9501, clinicaltrials@cytomx.com
Scientific contact	Clinical Development, CytomX Therapeutics, Inc, 001 650-515-3185, clinicaltrials@cytomx.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2020
Global end of trial reached?	Yes
Global end of trial date	10 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to determine the safety profile of CX-2009, the maximum tolerated dose (MTD) / Recommended Phase 2 Dose (RP2D), and the dose-limiting toxicities (DLTs) of CX-2009, when administered intravenously (IV) every 21 days as monotherapy to subjects with selected advanced or recurrent solid tumors.

Protection of trial subjects:

This study was conducted in full accordance with the World Medical Association Declaration of Helsinki concerning written informed consent and the protection of rights of human subjects. The investigators agreed to comply with Food and Drug Administration (FDA) Regulations, IRB/IEC Regulations and International Council of Harmonisation (ICH) Guidelines for Good Clinical Practices (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2017
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	United States: 64
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	99
EEA total number of subjects	26

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)	65
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 4 parts (Part A, Part A2, Part B, and Part C1). Enrolled patients continued on study through the follow-up period. Each study part consisted of 3 periods: a 30-day screening, a treatment period, and a follow-up period.

Pre-assignment

Screening details:

As of 09/April/2020, 99 patients had been enrolled and treated in the study (47 in Part A, 39 in Part A2, 3 in Part B, and 10 in Part C1); enrolled patients continued on study through the follow-up period. The study was terminated early after these subjects were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Group 1 (≤ 4 mg/kg (Q3W))

Arm description:

less than or equal to 4 mg/kg (Q3W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 2 (5 mg/kg (Q3W))
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Arm description:

5 mg/kg (Q3W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 3 (6 mg/kg (Q3W))
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Arm description:

6 mg/kg (Q3W)

Arm type	Experimental
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Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details:	
CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 4 (7 mg/kg (Q3W))
Arm description:	
7 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details:	
CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 5 (8 mg/kg (Q3W))
Arm description:	
8 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details:	
CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 6 (9 mg/kg (Q3W))
Arm description:	
9 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details:	
CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 7 (10 mg/kg (Q3W))
Arm description:	
10 mg/kg (Q3W)	
Arm type	Experimental

Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 8 (4 mg/kg (Q2W))
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Arm description:

4 mg/kg (Q2W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 9 (6 mg/kg (Q2W))
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Arm description:

6 mg/kg (Q2W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Number of subjects in period 1	Dose Group 1 (≤ 4 mg/kg (Q3W))	Dose Group 2 (5 mg/kg (Q3W))	Dose Group 3 (6 mg/kg (Q3W))
Started	20	9	9
Completed	14	7	7
Not completed	6	2	2
Adverse event, serious fatal	3	1	-
Termination by Sponsor	-	-	-
Consent withdrawn by subject	3	1	2
Unknown	-	-	-

Number of subjects in period 1	Dose Group 4 (7 mg/kg (Q3W))	Dose Group 5 (8 mg/kg (Q3W))	Dose Group 6 (9 mg/kg (Q3W))
Started	12	22	9
Completed	8	16	7
Not completed	4	6	2

Adverse event, serious fatal	2	4	1
Termination by Sponsor	1	-	-
Consent withdrawn by subject	-	2	-
Unknown	1	-	1

Number of subjects in period 1	Dose Group 7 (10 mg/kg (Q3W))	Dose Group 8 (4 mg/kg (Q2W))	Dose Group 9 (6 mg/kg (Q2W))
Started	8	4	6
Completed	8	4	4
Not completed	0	0	2
Adverse event, serious fatal	-	-	1
Termination by Sponsor	-	-	1
Consent withdrawn by subject	-	-	-
Unknown	-	-	-

Period 2

Period 2 title	Follow-Up Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Group 1 (≤ 4 mg/kg (Q3W))

Arm description:

less than or equal to 4 mg/kg (Q3W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 2 (5 mg/kg (Q3W))
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Arm description:

5 mg/kg (Q3W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of

sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 3 (6 mg/kg (Q3W))
Arm description: 6 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details: CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 4 (7 mg/kg (Q3W))
Arm description: 7 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details: CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 5 (8 mg/kg (Q3W))
Arm description: 8 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion
Dosage and administration details: CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL	
Arm title	Dose Group 6 (9 mg/kg (Q3W))
Arm description: 9 mg/kg (Q3W)	
Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 7 (10 mg/kg (Q3W))
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Arm description:

10 mg/kg (Q3W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 8 (4 mg/kg (Q2W))
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Arm description:

4 mg/kg (Q2W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Arm title	Dose Group 9 (6 mg/kg (Q2W))
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Arm description:

6 mg/kg (Q2W)

Arm type	Experimental
Investigational medicinal product name	CX-2009
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

CX-2009 was supplied as a lyophilized powder (cake) in 25 mg vials to be reconstituted with 5 mL of sterile water for injection to a final concentration of 5.0 mg/mL

Number of subjects in period 2	Dose Group 1 (≤ 4 mg/kg (Q3W))	Dose Group 2 (5 mg/kg (Q3W))	Dose Group 3 (6 mg/kg (Q3W))
Started	14	7	7
Completed	12	3	6
Not completed	2	4	1
Termination by Sponsor	1	-	-
Consent withdrawn by subject	1	-	-
Unknown	-	-	-
Lost to follow-up	-	4	1

Number of subjects in period 2	Dose Group 4 (7 mg/kg (Q3W))	Dose Group 5 (8 mg/kg (Q3W))	Dose Group 6 (9 mg/kg (Q3W))
Started	8	16	7
Completed	3	9	5
Not completed	5	7	2
Termination by Sponsor	1	5	-
Consent withdrawn by subject	4	1	1
Unknown	-	-	1
Lost to follow-up	-	1	-

Number of subjects in period 2	Dose Group 7 (10 mg/kg (Q3W))	Dose Group 8 (4 mg/kg (Q2W))	Dose Group 9 (6 mg/kg (Q2W))
Started	8	4	4
Completed	5	1	1
Not completed	3	3	3
Termination by Sponsor	-	3	2
Consent withdrawn by subject	3	-	1
Unknown	-	-	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Dose Group 1 (≤ 4 mg/kg (Q3W))
Reporting group description: less than or equal to 4 mg/kg (Q3W)	
Reporting group title	Dose Group 2 (5 mg/kg (Q3W))
Reporting group description: 5 mg/kg (Q3W)	
Reporting group title	Dose Group 3 (6 mg/kg (Q3W))
Reporting group description: 6 mg/kg (Q3W)	
Reporting group title	Dose Group 4 (7 mg/kg (Q3W))
Reporting group description: 7 mg/kg (Q3W)	
Reporting group title	Dose Group 5 (8 mg/kg (Q3W))
Reporting group description: 8 mg/kg (Q3W)	
Reporting group title	Dose Group 6 (9 mg/kg (Q3W))
Reporting group description: 9 mg/kg (Q3W)	
Reporting group title	Dose Group 7 (10 mg/kg (Q3W))
Reporting group description: 10 mg/kg (Q3W)	
Reporting group title	Dose Group 8 (4 mg/kg (Q2W))
Reporting group description: 4 mg/kg (Q2W)	
Reporting group title	Dose Group 9 (6 mg/kg (Q2W))
Reporting group description: 6 mg/kg (Q2W)	

Reporting group values	Dose Group 1 (≤ 4 mg/kg (Q3W))	Dose Group 2 (5 mg/kg (Q3W))	Dose Group 3 (6 mg/kg (Q3W))
Number of subjects	20	9	9
Age categorical			
Adult Subjects of at least 18 years of age and older			
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)	11	7	5
From 65-84 years	9	2	4
85 years and over	0	0	0

Gender categorical			
Units: Subjects			
Female	13	7	6
Male	7	2	3
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	18	8	8
More than one race	0	1	0
Unknown or Not Reported	0	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	2	0
Not Hispanic or Latino	18	7	8
Unknown or Not Reported	1	0	1

Reporting group values	Dose Group 4 (7 mg/kg (Q3W))	Dose Group 5 (8 mg/kg (Q3W))	Dose Group 6 (9 mg/kg (Q3W))
Number of subjects	12	22	9
Age categorical			
Adult Subjects of at least 18 years of age and older			
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)	7	15	5
From 65-84 years	5	7	4
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	12	18	7
Male	0	4	2
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	0
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	0	0	2
White	6	17	7
More than one race	0	1	0
Unknown or Not Reported	4	1	0
Ethnicity			
Units: Subjects			

Hispanic or Latino	1	1	2
Not Hispanic or Latino	9	20	7
Unknown or Not Reported	2	1	0

Reporting group values	Dose Group 7 (10 mg/kg (Q3W))	Dose Group 8 (4 mg/kg (Q2W))	Dose Group 9 (6 mg/kg (Q2W))
Number of subjects	8	4	6
Age categorical			
Adult Subjects of at least 18 years of age and older			
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)	7	3	5
From 65-84 years	1	1	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	7	4	4
Male	1	0	2
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	4	6
More than one race	1	0	0
Unknown or Not Reported	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	7	4	6
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	99		
Age categorical			
Adult Subjects of at least 18 years of age and older			
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)	65		
From 65-84 years	34		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	78		
Male	21		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	5		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	2		
White	81		
More than one race	3		
Unknown or Not Reported	6		
Ethnicity			
Units: Subjects			
Hispanic or Latino	8		
Not Hispanic or Latino	86		
Unknown or Not Reported	5		

End points

End points reporting groups

Reporting group title	Dose Group 1 (≤ 4 mg/kg (Q3W))
Reporting group description: less than or equal to 4 mg/kg (Q3W)	
Reporting group title	Dose Group 2 (5 mg/kg (Q3W))
Reporting group description: 5 mg/kg (Q3W)	
Reporting group title	Dose Group 3 (6 mg/kg (Q3W))
Reporting group description: 6 mg/kg (Q3W)	
Reporting group title	Dose Group 4 (7 mg/kg (Q3W))
Reporting group description: 7 mg/kg (Q3W)	
Reporting group title	Dose Group 5 (8 mg/kg (Q3W))
Reporting group description: 8 mg/kg (Q3W)	
Reporting group title	Dose Group 6 (9 mg/kg (Q3W))
Reporting group description: 9 mg/kg (Q3W)	
Reporting group title	Dose Group 7 (10 mg/kg (Q3W))
Reporting group description: 10 mg/kg (Q3W)	
Reporting group title	Dose Group 8 (4 mg/kg (Q2W))
Reporting group description: 4 mg/kg (Q2W)	
Reporting group title	Dose Group 9 (6 mg/kg (Q2W))
Reporting group description: 6 mg/kg (Q2W)	
Reporting group title	Dose Group 1 (≤ 4 mg/kg (Q3W))
Reporting group description: less than or equal to 4 mg/kg (Q3W)	
Reporting group title	Dose Group 2 (5 mg/kg (Q3W))
Reporting group description: 5 mg/kg (Q3W)	
Reporting group title	Dose Group 3 (6 mg/kg (Q3W))
Reporting group description: 6 mg/kg (Q3W)	
Reporting group title	Dose Group 4 (7 mg/kg (Q3W))
Reporting group description: 7 mg/kg (Q3W)	
Reporting group title	Dose Group 5 (8 mg/kg (Q3W))
Reporting group description: 8 mg/kg (Q3W)	
Reporting group title	Dose Group 6 (9 mg/kg (Q3W))
Reporting group description: 9 mg/kg (Q3W)	
Reporting group title	Dose Group 7 (10 mg/kg (Q3W))

Reporting group description:

10 mg/kg (Q3W)

Reporting group title	Dose Group 8 (4 mg/kg (Q2W))
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Reporting group description:

4 mg/kg (Q2W)

Reporting group title	Dose Group 9 (6 mg/kg (Q2W))
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Reporting group description:

6 mg/kg (Q2W)

Primary: The Number of Subjects Experiencing a Dose Limiting Toxicity at Various Dose Levels When Given CX-2009 as a Monotherapy

End point title	The Number of Subjects Experiencing a Dose Limiting Toxicity at Various Dose Levels When Given CX-2009 as a Monotherapy ^[1]
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End point description:

Determine the safety profile of CX-2009, the MTD/RP2D, and the DLTs of CX-2009 when administered IV every 14 or 21 days as monotherapy to participants with selected advanced or recurrent solid tumors. Adverse event collection and assessment will be evaluated for all participants receiving study drug to evaluate the safety, tolerability, and determine DLTs at MTD/RP2D.

End point type	Primary
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End point timeframe:

Every 14 or 21 days (dose limiting toxicity period)

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: The study was terminated early, but the RP2D was determined for CX-2009. The study commenced with accelerated dose titration in 1 single-subject cohort (0.25 mg/kg AIBQ), followed by a standard 3+3 design to determine the MTD, and then concluded using a Bayesian interval dose-finding design (mTPI-2) cohort with up to 38 subjects with demonstrated high CD166 expression to determine the RP2D. No other statistical analyses were done.

End point values	Dose Group 1 (≤ 4 mg/kg (Q3W))	Dose Group 2 (5 mg/kg (Q3W))	Dose Group 3 (6 mg/kg (Q3W))	Dose Group 4 (7 mg/kg (Q3W))
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	9	9	12
Units: Subjects				
Participants experiencing DLTs	0	0	0	0
Participants not experiencing DLTs	20	9	9	12

End point values	Dose Group 5 (8 mg/kg (Q3W))	Dose Group 6 (9 mg/kg (Q3W))	Dose Group 7 (10 mg/kg (Q3W))	Dose Group 8 (4 mg/kg (Q2W))
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	9	8	4
Units: Subjects				
Participants experiencing DLTs	1	0	0	0
Participants not experiencing DLTs	21	9	8	4

End point values	Dose Group 9 (6 mg/kg (Q2W))			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Participants experiencing DLTs	2			
Participants not experiencing DLTs	4			

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Subjects Experiencing Anti-cancer Activity (ORR) at Various Dose Levels When Given CX-2009 as a Monotherapy

End point title	The Percentage of Subjects Experiencing Anti-cancer Activity (ORR) at Various Dose Levels When Given CX-2009 as a Monotherapy ^[2]
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End point description:

Evaluate the efficacy of CX-2009 when administered IV every 21 days as monotherapy at the MTD/RP2D. Efficacy will be assessed via objective response rate (ORR) by RECIST version 1.1. ORR is defined as the proportion of patients with complete response (CR) or partial response (PR) on two consecutive tumor assessments with scan dates at least 4 weeks apart according to RECIST (version 1.1)

End point type	Secondary
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End point timeframe:

2 Years

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This study was terminated early due to the Covid Pandemic and the company's business decision to separate the Phase 2 (part B) course of the study to a separate, new Phase 2 study. The Phase 1 (part A) course of the study was completed and the RP2D was determined. Part B only enrolled 3 patients and the Secondary (ORR) and other Outcomes were not analyzed.

End point values	Dose Group 4 (7 mg/kg (Q3W))			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Not analysed	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Dosing Group 1 (≤ 4 mg/kg (Q3W))
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Reporting group description:

less than or equal to 4 mg/kg (Q3W)

Reporting group title	Dosing Group 2 (5 mg/kg (Q3W))
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Reporting group description:

5 mg/kg (Q3W)

Reporting group title	Dosing Group 3 (6 mg/kg (Q3W))
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Reporting group description:

6 mg/kg (Q3W)

Reporting group title	Dosing Group 4 (7 mg/kg (Q3W))
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Reporting group description:

7 mg/kg (Q3W)

Reporting group title	Dosing Group 5 (8 mg/kg (Q3W))
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Reporting group description:

8 mg/kg (Q3W)

Reporting group title	Dosing Group 6 (9 mg/kg (Q3W))
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Reporting group description:

9 mg/kg (Q3W)

Reporting group title	Dosing Group 7 (10 mg/kg (Q3W))
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Reporting group description:

10 mg/kg (Q3W)

Reporting group title	Dosing Group 8 (4 mg/kg (Q2W))
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Reporting group description:

4 mg/kg (Q2W)

Reporting group title	Dosing Group 9 (6 mg/kg (Q2W))
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Reporting group description:

6 mg/kg (Q2W)

Serious adverse events	Dosing Group 1 (≤ 4 mg/kg (Q3W))	Dosing Group 2 (5 mg/kg (Q3W))	Dosing Group 3 (6 mg/kg (Q3W))
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	2 / 9 (22.22%)	3 / 9 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour ulceration	Additional description: Tumour ulceration		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Vascular disorders			
Embolism	Additional description: Embolism		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
General disorders and administration site conditions			
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Pleural effusion	Additional description: Pleural effusion		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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 arrest	Additional description: Respiratory arrest		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Investigations			
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Injury, poisoning and procedural complications			
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Cardiac disorders			
Cardiac tamponade	Additional description: Cardiac tamponade		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders Haemorrhagic stroke			
	Additional description: Haemorrhagic stroke		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Intracranial haematoma			
	Additional description: Intracranial haematoma		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Neuropathy peripheral			
	Additional description: Neuropathy peripheral		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Neurotoxicity			
	Additional description: Neurotoxicity		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Seizure			
	Additional description: Seizure		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Blood and lymphatic system disorders Neutropenia			
	Additional description: Neutropenia		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Ear and labyrinth disorders Ear pain			
	Additional description: Ear pain		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0
Eye disorders Keratitis			
	Additional description: Keratitis		
	subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 0

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Hepatobiliary disorders			
Cholangitis	Additional description: Cholangitis		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Renal and urinary disorders			

Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion	Additional description: Inappropriate antidiuretic hormone secretion		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Haematoma muscle	Additional description: Haematoma muscle		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Infections and infestations			
Catheter site infection	Additional description: Catheter site infection		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (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
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Cellulitis orbital	Additional description: Cellulitis orbital		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Device related infection	Additional description: Device related infection		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Herpes zoster	Additional description: Herpes zoster		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Large intestine infection	Additional description: Large intestine infection		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Septic shock	Additional description: Septic shock		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (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	Dosing Group 4 (7)	Dosing Group 5 (8)	Dosing Group 6 (9)
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	mg/kg (Q3W))	mg/kg (Q3W))	mg/kg (Q3W))
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	10 / 22 (45.45%)	5 / 9 (55.56%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	1	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour ulceration	Additional description: Tumour ulceration		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Vascular disorders			
Embolism	Additional description: Embolism		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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			
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia	Additional description: Hypoxia		

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest	Additional description: Respiratory arrest		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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 failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Investigations			
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Injury, poisoning and procedural complications			
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac tamponade	Additional description: Cardiac tamponade		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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

Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Nervous system disorders			
Haemorrhagic stroke	Additional description: Haemorrhagic stroke		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Intracranial haematoma	Additional description: Intracranial haematoma		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Seizure	Additional description: Seizure		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Blood and lymphatic system disorders			
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Eye disorders			
Keratitis	Additional description: Keratitis		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Gastrointestinal disorders			
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 12 (8.33%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholangitis	Additional description: Cholangitis		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion	Additional description: Inappropriate antidiuretic hormone secretion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Haematoma muscle	Additional description: Haematoma muscle		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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			
Catheter site infection	Additional description: Catheter site infection		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Cellulitis orbital	Additional description: Cellulitis orbital		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Device related infection	Additional description: Device related infection		

subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (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
Large intestine infection	Additional description: Large intestine infection		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (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
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Septic shock	Additional description: Septic shock		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolism and nutrition disorders			
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (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
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia	Additional description: Hyponatraemia		

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dosing Group 7 (10 mg/kg (Q3W))	Dosing Group 8 (4 mg/kg (Q2W))	Dosing Group 9 (6 mg/kg (Q2W))
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour ulceration	Additional description: Tumour ulceration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Vascular disorders			
Embolism	Additional description: Embolism		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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			
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Dyspnoea	Additional description: Dyspnoea		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (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 / 1	0 / 0	0 / 0
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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 arrest	Additional description: Respiratory arrest		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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 failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Investigations			
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Injury, poisoning and procedural complications			
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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

Cardiac disorders			
Cardiac tamponade	Additional description: Cardiac tamponade		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Nervous system disorders			
Haemorrhagic stroke	Additional description: Haemorrhagic stroke		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (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
Intracranial haematoma	Additional description: Intracranial haematoma		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Blood and lymphatic system disorders			
Neutropenia	Additional description: Neutropenia		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Eye disorders			
Keratitis	Additional description: Keratitis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (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
Gastrointestinal disorders			
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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

Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Hepatobiliary disorders			
Cholangitis	Additional description: Cholangitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion	Additional description: Inappropriate antidiuretic hormone secretion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Musculoskeletal and connective tissue disorders			
Haematoma muscle	Additional description: Haematoma muscle		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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			
Catheter site infection	Additional description: Catheter site infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Cellulitis orbital	Additional description: Cellulitis orbital		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Device related infection	Additional description: Device related infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Large intestine infection	Additional description: Large intestine infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Septic shock	Additional description: Septic shock		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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			
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (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

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

Non-serious adverse events	Dosing Group 1 (≤ 4 mg/kg (Q3W))	Dosing Group 2 (5 mg/kg (Q3W))	Dosing Group 3 (6 mg/kg (Q3W))
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	9 / 9 (100.00%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma	Additional description: Lipoma		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malignant neoplasm progression	Additional description: Malignant neoplasm progression		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tumour pain	Additional description: Tumour pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Flushing	Additional description: Flushing		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypertension	Additional description: Hypertension		

subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Surgical and medical procedures			
Tooth extraction	Additional description: Tooth extraction		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Chills	Additional description: Chills		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	7 / 20 (35.00%)	6 / 9 (66.67%)	6 / 9 (66.67%)
occurrences (all)	9	8	8
Feeling cold	Additional description: Feeling cold		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Gait disturbance	Additional description: Gait disturbance		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infusion site erythema	Additional description: Infusion site erythema		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infusion site phlebitis	Additional description: Infusion site phlebitis		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Malaise	Additional description: Malaise		

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	1	2
Oedema	Additional description: Oedema		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	2 / 20 (10.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	3	2	0
Secretion discharge	Additional description: Secretion discharge		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pelvic pain	Additional description: Pelvic pain		

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain	Additional description: Vulvovaginal pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis	Additional description: Allergic bronchitis		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Aspiration	Additional description: Aspiration		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cough	Additional description: Cough		
subjects affected / exposed	0 / 20 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	8 / 20 (40.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	10	1	2
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haemoptysis	Additional description: Haemoptysis		

subjects affected / exposed	1 / 20 (5.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Laryngeal oedema	Additional description: Laryngeal oedema		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Pharyngeal hypoaesthesia	Additional description: Pharyngeal hypoaesthesia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pulmonary pain	Additional description: Pulmonary pain		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion	Additional description: Respiratory tract congestion		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sinus congestion	Additional description: Sinus congestion		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Tachypnoea	Additional description: Tachypnoea		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome	Additional description: Upper-airway cough syndrome		

subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Confusional state	Additional description: Confusional state		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Depression	Additional description: Depression		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	3 / 9 (33.33%)
occurrences (all)	0	3	9
Ammonia increased	Additional description: Ammonia increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	3 / 9 (33.33%)
occurrences (all)	1	3	8
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Blood calcium increased	Additional description: Blood calcium increased		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood creatine increased	Additional description: Blood creatine increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased	Additional description: Blood iron decreased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased	Additional description: International normalised ratio increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Neutrophil count decreased	Additional description: Neutrophil count decreased		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Concussion	Additional description: Concussion		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fall	Additional description: Fall		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	4 / 20 (20.00%)	1 / 9 (11.11%)	3 / 9 (33.33%)
occurrences (all)	4	1	3
Oral contusion	Additional description: Oral contusion		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Post procedural discomfort	Additional description: Post procedural discomfort		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac failure	Additional description: Cardiac failure		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness	Additional description: Dizziness		
subjects affected / exposed	3 / 20 (15.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Dysaesthesia	Additional description: Dysaesthesia		
subjects affected / exposed	0 / 20 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Dysarthria	Additional description: Dysarthria		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache	Additional description: Headache		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Lethargy	Additional description: Lethargy		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Memory impairment	Additional description: Memory impairment		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	2
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0

Paraesthesia subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Seizure subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all) Taste disorder subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	Additional description: Paraesthesia		
	0 / 20 (0.00%) 0	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0
	Additional description: Peripheral sensory neuropathy		
	1 / 20 (5.00%) 1	1 / 9 (11.11%) 1	1 / 9 (11.11%) 2
	Additional description: Seizure		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymph node pain subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	Additional description: Syncope		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Taste disorder		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Tremor		
	0 / 20 (0.00%) 0	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymph node pain subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	Additional description: Anaemia		
	2 / 20 (10.00%) 6	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Lymph node pain		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Neutropenia		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Ear and labyrinth disorders Ear disorder subjects affected / exposed occurrences (all) Ear pain	Additional description: Thrombocytopenia		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Ear disorder		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Ear and labyrinth disorders Ear disorder subjects affected / exposed occurrences (all) Ear pain	Additional description: Ear pain		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Asthenopia	Additional description: Asthenopia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Astigmatism	Additional description: Astigmatism		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cataract	Additional description: Cataract		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chalazion	Additional description: Chalazion		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Corneal infiltrates	Additional description: Corneal infiltrates		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Corneal toxicity	Additional description: Corneal toxicity		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	1	2
Eye pain	Additional description: Eye pain		
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Eyelid ptosis	Additional description: Eyelid ptosis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Glaucoma	Additional description: Glaucoma		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Keratitis	Additional description: Keratitis		
	1 / 20 (5.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
subjects affected / exposed	1	3	2
occurrences (all)			
Keratopathy	Additional description: Keratopathy		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Lacrimation increased	Additional description: Lacrimation increased		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Ocular hyperaemia	Additional description: Ocular hyperaemia		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Ocular hypertension	Additional description: Ocular hypertension		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Orbital cyst	Additional description: Orbital cyst		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Photophobia	Additional description: Photophobia		
	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
subjects affected / exposed	0	2	0
occurrences (all)			
Presbyopia	Additional description: Presbyopia		
	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
subjects affected / exposed	0	0	1
occurrences (all)			
Punctate keratitis	Additional description: Punctate keratitis		
	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
subjects affected / exposed	0	1	0
occurrences (all)			
Pupillary reflex impaired	Additional description: Pupillary reflex impaired		
	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	1	0	0
occurrences (all)			
Retinal degeneration	Additional description: Retinal degeneration		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Retinal detachment	Additional description: Retinal detachment		
	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			

Vision blurred subjects affected / exposed occurrences (all)	Additional description: Vision blurred		
	3 / 20 (15.00%) 3	2 / 9 (22.22%) 2	0 / 9 (0.00%) 0
Visual impairment subjects affected / exposed occurrences (all)	Additional description: Visual impairment		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Gastrointestinal disorders			
	Additional description: Abdominal discomfort		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Abdominal distension		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	1 / 9 (11.11%) 1
	Additional description: Abdominal pain		
	3 / 20 (15.00%) 4	1 / 9 (11.11%) 1	1 / 9 (11.11%) 1
	Additional description: Abdominal pain lower		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Abdominal pain upper		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Aphthous ulcer		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Ascites		
	3 / 20 (15.00%) 3	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	Additional description: Constipation		
	5 / 20 (25.00%) 5	2 / 9 (22.22%) 2	2 / 9 (22.22%) 2
Diarrhoea subjects affected / exposed occurrences (all)	Additional description: Diarrhoea		
	5 / 20 (25.00%) 6	1 / 9 (11.11%) 1	3 / 9 (33.33%) 4
Dry mouth	Additional description: Dry mouth		

subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	3
Flatulence	Additional description: Flatulence		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastritis	Additional description: Gastritis		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding	Additional description: Gingival bleeding		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Large intestinal obstruction	Additional description: Large intestinal obstruction		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nausea	Additional description: Nausea		
subjects affected / exposed	9 / 20 (45.00%)	2 / 9 (22.22%)	4 / 9 (44.44%)
occurrences (all)	14	2	8
Odynophagia	Additional description: Odynophagia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Toothache	Additional description: Toothache		

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	5 / 20 (25.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	8	4	3
Hepatobiliary disorders			
Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Blister	Additional description: Blister		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dry skin	Additional description: Dry skin		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Ecchymosis	Additional description: Ecchymosis		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Erythema	Additional description: Erythema		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Night sweats	Additional description: Night sweats		
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Rash	Additional description: Rash		

subjects affected / exposed	3 / 20 (15.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash papular	Additional description: Rash papular		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation	Additional description: Skin exfoliation		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Skin mass	Additional description: Skin mass		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Bladder pain	Additional description: Bladder pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Dysuria	Additional description: Dysuria		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Haematuria	Additional description: Haematuria		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

Micturition urgency subjects affected / exposed occurrences (all)	Additional description: Micturition urgency		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	Additional description: Urinary incontinence		
	0 / 20 (0.00%) 0	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	Additional description: Urinary retention		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Urinary tract pain subjects affected / exposed occurrences (all)	Additional description: Urinary tract pain		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Endocrine disorders Addison's disease subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all) Inappropriate antidiuretic hormone secretion subjects affected / exposed occurrences (all) Primary adrenal insufficiency subjects affected / exposed occurrences (all)			
	Additional description: Addison's disease		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Hypothyroidism		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	1 / 9 (11.11%) 1
	Additional description: Inappropriate antidiuretic hormone secretion		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Flank pain subjects affected / exposed occurrences (all) Joint stiffness			
	Additional description: Arthralgia		
	3 / 20 (15.00%) 3	1 / 9 (11.11%) 1	1 / 9 (11.11%) 1
	Additional description: Back pain		
	5 / 20 (25.00%) 6	1 / 9 (11.11%) 1	3 / 9 (33.33%) 4
	Additional description: Flank pain		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Joint stiffness		

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Myositis	Additional description: Myositis		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
Pain in jaw	Additional description: Pain in jaw		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Spinal pain	Additional description: Spinal pain		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Adenoviral conjunctivitis subjects affected / exposed occurrences (all)	Additional description: Adenoviral conjunctivitis		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Candida infection subjects affected / exposed occurrences (all)	Additional description: Candida infection		
	1 / 20 (5.00%) 1	1 / 9 (11.11%) 1	1 / 9 (11.11%) 1
Cellulitis subjects affected / exposed occurrences (all)	Additional description: Cellulitis		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Conjunctivitis subjects affected / exposed occurrences (all)	Additional description: Conjunctivitis		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Lip infection subjects affected / exposed occurrences (all)	Additional description: Lip infection		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Ophthalmic herpes zoster subjects affected / exposed occurrences (all)	Additional description: Ophthalmic herpes zoster		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Oral infection subjects affected / exposed occurrences (all)	Additional description: Oral infection		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	Additional description: Pneumonia		
	1 / 20 (5.00%) 1	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Pneumonia viral subjects affected / exposed occurrences (all)	Additional description: Pneumonia viral		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Stoma site infection subjects affected / exposed occurrences (all)	Additional description: Stoma site infection		
	0 / 20 (0.00%) 0	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: Upper respiratory tract infection		
	0 / 20 (0.00%) 0	0 / 9 (0.00%) 0	0 / 9 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	Additional description: Urinary tract infection		
	2 / 20 (10.00%) 2	0 / 9 (0.00%) 0	1 / 9 (11.11%) 2

Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	8 / 20 (40.00%)	2 / 9 (22.22%)	4 / 9 (44.44%)
occurrences (all)	10	2	5
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Fluid overload	Additional description: Fluid overload		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia	Additional description: Hypercholesterolaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypermagnesaemia	Additional description: Hypermagnesaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia	Additional description: Hypernatraemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia	Additional description: Hyperuricaemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	3 / 20 (15.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	3 / 20 (15.00%)	0 / 9 (0.00%)	3 / 9 (33.33%)
occurrences (all)	3	0	3
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Dosing Group 4 (7 mg/kg (Q3W))	Dosing Group 5 (8 mg/kg (Q3W))	Dosing Group 6 (9 mg/kg (Q3W))
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	22 / 22 (100.00%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma	Additional description: Lipoma		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Malignant neoplasm progression	Additional description: Malignant neoplasm progression		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tumour pain	Additional description: Tumour pain		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Flushing	Additional description: Flushing		

subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 12 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Surgical and medical procedures			
Tooth extraction	Additional description: Tooth extraction		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 12 (0.00%)	2 / 22 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	3	5
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chills	Additional description: Chills		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	7 / 12 (58.33%)	10 / 22 (45.45%)	4 / 9 (44.44%)
occurrences (all)	8	15	4
Feeling cold	Additional description: Feeling cold		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gait disturbance	Additional description: Gait disturbance		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Infusion site erythema	Additional description: Infusion site erythema		

subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infusion site phlebitis	Additional description: Infusion site phlebitis		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	2 / 12 (16.67%)	3 / 22 (13.64%)	1 / 9 (11.11%)
occurrences (all)	2	4	1
Pain	Additional description: Pain		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	4 / 12 (33.33%)	2 / 22 (9.09%)	1 / 9 (11.11%)
occurrences (all)	5	2	1
Secretion discharge	Additional description: Secretion discharge		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pelvic pain	Additional description: Pelvic pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pain	Additional description: Vulvovaginal pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis	Additional description: Allergic bronchitis		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aspiration	Additional description: Aspiration		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cough	Additional description: Cough		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	3 / 12 (25.00%)	2 / 22 (9.09%)	2 / 9 (22.22%)
occurrences (all)	6	2	2
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Epistaxis	Additional description: Epistaxis		

subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Laryngeal oedema	Additional description: Laryngeal oedema		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pharyngeal hypoaesthesia	Additional description: Pharyngeal hypoaesthesia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pulmonary pain	Additional description: Pulmonary pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion	Additional description: Respiratory tract congestion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sinus congestion	Additional description: Sinus congestion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tachypnoea	Additional description: Tachypnoea		

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Upper-airway cough syndrome	Additional description: Upper-airway cough syndrome		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Wheezing	Additional description: Wheezing		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	3 / 22 (13.64%) 3	0 / 9 (0.00%) 0
Confusional state	Additional description: Confusional state		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Depression	Additional description: Depression		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Insomnia	Additional description: Insomnia		
subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	4 / 22 (18.18%) 5	1 / 9 (11.11%) 1
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	7 / 22 (31.82%) 16	2 / 9 (22.22%) 2
Ammonia increased	Additional description: Ammonia increased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	9 / 22 (40.91%) 32	2 / 9 (22.22%) 2
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		

subjects affected / exposed	1 / 12 (8.33%)	5 / 22 (22.73%)	1 / 9 (11.11%)
occurrences (all)	1	7	2
Blood calcium increased	Additional description: Blood calcium increased		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood creatine increased	Additional description: Blood creatine increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood iron decreased	Additional description: Blood iron decreased		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased	Additional description: International normalised ratio increased		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	1 / 9 (11.11%) 1
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	0 / 9 (0.00%) 0
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	4 / 22 (18.18%) 5	2 / 9 (22.22%) 2
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Injury, poisoning and procedural complications			
Concussion	Additional description: Concussion		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Fall	Additional description: Fall		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 22 (0.00%) 0	1 / 9 (11.11%) 1
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	5 / 22 (22.73%) 5	0 / 9 (0.00%) 0
Oral contusion	Additional description: Oral contusion		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Post procedural discomfort	Additional description: Post procedural discomfort		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Cardiac disorders			

Atrial fibrillation subjects affected / exposed occurrences (all)	Additional description: Atrial fibrillation		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Cardiac failure subjects affected / exposed occurrences (all)	Additional description: Cardiac failure		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
Pericardial effusion subjects affected / exposed occurrences (all)	Additional description: Pericardial effusion		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Nervous system disorders			
	Additional description: Dizziness		
	0 / 12 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
	0	2	0
	Additional description: Dysaesthesia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
	Additional description: Dysarthria		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
	Additional description: Dysgeusia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
	0	0	1
	Additional description: Headache		
	1 / 12 (8.33%)	3 / 22 (13.64%)	1 / 9 (11.11%)
	1	3	1
	Additional description: Hypoaesthesia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
	Additional description: Lethargy		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
	Additional description: Memory impairment		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
	Additional description: Neuropathy peripheral		

subjects affected / exposed	2 / 12 (16.67%)	6 / 22 (27.27%)	3 / 9 (33.33%)
occurrences (all)	3	8	4
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 12 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	2 / 9 (22.22%)
occurrences (all)	1	1	3
Seizure	Additional description: Seizure		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Taste disorder	Additional description: Taste disorder		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Tremor	Additional description: Tremor		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	2 / 12 (16.67%)	5 / 22 (22.73%)	0 / 9 (0.00%)
occurrences (all)	6	13	0
Lymph node pain	Additional description: Lymph node pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Ear and labyrinth disorders			
Ear disorder	Additional description: Ear disorder		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Asthenopia	Additional description: Asthenopia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Astigmatism	Additional description: Astigmatism		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cataract	Additional description: Cataract		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Chalazion	Additional description: Chalazion		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Corneal infiltrates	Additional description: Corneal infiltrates		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Corneal toxicity	Additional description: Corneal toxicity		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	0 / 12 (0.00%)	2 / 22 (9.09%)	2 / 9 (22.22%)
occurrences (all)	0	3	2
Eye pain	Additional description: Eye pain		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Eyelid ptosis	Additional description: Eyelid ptosis		

subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Glaucoma	Additional description: Glaucoma		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Keratitis	Additional description: Keratitis		
subjects affected / exposed	1 / 12 (8.33%)	7 / 22 (31.82%)	2 / 9 (22.22%)
occurrences (all)	1	13	8
Keratopathy	Additional description: Keratopathy		
subjects affected / exposed	0 / 12 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	6	0
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia	Additional description: Ocular hyperaemia		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ocular hypertension	Additional description: Ocular hypertension		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Orbital cyst	Additional description: Orbital cyst		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Photophobia	Additional description: Photophobia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Presbyopia	Additional description: Presbyopia		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis	Additional description: Punctate keratitis		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Pupillary reflex impaired	Additional description: Pupillary reflex impaired		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Retinal degeneration	Additional description: Retinal degeneration		

subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Retinal detachment	Additional description: Retinal detachment		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vision blurred	Additional description: Vision blurred		
subjects affected / exposed	1 / 12 (8.33%)	4 / 22 (18.18%)	2 / 9 (22.22%)
occurrences (all)	1	5	3
Visual impairment	Additional description: Visual impairment		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	1 / 12 (8.33%)	3 / 22 (13.64%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 12 (16.67%)	5 / 22 (22.73%)	2 / 9 (22.22%)
occurrences (all)	2	7	3
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	1 / 12 (8.33%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Constipation	Additional description: Constipation		
subjects affected / exposed	4 / 12 (33.33%)	4 / 22 (18.18%)	1 / 9 (11.11%)
occurrences (all)	5	5	1

Diarrhoea	Additional description: Diarrhoea		
	2 / 12 (16.67%)	7 / 22 (31.82%)	4 / 9 (44.44%)
subjects affected / exposed	2	9	5
occurrences (all)			
Dry mouth	Additional description: Dry mouth		
	1 / 12 (8.33%)	3 / 22 (13.64%)	1 / 9 (11.11%)
subjects affected / exposed	1	3	1
occurrences (all)			
Dyspepsia	Additional description: Dyspepsia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	2 / 9 (22.22%)
subjects affected / exposed	0	0	2
occurrences (all)			
Flatulence	Additional description: Flatulence		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Gastritis	Additional description: Gastritis		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
subjects affected / exposed	0	1	0
occurrences (all)			
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Gingival bleeding	Additional description: Gingival bleeding		
	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
subjects affected / exposed	0	0	1
occurrences (all)			
Large intestinal obstruction	Additional description: Large intestinal obstruction		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
subjects affected / exposed	0	1	0
occurrences (all)			
Nausea	Additional description: Nausea		
	6 / 12 (50.00%)	10 / 22 (45.45%)	6 / 9 (66.67%)
subjects affected / exposed	7	12	7
occurrences (all)			
Odynophagia	Additional description: Odynophagia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Proctalgia	Additional description: Proctalgia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			
Small intestinal obstruction	Additional description: Small intestinal obstruction		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
subjects affected / exposed	0	0	0
occurrences (all)			

Stomatitis subjects affected / exposed occurrences (all)	Additional description: Stomatitis		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
Toothache subjects affected / exposed occurrences (all)	Additional description: Toothache		
	0 / 12 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
	0	0	1
Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	Additional description: Upper gastrointestinal haemorrhage		
	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	1	0	0
Vomiting subjects affected / exposed occurrences (all)	Additional description: Vomiting		
	3 / 12 (25.00%)	6 / 22 (27.27%)	2 / 9 (22.22%)
	4	9	2
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	Additional description: Hyperbilirubinaemia		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all)	Additional description: Blister		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Dermatitis acneiform subjects affected / exposed occurrences (all)	Additional description: Dermatitis acneiform		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
Dry skin subjects affected / exposed occurrences (all)	Additional description: Dry skin		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Ecchymosis subjects affected / exposed occurrences (all)	Additional description: Ecchymosis		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Erythema subjects affected / exposed occurrences (all)	Additional description: Erythema		
	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
	0	1	0
Night sweats subjects affected / exposed occurrences (all)	Additional description: Night sweats		
	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
	0	0	0
Pruritus	Additional description: Pruritus		

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Rash	Additional description: Rash		
subjects affected / exposed	1 / 12 (8.33%)	2 / 22 (9.09%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Rash papular	Additional description: Rash papular		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation	Additional description: Skin exfoliation		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin mass	Additional description: Skin mass		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Bladder pain	Additional description: Bladder pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Haematuria subjects affected / exposed occurrences (all)	Additional description: Haematuria		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Micturition urgency		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	1 / 9 (11.11%) 1
	Additional description: Urinary incontinence		
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Urinary retention		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
	Additional description: Urinary tract pain		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	1 / 9 (11.11%) 1
Endocrine disorders Addison's disease subjects affected / exposed occurrences (all)	Additional description: Addison's disease		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
	Additional description: Hypothyroidism		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Inappropriate antidiuretic hormone secretion		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Primary adrenal insufficiency		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Arthralgia		
	3 / 12 (25.00%) 7	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
	Additional description: Back pain		
	1 / 12 (8.33%) 1	3 / 22 (13.64%) 3	0 / 9 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	Additional description: Flank pain		
Flank pain			

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Joint stiffness	Additional description: Joint stiffness		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	2 / 12 (16.67%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
Myositis	Additional description: Myositis		
subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	1 / 12 (8.33%)	0 / 22 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	4
Pain in jaw	Additional description: Pain in jaw		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Spinal pain	Additional description: Spinal pain		

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Infections and infestations	Additional description: Adenoviral conjunctivitis		
Adenoviral conjunctivitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Candida infection	Additional description: Candida infection		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	0 / 9 (0.00%) 0
Lip infection	Additional description: Lip infection		
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Ophthalmic herpes zoster	Additional description: Ophthalmic herpes zoster		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Oral infection	Additional description: Oral infection		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Pneumonia viral	Additional description: Pneumonia viral		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Stoma site infection	Additional description: Stoma site infection		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	0 / 9 (0.00%) 0

Urinary tract infection subjects affected / exposed occurrences (all)	Additional description: Urinary tract infection		
	4 / 12 (33.33%) 4	0 / 22 (0.00%) 0	1 / 9 (11.11%) 1
Metabolism and nutrition disorders	Additional description: Decreased appetite		
	4 / 12 (33.33%) 4	8 / 22 (36.36%) 9	5 / 9 (55.56%) 5
	Additional description: Dehydration		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	1 / 9 (11.11%) 1
	Additional description: Fluid overload		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Hypercalcaemia		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	1 / 9 (11.11%) 2
	Additional description: Hypercholesterolaemia		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 1	0 / 9 (0.00%) 0
	Additional description: Hyperglycaemia		
	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	0 / 9 (0.00%) 0
	Additional description: Hyperkalaemia		
	1 / 12 (8.33%) 1	1 / 22 (4.55%) 2	0 / 9 (0.00%) 0
	Additional description: Hypermagnesaemia		
	0 / 12 (0.00%) 0	1 / 22 (4.55%) 2	0 / 9 (0.00%) 0
	Additional description: Hyponatraemia		
	0 / 12 (0.00%) 0	0 / 22 (0.00%) 0	0 / 9 (0.00%) 0
	Additional description: Hyperuricaemia		
	0 / 12 (0.00%) 0	2 / 22 (9.09%) 2	0 / 9 (0.00%) 0
	Additional description: Hypoalbuminaemia		

subjects affected / exposed	0 / 12 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	4 / 12 (33.33%)	2 / 22 (9.09%)	4 / 9 (44.44%)
occurrences (all)	4	3	4
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	2 / 12 (16.67%)	0 / 22 (0.00%)	3 / 9 (33.33%)
occurrences (all)	4	0	4
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	3 / 12 (25.00%)	3 / 22 (13.64%)	2 / 9 (22.22%)
occurrences (all)	3	5	2
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 12 (8.33%)	1 / 22 (4.55%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	0 / 12 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dosing Group 7 (10 mg/kg (Q3W))	Dosing Group 8 (4 mg/kg (Q2W))	Dosing Group 9 (6 mg/kg (Q2W))
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	4 / 4 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma	Additional description: Lipoma		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malignant neoplasm progression	Additional description: Malignant neoplasm progression		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tumour pain	Additional description: Tumour pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vascular disorders			

Deep vein thrombosis subjects affected / exposed occurrences (all)	Additional description: Deep vein thrombosis		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Flushing subjects affected / exposed occurrences (all)	Additional description: Flushing		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Hot flush subjects affected / exposed occurrences (all)	Additional description: Hot flush		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	Additional description: Hypertension		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Hypotension subjects affected / exposed occurrences (all)	Additional description: Hypotension		
	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 6 (0.00%) 0
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	Additional description: Tooth extraction		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	Additional description: Asthenia		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	Additional description: Chest pain		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	Additional description: Chills		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
Fatigue subjects affected / exposed occurrences (all)	Additional description: Fatigue		
	2 / 8 (25.00%) 2	1 / 4 (25.00%) 2	3 / 6 (50.00%) 6
Feeling cold subjects affected / exposed occurrences (all)	Additional description: Feeling cold		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Gait disturbance	Additional description: Gait disturbance		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema	Additional description: Infusion site erythema		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion site phlebitis	Additional description: Infusion site phlebitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	3
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 8 (12.50%)	3 / 4 (75.00%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Secretion discharge	Additional description: Secretion discharge		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	Additional description: Seasonal allergy		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Reproductive system and breast disorders			
	Additional description: Erectile dysfunction		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Pelvic pain		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Vaginal discharge		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Vaginal haemorrhage		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Vulvovaginal pain		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Respiratory, thoracic and mediastinal disorders			
	Additional description: Allergic bronchitis		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Aspiration		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Cough		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Dysphonia		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Dyspnoea		
	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
	0	0	2
	Additional description: Dyspnoea exertional		

subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Laryngeal oedema	Additional description: Laryngeal oedema		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngeal hypoaesthesia	Additional description: Pharyngeal hypoaesthesia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pulmonary pain	Additional description: Pulmonary pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion	Additional description: Respiratory tract congestion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion	Additional description: Sinus congestion		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachypnoea	Additional description: Tachypnoea		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome	Additional description: Upper-airway cough syndrome		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression	Additional description: Depression		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 8 (12.50%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	2	1	4
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	12	0	3
Ammonia increased	Additional description: Ammonia increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		

subjects affected / exposed	3 / 8 (37.50%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	14	0	6
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood calcium increased	Additional description: Blood calcium increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatine increased	Additional description: Blood creatine increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased	Additional description: Blood iron decreased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
International normalised ratio increased	Additional description: International normalised ratio increased		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Concussion	Additional description: Concussion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall	Additional description: Fall		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	1 / 8 (12.50%)	2 / 4 (50.00%)	2 / 6 (33.33%)
occurrences (all)	1	2	2
Oral contusion	Additional description: Oral contusion		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural discomfort	Additional description: Post procedural discomfort		

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
Cardiac failure	Additional description: Cardiac failure		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
Nervous system disorders			
Dizziness	Additional description: Dizziness		
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dysaesthesia	Additional description: Dysaesthesia		
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dysarthria	Additional description: Dysarthria		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Headache	Additional description: Headache		
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 4 (25.00%) 1	2 / 6 (33.33%) 2
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Lethargy	Additional description: Lethargy		
subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Memory impairment	Additional description: Memory impairment		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	9
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Taste disorder	Additional description: Taste disorder		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor	Additional description: Tremor		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymph node pain	Additional description: Lymph node pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2

Thrombocytopenia subjects affected / exposed occurrences (all)	Additional description: Thrombocytopenia		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Ear and labyrinth disorders Ear disorder subjects affected / exposed occurrences (all) Ear pain subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all)	Additional description: Ear disorder		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Ear pain		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Tinnitus		
	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	1	0	0
Eye disorders Asthenopia subjects affected / exposed occurrences (all) Astigmatism subjects affected / exposed occurrences (all) Cataract subjects affected / exposed occurrences (all) Chalazion subjects affected / exposed occurrences (all) Corneal infiltrates subjects affected / exposed occurrences (all) Corneal toxicity subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all) Eye pain	Additional description: Asthenopia		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Astigmatism		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Cataract		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Chalazion		
	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
	0	0	1
	Additional description: Corneal infiltrates		
	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
	0	0	1
	Additional description: Corneal toxicity		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Dry eye		
	0 / 8 (0.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
	0	2	1
	Additional description: Eye pain		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis	Additional description: Eyelid ptosis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glaucoma	Additional description: Glaucoma		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Keratitis	Additional description: Keratitis		
subjects affected / exposed	4 / 8 (50.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	11	0	16
Keratopathy	Additional description: Keratopathy		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia	Additional description: Ocular hyperaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ocular hypertension	Additional description: Ocular hypertension		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Orbital cyst	Additional description: Orbital cyst		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Photophobia	Additional description: Photophobia		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Presbyopia	Additional description: Presbyopia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis	Additional description: Punctate keratitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired	Additional description: Pupillary reflex impaired		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retinal degeneration	Additional description: Retinal degeneration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retinal detachment	Additional description: Retinal detachment		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred	Additional description: Vision blurred		
subjects affected / exposed	5 / 8 (62.50%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	6	0	1
Visual impairment	Additional description: Visual impairment		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 8 (12.50%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Constipation	Additional description: Constipation		
	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	3 / 6 (50.00%) 5
Diarrhoea	Additional description: Diarrhoea		
	3 / 8 (37.50%) 3	2 / 4 (50.00%) 2	1 / 6 (16.67%) 1
Dry mouth	Additional description: Dry mouth		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dyspepsia	Additional description: Dyspepsia		
	2 / 8 (25.00%) 2	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
Flatulence	Additional description: Flatulence		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 2
Gastritis	Additional description: Gastritis		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Gingival bleeding	Additional description: Gingival bleeding		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Large intestinal obstruction	Additional description: Large intestinal obstruction		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Nausea	Additional description: Nausea		
	5 / 8 (62.50%) 6	0 / 4 (0.00%) 0	2 / 6 (33.33%) 2
Odynophagia	Additional description: Odynophagia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Proctalgia	Additional description: Proctalgia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0

Small intestinal obstruction subjects affected / exposed occurrences (all)	Additional description: Small intestinal obstruction		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	Additional description: Stomatitis		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	Additional description: Toothache		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	Additional description: Upper gastrointestinal haemorrhage		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	Additional description: Vomiting		
	3 / 8 (37.50%) 3	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	Additional description: Hyperbilirubinaemia		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all)	Additional description: Blister		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dermatitis acneiform subjects affected / exposed occurrences (all)	Additional description: Dermatitis acneiform		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	Additional description: Dry skin		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Ecchymosis subjects affected / exposed occurrences (all)	Additional description: Ecchymosis		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	Additional description: Erythema		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Night sweats	Additional description: Night sweats		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash	Additional description: Rash		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash papular	Additional description: Rash papular		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation	Additional description: Skin exfoliation		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin mass	Additional description: Skin mass		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bladder pain	Additional description: Bladder pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Dysuria subjects affected / exposed occurrences (all)	Additional description: Dysuria		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Haematuria		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Micturition urgency subjects affected / exposed occurrences (all)	Additional description: Micturition urgency		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Urinary incontinence		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Urinary retention subjects affected / exposed occurrences (all)	Additional description: Urinary retention		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Urinary tract pain		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
Endocrine disorders Addison's disease subjects affected / exposed occurrences (all)	Additional description: Addison's disease		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Hypothyroidism		
	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
	0	0	1
Inappropriate antidiuretic hormone secretion subjects affected / exposed occurrences (all)	Additional description: Inappropriate antidiuretic hormone secretion		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0
	Additional description: Primary adrenal insufficiency		
	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
	0	0	1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	Additional description: Arthralgia		
	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
	0	1	2
	Additional description: Back pain		
	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
	0	0	0

subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Flank pain	Additional description: Flank pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint stiffness	Additional description: Joint stiffness		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Myalgia	Additional description: Myalgia		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	4
Myositis	Additional description: Myositis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Pain in jaw	Additional description: Pain in jaw		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Spinal pain	Additional description: Spinal pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Adenoviral conjunctivitis	Additional description: Adenoviral conjunctivitis		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Candida infection	Additional description: Candida infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip infection	Additional description: Lip infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ophthalmic herpes zoster	Additional description: Ophthalmic herpes zoster		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral infection	Additional description: Oral infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia viral	Additional description: Pneumonia viral		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Stoma site infection	Additional description: Stoma site infection		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: Upper respiratory tract infection		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	Additional description: Urinary tract infection		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
	Additional description: Decreased appetite		
	2 / 8 (25.00%) 3	1 / 4 (25.00%) 1	0 / 6 (0.00%) 0
	Additional description: Dehydration		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
	Additional description: Fluid overload		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
	Additional description: Hypercalcaemia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
	Additional description: Hypercholesterolaemia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
	Additional description: Hyperglycaemia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
	Additional description: Hyperkalaemia		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	1 / 6 (16.67%) 1
	Additional description: Hypermagnesaemia		
	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
	Additional description: Hypernatraemia		
	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 6 (0.00%) 0
	Additional description: Hyperuricaemia		

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2017	<p>Amendment 1 (version 2) (Global) (15 May 2017)</p> <p>The protocol was revised to:</p> <ul style="list-style-type: none">• Update the statistical section for Part B of the study;• Modify the inclusion criteria for subject eligibility;• Add exclusion criteria for advanced or metastatic Stage IV non-small cell lung carcinoma subjects with epidermal growth factor receptor or anaplastic lymphoma kinase genomic alterations;• Update restricted medications section to include cytochrome P450 3A inhibitors and substrates;• Add a section to describe potential important drug-drug interactions;• Add time points for pharmacokinetic assessments.
31 October 2017	<p>Amendment 2 (Global) (31 October 2017)</p> <p>The protocol was revised to:</p> <ul style="list-style-type: none">• Update the study objectives;• Add a cohort (Part A2) to the study to refine the selection of the recommended Phase 2 dose and update the study design for Part A and Part B to reflect the addition of Part A2;• Update the study design to not allow for over-enrollment in any cohort;• Update the inclusion/exclusion criteria;• Clarify study drug administration;• Update ocular toxicity section to include protective measures for subjects who report ocular symptoms;• Update the use of live vaccines in the excluded medications section to;• Update the dose of glucocorticoids in the restricted medications section;• Update Section 7 to exclude the term pharmacodynamic;• Update module specified events;• Update sample size and statistical analyses
09 March 2018	<p>Amendment 3 (Global) (09 March 2018)</p> <p>The protocol was revised to:</p> <ul style="list-style-type: none">• Update the study design to allow additional dose levels to be tested in Part A and Part A2 <p>and to include that Germany will only participate in Part B of the study;</p> <ul style="list-style-type: none">• Add endometrial carcinoma as a subject's tumor type to Part A2;• Update the inclusion/exclusion criteria;• Update rationale for dosing section;• Update ocular toxicity section to make protective measures mandatory for subjects who report treatment-emergent ocular symptoms and allow subjects with Grade 2 ocular toxicity to continue treatment upon resolution of symptoms to Grade 1 or baseline;• Clarify exposure in utero and documentation of adverse events by Investigator sections;• Clarify radiology language in the Schedule of Procedures table; and• Update sample size.

10 September 2018	<p>Amendment 4 (Global) (10 September 2018)</p> <p>The protocol was revised to:</p> <ul style="list-style-type: none"> • Include subjects in Part B who have high CD166 expression to ensure the presence of target antigen on tumors which is expected to be necessary for biological activity of CX-2009. • Define CD166 high expression in tumor cells. • Update inclusion criterion for subjects with non-small cell lung cancer in Part B to clarify that subjects must have progressed on anti-programmed cell death protein 1 or anti-programmed cell death ligand 1 therapy. • Clarify recording of adverse events including on-study deaths due to progressive disease. • Update dose management for CX-2009 section to include a process for dose reduction. • Update ocular toxicity section to require mandatory ocular prophylaxis for all subjects being dosed with CX-2009 due to increased rate of ocular toxicity observed at higher dose levels. • Clarify guidelines for CX-2009 dose modifications for Grade 3 treatment-emergent ocular disorders in Table 8. • Clarify that tumor biopsies collected will be fixed and frozen. • Update rapid notification of adverse events of special interest section to include Grade 2 infusion reactions (instead of previously stated Grade 3 and Grade 4) to be reported to the Sponsor or its designee within 24 hours. • Include Appendix I to clarify the process of assessment of CD166 status.
13 February 2019	<p>Amendment 5 (Global) (13 February 2019)</p> <p>The protocol was revised to:</p> <ul style="list-style-type: none"> • Add 2 cohorts (Parts C1 and C2) to the study to allow evaluation of an every 14-day dosing regimen of CX-2009; • Include subjects in the modified toxicity probability interval (mTPI-2) cohort of Part A who have high CD166 expression since preliminary data from this study shows a trend towards activity of CX-2009 in subjects with high CD166 expressing tumors; • Increase the number of subjects in the mTPI-2 cohort of Part A to further refine the recommended Phase 2 dose selection; • Update the inclusion/exclusion criteria to include Parts C1 and C2; • Update ocular toxicity section based on antibody drug conjugate ophthalmology consultant's guidance on management of N2-deacetyl-N2-(4-mercapto-4-methyl-1-oxopentyl)-maytansine toxin-related ocular toxicities; • Update dose reduction section to include guidance on dose reduction for Parts C1 and C2; and • Update sample size.

09 August 2019	<p>Amendment 6 (Global) (09 August 2019)</p> <p>The protocol has been amended to:</p> <ul style="list-style-type: none"> • Add study Parts D1 and D2 (for a new total of 7 study parts) to evaluate the combination of CX-2009 plus CX-072, with Part D1 comprising dose escalation and Part D2 comprising dose expansion; • Revise eligibility criteria; • Update tumor types eligible for enrollment in Parts B and C2 expansion cohorts to align with new Part D2; • Increase sample size in Part B from up to 14 subjects in each of 7 tumor types (ie, ≤ 98 subjects) to up to total of 40 subjects in each of 5 tumor types; • For Part C1, add a provision to characterize protease activity in optional pretreatment tumor biopsies; • In Parts C1 and D1, add a specification that prior to dose escalation a minimum of 3 evaluable subjects must be assessed per the modified toxicity interval 2 (mTPI-2) algorithm • Increase sample size in Part C2 from up to 14 subjects in 1 tumor types (ie, ≤ 14 subjects) to up to total of 40 subjects in each of 5 tumor types; • Add stipulation that dose expansion for monotherapy would occur under Part B or C2; • Add safety stopping rules for the first 6 subjects enrolled in Parts B, C2, and D2 (dose expansion cohorts); • Update clinical experience for CX-2009 and add clinical experience and toxicity management guidelines for CX-072; • Align biopsy collection schedule (optional and mandatory) across all study parts; • Update existing Schedule of Procedures (Appendix B) to incorporate information previously communicated through administrative memos or in accordance with changes made within this amendment; • Update Schedule of Vital Sign Measurements to remove cycle day from table, clarify when height should be collected, and clarify when to measure vital signs in case of an IRR; • Update schedule of pharmacokinetics (PK) and antidrug antibody (ADA) assessment tables
16 December 2019	<p>Amendment 6.1 (Global) (16 December 2019)</p> <p>The protocol has been amended to:</p> <ul style="list-style-type: none"> • Clarify the intention to de-escalate the cohort in Part C1 • Clarify that Parts D1 and D2 will not open for enrollment in UK • Update ocular prophylaxis language to align with published prophylaxis regimen for management of antibody-drug conjugate-induced corneal abnormalities
20 February 2020	<p>Amendment 7 (Global) (20 February 2020)</p> <p>The protocol has been amended to:</p> <ul style="list-style-type: none"> • Update specifications relevant to each section for newly added Parts E1 and E2; • Clarify Part C1 dose de-escalation/escalation based on available safety information; • Clarify Part B – Indication and dose, Part E – Combination of CX-2009 and CX-072 in an every 21-day schedule, Ocular treatment guidelines, Inclusion and exclusion criteria; • Clarify Determination of cluster of differentiation 166 (CD166) expression during the screening period, Biopsy for CD166 determination, Part C1 dose reduction, Part D1 starting dose, Determination of PD-L1 expression for Part D, Co-administration of CX-2009 and CX-072 (Parts D and E)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
09 April 2020	Enrollment into the study was terminated in April 2020 due to a strategic business decision and the Covid Pandemic. The study was terminated by CytomX before patients were enrolled into Parts C2, D1, or D2.	-

Notes:

Limitations and caveats

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

Additional study parts added in Amendments 5, 6, 6.1, and 7 did not enroll any patients and are not further discussed. Enrollment into the study was terminated in April 2020 and did not complete all planned secondary outcomes.
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Notes: