Clinical trial results:
A Phase I/IIa, multicentre, open label study designed to evaluate the safety and tolerability of escalating doses of AGI-134 in unresectable/metastatic solid tumours.

Summary

EudraCT number	2018-001032-22
Trial protocol	GB
Global end of trial date	31 December 2023

Results information

Result version number	v1 (current)
This version publication date	30 January 2025
First version publication date	30 January 2025

Trial information

Trial identification

Sponsor protocol code	AGI-134.FIM.101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03593226
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Agalimmune Ltd
Sponsor organisation address	1st Floor Thavies Inn House, 3-4 Holborn Circus, London, United Kingdom, EC1N 2HA
Public contact	VP Clinical & Medical, BioLineRx Ltd, 972 8642910, clinicaltrials@biolinerx.com
Scientific contact	VP Clinical & Medical, BioLineRx Ltd, 972 8642910, clinicaltrials@biolinerx.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	08 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2022
Global end of trial reached?	Yes
Global end of trial date	31 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of AGI-134 administered by intratumoural injection and to determine the maximum tolerated dose (MTD) and recommended Part 2 dose (RP2D).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding Ethical Committee review, Informed Consent and the protection of human subjects participating in research.
Only subjects that met all the study inclusion criteria and none of the exclusion criteria were enrolled.

Background therapy:

AGI-134 is a synthetic glycophospholipid comprised of an alpha-gal epitope (Galα-1,3-Galβ-1,4-GlcNAc) linked to a lipid tail via adipate, designed to be administrated IT to solid tumors and label cells with alpha-gal, with the aim of triggering innate immune responses.

Evidence for comparator: -

Actual start date of recruitment	01 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	United Kingdom: 24
Worldwide total number of subjects	38
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

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

Adults (18-64 years)	20
From 65 to 84 years	17
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted in two parts: Part 1 and Part 2
Part 1 included 5 Patients in Israel and UK; First ICF Consent Date (in Israel): 15-Nov-2018; Last Discontinuation Date (in UK): 30-Sep-2019
Part 2 included 33 Patients in Israel, UK and Spain; First ICF Consent Date (in UK): 12-Sep-2019; Last Discontinuation Date: 06-Apr-2022

Pre-assignment

Screening details:

ICF, Inclusion/Exclusion Criteria, Demographics, Medical/Disease/Treatment History, Prior & Concomitant Medications, AEs, ECG, Full Physical Examination, Vital Signs, Weight, Height, Urine, ECOG, Blood (Pregnancy, FSH, Disease Markers, HPV, PT/INR, aPTT, CBC, Biochemistry, T3, Free T4 & TSH, HIV, HBV & HCV, Anti-Gal IgE), Tumor Imaging, RECIST

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	25 mg

Arm description:

25 mg AGI-134 (1 mL)

Arm type	Experimental
Investigational medicinal product name	AGI-134
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

One dose of 25 mg AGI-134 (1 mL) per cycle; three weeks per cycle; dosing will be given for 4 cycles.

Arm title	50 mg

Arm description:

50 mg AGI-134 (2 mL)

Arm type	Experimental
Investigational medicinal product name	AGI-134
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

One dose of 50 mg AGI-134 (2 mL) per cycle; three weeks per cycle; dosing will be given for 4 cycles.

Arm title	100 mg

Arm description:

100 mg AGI-134 (4 mL)

Arm type	Experimental

Investigational medicinal product name	AGI-134
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

One dose of 100 mg AGI-134 (4 mL) per cycle; three weeks per cycle; dosing will be given for 4 cycles.

Arm title	200 mg

Arm description:

200 mg AGI-134 (8 mL)

Arm type	Experimental
Investigational medicinal product name	AGI-134
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

One dose of 200 mg AGI-134 (8 mL) per cycle; three weeks per cycle; dosing will be given for 4 cycles.

Number of subjects in period 1	25 mg	50 mg	100 mg
Started	6	19	7
Completed	0	0	0
Not completed	6	19	7
Physician decision	-	1	-
Consent withdrawn by subject	-	4	1
Disease progression	6	13	5
Adverse event, non-fatal	-	1	-
Clinical disease progression	-	-	1

Number of subjects in period 1	200 mg
Started	6
Completed	0
Not completed	6
Physician decision	-
Consent withdrawn by subject	-
Disease progression	6
Adverse event, non-fatal	-
Clinical disease progression	-

Baseline characteristics

Reporting groups	
Reporting group title	25 mg
Reporting group description: 25 mg AGI-134 (1 mL)	
Reporting group title	50 mg
Reporting group description: 50 mg AGI-134 (2 mL)	
Reporting group title	100 mg
Reporting group description: 100 mg AGI-134 (4 mL)	
Reporting group title	200 mg
Reporting group description: 200 mg AGI-134 (8 mL)	

Reporting group values	25 mg	50 mg	100 mg
Number of subjects	6	19	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	11	5
From 65-84 years	5	7	2
85 years and over	0	1	0
Age continuous Units: years			
arithmetic mean	67.8	59.95	54
standard deviation	± 8.2	± 13.4	± 11
Gender categorical Units: Subjects			
Female	1	11	2
Male	5	8	5

Reporting group values	200 mg	Total	
Number of subjects	6	38	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	

Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	20	
From 65-84 years	3	17	
85 years and over	0	1	
Age continuous			
Units: years			
arithmetic mean	59.2		
standard deviation	± 18.5	-	
Gender categorical			
Units: Subjects			
Female	3	17	
Male	3	21	

End points

End points reporting groups

Reporting group title	25 mg
Reporting group description: 25 mg AGI-134 (1 mL)	
Reporting group title	50 mg
Reporting group description: 50 mg AGI-134 (2 mL)	
Reporting group title	100 mg
Reporting group description: 100 mg AGI-134 (4 mL)	
Reporting group title	200 mg
Reporting group description: 200 mg AGI-134 (8 mL)	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: All enrolled subjects who received at least one dose of study drug.	

Primary: Safety and Tolerability of AGI-134

End point title	Safety and Tolerability of AGI-134[1]
End point description: Participants who experiences a dose-limiting toxicity (DLT); DLTs assessed during the first cycle (21 days)	
End point type	Primary
End point timeframe: Up to 3 weeks at each dose level	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this end point, only descriptive data were planned to be analyzed for this endpoint.

End point values	25 mg	50 mg	100 mg	200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	19	7	6
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Discontinuation of Study Drug Due to an Adverse Events

End point title	Discontinuation of Study Drug Due to an Adverse Events[2]
End point description: Participants Who Discontinued Study Drug Due to an Adverse Event (AE). AEs are defined as any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of study treatment or protocol-	

specified procedure, whether or not considered related to the study treatment or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition that is temporally associated with the use of the study treatment, is also an AE.

End point type	Primary

End point timeframe:

54 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this end point, only descriptive data were planned to be analyzed for this endpoint.

End point values	25 mg	50 mg	100 mg	200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	19	7	6
Units: Subjects	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs collected during the course of the study from ICF signature time until study completed or ceased, approximately 12 months.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	25 mg
Reporting group description: 25 mg AGI-134 (1 mL)	
Reporting group title	50 mg
Reporting group description: 50 mg AGI-134 (2 mL)	
Reporting group title	100 mg
Reporting group description: 100 mg AGI-134 (4 mL)	
Reporting group title	200 mg
Reporting group description: 200 mg AGI-134 (8 mL)	

Serious adverse events	25 mg	50 mg	100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	8 / 19 (42.11%)	2 / 7 (28.57%)
number of deaths (all causes)	3	16	6
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected neoplasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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			
Hypotension			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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
Chills			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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			
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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
Pleural effusion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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			
Injection related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
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			
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (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
Groin infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Lower respiratory tract infection			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Localised infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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
Injection site infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (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			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (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			
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	200 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected neoplasm			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vascular disorders				
Hypotension				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Pelvic pain				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Groin infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injection site infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyponatraemia				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	25 mg	50 mg	100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	19 / 19 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infected neoplasm			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Tumour ulceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin neoplasm bleeding			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0

Flushing			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 7 (0.00%)
occurrences (all)	0	4	0
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Systolic hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	6 / 19 (31.58%)	4 / 7 (57.14%)
occurrences (all)	3	13	5
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 7 (0.00%)
occurrences (all)	0	4	0
Chills			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Injection site discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site discomfort			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Injection site erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Injection site oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	2 / 6 (33.33%)	2 / 19 (10.53%)	3 / 7 (42.86%)
occurrences (all)	3	2	4
Injection site swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nodule			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Chest pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Cough			
subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Aspiration			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Increased upper airway secretion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Libido increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Investigations			
Activated partial thromboplastin time shortened			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Past-pointing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood albumin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase			

decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Protein urine present			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Neutrophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Incision site pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Post procedural contusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Supraventricular extrasystoles			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dyskinesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	4 / 7 (57.14%)
occurrences (all)	0	2	4
Memory impairment			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	5 / 19 (26.32%)	1 / 7 (14.29%)
occurrences (all)	1	6	1
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 19 (21.05%)	1 / 7 (14.29%)
occurrences (all)	1	12	1
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Lymph node pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Periorbital oedema			

subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Asthenopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	1	3	1
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	0	4	1
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	1 / 7 (14.29%)
occurrences (all)	0	3	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	4 / 19 (21.05%)	2 / 7 (28.57%)
occurrences (all)	3	5	2
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	6 / 19 (31.58%)	2 / 7 (28.57%)
occurrences (all)	0	8	3
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Lip pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Parotid gland haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Tongue movement disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatomegaly			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	3 / 19 (15.79%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Skin exfoliation			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	4 / 19 (21.05%)	3 / 7 (42.86%)
occurrences (all)	1	6	4
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Skin mass			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Bladder dilatation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Urinary tract discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Arthralgia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	3
Joint range of motion decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	1 / 7 (14.29%)
occurrences (all)	1	3	1
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 7 (14.29%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	3 / 19 (15.79%)	1 / 7 (14.29%)
occurrences (all)	1	5	2
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	5	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	5	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	1 / 7 (14.29%)
occurrences (all)	0	4	3
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 7 (0.00%)
occurrences (all)	0	2	0

COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hepatic infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Groin infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injection site infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Pseudomonas infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	1 / 7 (14.29%)
occurrences (all)	0	4	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	6 / 19 (31.58%)	1 / 7 (14.29%)
occurrences (all)	0	6	2
Increased appetite			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 7 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infected neoplasm			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tumour ulceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin neoplasm bleeding			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Systolic hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Hypotension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	6		
Chills			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site discharge			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site discomfort			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	4		
Injection site swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nodule			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Pelvic pain			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vulvovaginal inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aspiration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Increased upper airway secretion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphonia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Libido increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time shortened			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fibrin D dimer increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Past-pointing			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Weight decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Platelet count increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Blood albumin increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
C-reactive protein increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Protein total decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood urea increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Blood alkaline phosphatase decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Blood lactate dehydrogenase increased				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	3			
Protein urine present				

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Neutrophil count increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Injury, poisoning and procedural complications			
Ligament sprain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Muscle strain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Incision site pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Post procedural contusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin laceration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Cardiac disorders			

Bradycardia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Supraventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyskinesia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Paraesthesia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lymph node pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Asthenopia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			

subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	5			
Dyspepsia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Abdominal pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Nausea				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	4			
Vomiting				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	5			
Mouth haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lip pain				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Oral pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Parotid gland haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Tongue movement disturbance				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hepatomegaly			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Purpura			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rash			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin mass			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin burning sensation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Bladder dilatation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Joint range of motion decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Muscle spasms			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatic infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Groin infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pseudomonas infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperchloraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	4		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2018	AMENDMENT 1 (Protocol version 1.1) - dated 21-Jun-2018 (not submitted): - Update of Sponsor staff - Clarifications regarding study procedure assessment visits - Additional optional biopsy was added on Week 27 - Additional blood collection for PBMC isolation was added on Baseline Visit, Cycle 3, and Termination - PK timepoint was added on Cycles 2 and 3 (2 hours post-dose) - Clarifications and detail regarding exploratory endpoints
05 November 2018	AMENDMENT 2 (Protocol version 1.2) - submitted in UK only (on 05-Nov-2018): - Clarification of dose-limiting toxicity and AGI-134-related adverse event - Clarification on the Recommended Part 2 Dose and safety committee meeting schedule - Clarification of procedure to contact sponsor in case of moderate, clinically significant and AGI-134 related AEs - Update of medical monitor and PhV contact information - Update of vital signs timepoint prior to AGI-134 administration - Update of NCI-CTCAE version used to 5.0 and MedDRA version used to 21.1 - Add term LPLV in Glossary and text to replace "last patient out" - Clarification of inclusion criteria re. type and number of lesions - Clarification of Survival Status and Post-study Anti-cancer Therapy Status, to be completed in cases of early termination - Clarification of Collection of Mutational and dMMR/MSI status
28 January 2019	AMENDMENT 3 (Protocol version 1.3) - submitted in UK only (approved by UK REC on 28-Jan-2019): - Clarification of the escalation rules specifying expansion in case of a DLT event during the accelerated escalation - Clarification of contraception requirements and the definition of abstinence - General stopping rules of the study were updated to include a change in the risk/benefit ratio - Subjects are not allowed to receive live vaccines 90 days after last dose - Dose modification guidance for pembrolizumab was updated to indicate that pembrolizumab should be withheld in case of hypothyroidism Grade 4

23 April 2019	AMENDMENT 4 (Protocol version 2.0) - submitted in UK and US (approved by UK REC 23-Apr-2019): - Update countries and sites in the study. - Clarification of language describing type of injectable lesion in Part 2 of the study to deep or superficial in Inclusion Criterion No. 3. - Clarification of the language defining non-childbearing potential in Inclusion Criterion No. 11. - Clarification of prior therapies excluded in Exclusion Criteria Nos. 18 and 19. - Clarifications and additions to study procedures/assessments and visits: adding safety assessment follow up activities, including physical examinations and examination of injection site, photography of lesions and safety labs - Clarifications regarding examination and photography of superficial injected lesions, added time specifications; 1 hour (± 30 min) pre- and post-dose - Clarification of FSH lab required only for women who reported menopause less than two years - Blood for PBMC isolation, immunophenotyping by FACS and for DNA and RNA was added to Visit on week 27 - Clarification regarding Safety interim analyses timelines. - Clarification that immune checkpoint inhibitor refers to pembrolizumab throughout the protocol. - Clarification of language describing DLT assessment period. - Added measurement of LDH as part of biochemistry panel. - Clarification of the timing of biopsy collection and tumor imaging during Cycle 3. - Update to the definition of "Events of Clinical Interest" removing liver enzyme-related events.
16 May 2019	AMENDMENT 5 (Protocol version 2.1) - submitted in US only (on 16-May-2019): - Clarification of language describing previous treatment in Inclusion Criteria No. 2. - Addition of definition for deep lesions - Limitation of HNSCC patients to include only those with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy in Inclusion Criteria No. 3 - The reference to the manual for administration of AGI-134 has been updated for clarity in Section 3. - Clarification of DLT definition - Adding a statement of compliance with regulations per 21 CFR 312.32 regarding IND safety reporting for SUSAR to the FDA
25 October 2019	AMENDMENT 6 (Protocol version 3.0) - submitted in UK and US (approved by UK REC 25-Oct-2019): - Change in treatment arms, removal of combination therapy and increase of the number of subjects in the basket monotherapy. - Additional biopsy for superficial lesions only between 48-72 hours post-AGI-134 administration was added. - The window for Baseline biopsy was changed from 3 days to 7 days before the first dose of AGI-134. - Optional biopsy was moved from Week 27 to Week 18. - Blood sampling for biomarkers, concomitant with biopsies, was added for Cycle 1, Cycle 3 and Week 18. - PK for metabolites was added.
17 March 2020	AMENDMENT 7 (Protocol version 4.0) - submitted in UK, ES and US (approved by UK REC 17-Mar-2020): - Addition of definition of deep lesions - Addition of photography of superficial lesion if applicable in Cycle 1 Day 3 - Clarification of study procedures and assessments, definition of causality, the relationship of AEs to the study medication, study procedure - Clarification of definition of significant medical events as excess dosing of investigational product - Addition of a statistical analysis for predefined subpopulation of melanoma to support the new data from subpopulation - Appendix – SoA Part 2: Addition of review of AEs on the first survival follow-up visit (defining the reporting of AEs more appropriately). - Addition of optional radiologic imaging: In the event that a radiological imaging verifies initial PD, at PI's discretion, tumor assessment can be repeated ≥4 weeks later and no later than the next schedule CT scan in order to confirm PD with the option of continuing treatment.

05 February 2021	AMENDMENT 8 (Protocol version 5.0) - submitted in UK, US and ES (approved by UK REC 05-Feb-2021): - Change of Sponsor address - General instructions before study drug administration were added to the synopsis and to the body of protocol. - Omission of the exclusion criterion related to live vaccines
19 May 2021	AMENDMENT 9 (Protocol version 6.0) - submitted in UK only and withdrawn due to mistake in Inclusion Criteria: - Change of Sponsor address - Addition of Spain to study sites, removal of USA. - Small changes in wording of Study Design and MedDRA version updated to 24.0. - Redefinition of timepoint of safety assessment for SAEs and AEs. - Removal of predefined subpopulation of melanoma second line.
24 June 2021	AMENDMENT 10 (Protocol version 6.1) - submitted in UK and ES (approved by UK REC 11-Jun-2021): - Change in wording of Inclusion Criterion 7:"Tumor dimensions should allow injection of a minimum of 1 mL" - Clarification of instruction for the AGI-134 administration added: "AGI-134 administration, every effort should be made to inject the same lesion as in previous cycle." - Reference to the Administration of AGI-134 and Tumor Biopsy Procedures in Study AGI-134.FIM.101 document was added - Section 5.12.2, the sentence: "Optional biopsies from the injected and un-injected lesion may be performed on Week 18." was removed, as it was left in section 5.12.2 by error in protocol version 6.0.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 March 2020	Temporary hold on the recruitment of new subjects to the ongoing study in light of the world-wide outbreak of COVID-19. This also included subjects who signed an ICF but did not start dosing with the investigational product.	07 July 2020

Notes:

Limitations and caveats

None reported