Clinical trial results:
TAX-TORC: A Phase I multi-centre trial of the combination of AZD2014 (dual TORC1 and TORC2 inhibitor) and weekly paclitaxel in patients with solid tumours

Summary

EudraCT number	2012-003896-20
Trial protocol	GB
Global end of trial date	04 February 2019

Results information

Result version number	v1 (current)
This version publication date	23 September 2020
First version publication date	23 September 2020

Trial information

Trial identification

Sponsor protocol code	CCR3667

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	The Institute of Cancer Research
Sponsor organisation address	15 Cotwold Road, Sutton, United Kingdom,
Public contact	Alison Turner, Royal Marsden Hospital Drug Development Unit, +44 2086613752, alison.turner@icr.ac.uk
Scientific contact	Alison Turner, Royal Marsden Hospital Drug Development Unit, +44 2086613752, alison.turner@icr.ac.uk

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	04 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 February 2019
Global end of trial reached?	Yes
Global end of trial date	04 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the MTD and recommended dose of two intermittent dosing schedules of AZD2014: 3 days on/4days off and 2 days on 5 days off in combination with weekly paclitaxel in patients with solid tumours. To assess the safety and toxicity profile of the combination of AZD2014 and weekly paclitaxel.

Protection of trial subjects:

As this is a phase I trial, there are stopping rules for toxicity during this study (parts A and B): Regular weekly to 2-weekly safety reviews will be conducted between the Principal Investigator or delegate from each investigational site and DDU Clinical Trials Manager or delegate. Decisions will be based on all relevant data available from all dose levels evaluated in the ongoing study including safety information, DLTs, all CTCAE Grade ≥ 2 toxicity data, available PK, and PD data from evaluable patients. If at any time, 2 or more DLTs have occurred in a specific dose level, one of the following actions will be implemented:
- Proceed with dose escalation
- Expand the cohort to a maximum of 6 evaluable patients
- De-escalate the dose
- Define the MTD (where 6 evaluable patients are assessed)
- Stop the study

Formal review of toxicity and intrapatient dose escalation data will be undertaken by the SRC when 3 patients have completed approximately 9 weeks of treatment on either schedule, and at the end of the dose escalation phase, for selection of the dose expansion schedule. During dose expansion, SRC meetings will be held regularly for safety review (e.g. every 5-10 patients). Additional SRC meetings will be organised in the event of safety concerns, e.g. with the intrapatient dose escalation strategy, for consideration of reverting to a classic 3+3 phase I dose escalation scheme.
The SRC will consist of:
- Chief Investigator or delegate
- Principal Investigator or delegate from each investigational site
- DDU Pharmacovigilance Officer or delegate
- DDU Clinical Trials Manager or delegate
- Senior ECMC clinician (who is not CI)

Representatives of AstraZeneca and Cancer Research UK's Drug Development Office will also be invited to attend the SRC meetings as non-voting participants. Further internal or external experts may be consulted by the SRC as necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2013
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	United Kingdom: 97

Worldwide total number of subjects	97
EEA total number of subjects	97

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)	49
From 65 to 84 years	47
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Adult patients with solid tumours will be enrolled into the dose escalation phase of the study. Patients with ovarian cancer and patients with squamous lung cancer will be enrolled in the expansion phase.

Pre-assignment

Screening details:

The patient must fulfil the eligibility criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Escalation: 3 days on, 4 days off (Schedule A)

Arm description: -

Arm type	Dosing Schedule
Investigational medicinal product name	AZD2014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BD intermittent 3 days on 4 days off schedule (Schedule A): AZD2014 (25 mg, 50 mg and 75 mg)

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BD intermittent 3 days on 4 days off schedule (Schedule A): paclitaxel (80mg/m2) intravenously every week (D1, D8, D15, D22, D29, D36) for 6 weeks followed by a 1 week break (1 cycle).

Arm title	Escalation: 2 days on, 5 days off (Schedule B)

Arm description: -

Arm type	Dosing schedule
Investigational medicinal product name	AZD2014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BD intermittent 2 days on 5 days off schedule (Schedule B): AZD2014 (25 mg, 50 mg, 75 mg and 100mg)

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BD intermittent 2 days on 5 days off schedule (Schedule B): paclitaxel (80mg/m2) intravenously every week (D1, D8, D15, D22, D29, D36) for 6 weeks followed by a 1 week break (1 cycle).

Arm title	Expansion: 3 days on, 4 days off (Schedule A)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AZD2014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BD intermittent 3 days on 4 days off schedule (Schedule A): AZD2014 (25 mg, 50 mg and 75 mg)

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BD intermittent 3 days on 4 days off schedule (Schedule A): paclitaxel (80mg/m2) intravenously every week (D1, D8, D15, D22, D29, D36) for 6 weeks followed by a 1 week break (1 cycle).

Number of subjects in period 1	Escalation: 3 days on, 4 days off (Schedule A)	Escalation: 2 days on, 5 days off (Schedule B)	Expansion: 3 days on, 4 days off (Schedule A)
Started	12	11	74
Completed	11	10	69
Not completed	1	1	5
Physician decision	1	1	2
Adverse event, non-fatal	-	-	2
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	97	97	
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)	49	49	
From 65-84 years	47	47	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	65	65	
Male	32	32	

End points

End points reporting groups

Reporting group title	Escalation: 3 days on, 4 days off (Schedule A)
Reporting group description: -	
Reporting group title	Escalation: 2 days on, 5 days off (Schedule B)
Reporting group description: -	
Reporting group title	Expansion: 3 days on, 4 days off (Schedule A)
Reporting group description: -	

Primary: To determine a dose at which no more than one patient out of up to six patients at the same dose level experience a drug-related DLT

End point title	To determine a dose at which no more than one patient out of up to six patients at the same dose level experience a drug-related DLT[1][2]
End point description:	
End point type	Primary
End point timeframe:	
28 days	

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 analysis was required when assessing the number of DLTs. The Safety Review Committee made the decision to escalate the dose of AZD2014 maximum tolerated dose), thereby assessing the safest schedule to take forward into expansion.
[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: Patient disposition arms presented as:
Escalation: 3d on, 4d off (Sch. A)
Escalation: 2d on, 5d off (Sch. B)
Expansion: 3d on, 4d off (Sch. A)

AE's and SAE's the arms are split further into each schedule dosing groups and the expansion in the tumour types (Lung 25mg & 50mg and Ovarian 50mg):
Escalation 3/4 25mg
Escalation 3/4 50mg
Escalation 3/4 75mg
Escalation 2/5 50mg
Escalation 2/5 75mg
Escalation 2/5 100mg
Ovarian expansion 50mg
Lung expansion 25mg
Lung expansion 50mg

End point values	Escalation: 3 days on, 4 days off (Schedule A)	Escalation: 2 days on, 5 days off (Schedule B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: DLT				
number (not applicable)	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: To determine causality of each adverse event to the combination of AZD2014 and weekly paclitaxel and grading severity according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

End point title	To determine causality of each adverse event to the combination of AZD2014 and weekly paclitaxel and grading severity according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.[3][4]

End point description:

End point type	Primary

End point timeframe:

From treatment.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was required for this endpoint as the n number per each AE is not significant.
[4] - 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: Patient disposition arms presented as:
Escalation: 3d on, 4d off (Sch. A)
Escalation: 2d on, 5d off (Sch. B)
Expansion: 3d on, 4d off (Sch. A)

AE's and SAE's the arms are split further into each schedule dosing groups and the expansion in the tumour types (Lung 25mg & 50mg and Ovarian 50mg):
Escalation 3/4 25mg
Escalation 3/4 50mg
Escalation 3/4 75mg
Escalation 2/5 50mg
Escalation 2/5 75mg
Escalation 2/5 100mg
Ovarian expansion 50mg
Lung expansion 25mg
Lung expansion 50mg

End point values	Escalation: 3 days on, 4 days off (Schedule A)	Escalation: 2 days on, 5 days off (Schedule B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Treatment related AE's				
number (not applicable)	11	10		

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Ovarian expansion 50mg
Reporting group description: -	
Reporting group title	Lung expansion 50mg
Reporting group description: -	
Reporting group title	Escalation 3/4 50mg
Reporting group description: -	
Reporting group title	Escalation 3/4 25mg
Reporting group description: -	
Reporting group title	Lung expansion 25mg
Reporting group description: -	
Reporting group title	Escalation 2/5 100mg
Reporting group description: -	
Reporting group title	Escalation 3/4 75mg
Reporting group description: -	
Reporting group title	Escalation 2/5 75mg
Reporting group description: -	
Reporting group title	Escalation 2/5 50mg
Reporting group description: -	

Serious adverse events	Ovarian expansion 50mg	Lung expansion 50mg	Escalation 3/4 50mg
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 27 (62.96%)	10 / 17 (58.82%)	3 / 6 (50.00%)
number of deaths (all causes)	1	3	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian epithelial cancer	Additional description: Ovarian epithelial cancer		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Disease progression	Additional description: Disease progression		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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 / 27 (0.00%)	0 / 17 (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
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	0 / 6 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	0 / 6 (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
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	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 tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Pulmonary function test decreased	Additional description: Pulmonary function test decreased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Fall	Additional description: Fall		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Nervous system disorders			
Cerebrovascular accident	Additional description: Cerebrovascular accident		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Spinal cord compression	Additional description: Spinal cord compression		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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			
Febrile neutropenia	Additional description: Febrile neutropenia		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites	Additional description: Ascites		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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 / 27 (0.00%)	0 / 17 (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
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	3 / 27 (11.11%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	2 / 3	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal toxicity	Additional description: Gastrointestinal toxicity		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Stomatitis	Additional description: Stomatitis		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Skin and subcutaneous tissue disorders			
Rash macular	Additional description: Rash macular		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Infections and infestations			
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Device related sepsis	Additional description: Device related sepsis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	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
Influenza	Additional description: Influenza		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		

subjects affected / exposed	3 / 27 (11.11%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis	Additional description: Periorbital cellulitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (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
Sepsis	Additional description: Sepsis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (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
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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	1 / 27 (3.70%)	0 / 17 (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

Serious adverse events	Escalation 3/4 25mg	Lung expansion	Escalation 2/5

		25mg	100mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	12 / 24 (50.00%)	3 / 3 (100.00%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian epithelial cancer	Additional description: Ovarian epithelial cancer		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Vascular disorders			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression	Additional description: Disease progression		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: Fatigue		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Pneumonitis	Additional description: Pneumonitis		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (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
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Pulmonary function test decreased	Additional description: Pulmonary function test decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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			
Fall	Additional description: Fall		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Nervous system disorders			
Cerebrovascular accident	Additional description: Cerebrovascular accident		

subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (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
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Spinal cord compression	Additional description: Spinal cord compression		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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			
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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			
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 toxicity	Additional description: Gastrointestinal toxicity		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Intestinal obstruction	Additional description: Intestinal obstruction		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Skin and subcutaneous tissue disorders			
Rash macular	Additional description: Rash macular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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 sepsis	Additional description: Device related sepsis		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Influenza	Additional description: Influenza		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	6 / 24 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis	Additional description: Periorbital cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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			
Dehydration	Additional description: Dehydration		

subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (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	Escalation 3/4 75mg	Escalation 2/5 75mg	Escalation 2/5 50mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	1 / 1 (100.00%)
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)			
Ovarian epithelial cancer	Additional description: Ovarian epithelial cancer		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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	Additional description: Hypotension		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Lymphoedema	Additional description: Lymphoedema		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Disease progression	Additional description: Disease progression		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (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
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Pulmonary function test decreased	Additional description: Pulmonary function test decreased		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Fall	Additional description: Fall		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (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
Cardiac disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Cerebrovascular accident	Additional description: Cerebrovascular accident		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Spinal cord compression	Additional description: Spinal cord compression		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (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
Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Ascites	Additional description: Ascites		

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 toxicity	Additional description: Gastrointestinal toxicity		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	1 / 6 (16.67%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (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
Skin and subcutaneous tissue disorders			
Rash macular	Additional description: Rash macular		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (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
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 sepsis	Additional description: Device related sepsis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Influenza	Additional description: Influenza		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Periorbital cellulitis	Additional description: Periorbital cellulitis		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (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: 0 %

Non-serious adverse events	Ovarian expansion 50mg	Lung expansion 50mg	Escalation 3/4 50mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 27 (100.00%)	17 / 17 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acral lentiginous melanoma	Additional description: Acral lentiginous melanoma		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post thrombotic syndrome	Additional description: Post thrombotic syndrome		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dry skin prophylaxis	Additional description: Dry skin prophylaxis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 27 (3.70%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	1	6	0
Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Early satiety	Additional description: Early satiety		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Extravasation	Additional description: Extravasation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Face oedema	Additional description: Face oedema		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	20 / 27 (74.07%)	13 / 17 (76.47%)	5 / 6 (83.33%)
occurrences (all)	65	47	14
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	3 / 27 (11.11%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Localised oedema	Additional description: Localised oedema		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Mass	Additional description: Mass		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	1 / 27 (3.70%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	4 / 27 (14.81%)	3 / 17 (17.65%)	1 / 6 (16.67%)
occurrences (all)	6	6	2
Pain	Additional description: Pain		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	14 / 27 (51.85%)	6 / 17 (35.29%)	3 / 6 (50.00%)
occurrences (all)	20	7	4
Suprapubic pain	Additional description: Suprapubic pain		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Thirst	Additional description: Thirst		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Breast haemorrhage	Additional description: Breast haemorrhage		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Perineal pain	Additional description: Perineal pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Vaginal inflammation	Additional description: Vaginal inflammation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort	Additional description: Vulvovaginal discomfort		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough	Additional description: Cough		
subjects affected / exposed	8 / 27 (29.63%)	9 / 17 (52.94%)	1 / 6 (16.67%)
occurrences (all)	11	16	1
Dry throat	Additional description: Dry throat		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	2 / 27 (7.41%)	9 / 17 (52.94%)	2 / 6 (33.33%)
occurrences (all)	2	18	2

Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	6 / 27 (22.22%)	2 / 17 (11.76%)	1 / 6 (16.67%)
occurrences (all)	7	4	1
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 27 (0.00%)	3 / 17 (17.65%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngospasm	Additional description: Laryngospasm		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Nasal discomfort	Additional description: Nasal discomfort		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	4 / 27 (14.81%)	2 / 17 (11.76%)	1 / 6 (16.67%)
occurrences (all)	5	2	3
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	2 / 27 (7.41%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Productive cough	Additional description: Productive cough		
subjects affected / exposed	2 / 27 (7.41%)	2 / 17 (11.76%)	2 / 6 (33.33%)
occurrences (all)	3	2	6
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Stridor	Additional description: Stridor		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (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 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract congestion	Additional description: Upper respiratory tract congestion		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depression	Additional description: Depression		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hallucination	Additional description: Hallucination		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nightmare	Additional description: Nightmare		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	1	3	1
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	1	2	2
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		

subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased	Additional description: Blood sodium decreased		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased	Additional description: Blood triglycerides increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CD4 lymphocytes decreased	Additional description: CD4 lymphocytes decreased		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1

Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal	Additional description: Liver function test abnormal		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased	Additional description: Neutrophil count increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	5 / 27 (18.52%)	4 / 17 (23.53%)	0 / 6 (0.00%)
occurrences (all)	8	5	0
Weight increased	Additional description: Weight increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
White blood cell count increased	Additional description: White blood cell count increased		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cystitis radiation	Additional description: Cystitis radiation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall	Additional description: Fall		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction	Additional description: Infusion related reaction		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonitis chemical	Additional description: Pneumonitis chemical		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Skin injury	Additional description: Skin injury		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound	Additional description: Wound		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Hand-foot-genital syndrome	Additional description: Hand-foot-genital syndrome		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Atrial tachycardia	Additional description: Atrial tachycardia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia	Additional description: Sinus tachycardia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		

subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Amnesia	Additional description: Amnesia		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Aphasia	Additional description: Aphasia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ataxia	Additional description: Ataxia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cluster headache	Additional description: Cluster headache		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cognitive disorder	Additional description: Cognitive disorder		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dizziness	Additional description: Dizziness		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Dizziness postural	Additional description: Dizziness postural		
subjects affected / exposed	3 / 27 (11.11%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	4 / 27 (14.81%)	2 / 17 (11.76%)	4 / 6 (66.67%)
occurrences (all)	6	4	4
Headache	Additional description: Headache		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	1	1	1

Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Hypokinesia	Additional description: Hypokinesia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lethargy	Additional description: Lethargy		
subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Migraine	Additional description: Migraine		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	9 / 27 (33.33%)	5 / 17 (29.41%)	3 / 6 (50.00%)
occurrences (all)	13	10	3
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Peripheral motor neuropathy	Additional description: Peripheral motor neuropathy		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	3 / 27 (11.11%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Presyncope	Additional description: Presyncope		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Somnolence	Additional description: Somnolence		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Trigeminal nerve disorder	Additional description: Trigeminal nerve disorder		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	10 / 27 (37.04%)	5 / 17 (29.41%)	5 / 6 (83.33%)
occurrences (all)	18	13	13
Blood disorder	Additional description: Blood disorder		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bone marrow failure	Additional description: Bone marrow failure		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 27 (0.00%)	3 / 17 (17.65%)	1 / 6 (16.67%)
occurrences (all)	0	12	1
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	8 / 27 (29.63%)	4 / 17 (23.53%)	3 / 6 (50.00%)
occurrences (all)	20	8	12
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis	Additional description: Blepharitis		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dry eye	Additional description: Dry eye		

subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Eye discharge	Additional description: Eye discharge		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye pain	Additional description: Eye pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes	Additional description: Foreign body sensation in eyes		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	2	1	3
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Abdominal mass	Additional description: Abdominal mass		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	7 / 27 (25.93%)	1 / 17 (5.88%)	2 / 6 (33.33%)
occurrences (all)	17	1	2
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 27 (3.70%)	2 / 17 (11.76%)	1 / 6 (16.67%)
occurrences (all)	2	2	1
Anorectal discomfort	Additional description: Anorectal discomfort		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Constipation	Additional description: Constipation		
subjects affected / exposed	12 / 27 (44.44%)	5 / 17 (29.41%)	3 / 6 (50.00%)
occurrences (all)	24	10	8
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	16 / 27 (59.26%)	9 / 17 (52.94%)	5 / 6 (83.33%)
occurrences (all)	58	22	18
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	5 / 27 (18.52%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	9	2	0
Duodenogastric reflux	Additional description: Duodenogastric reflux		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	8 / 27 (29.63%)	2 / 17 (11.76%)	1 / 6 (16.67%)
occurrences (all)	9	2	3
Epigastric discomfort	Additional description: Epigastric discomfort		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eructation	Additional description: Eructation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence	Additional description: Flatulence		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Mouth ulceration	Additional description: Mouth ulceration		
subjects affected / exposed	3 / 27 (11.11%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	3	5	0
Nausea	Additional description: Nausea		
subjects affected / exposed	12 / 27 (44.44%)	5 / 17 (29.41%)	4 / 6 (66.67%)
occurrences (all)	23	11	11
Oral pain	Additional description: Oral pain		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Paraesthesia oral	Additional description: Paraesthesia oral		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sensitivity of teeth	Additional description: Sensitivity of teeth		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	8 / 27 (29.63%)	3 / 17 (17.65%)	2 / 6 (33.33%)
occurrences (all)	19	3	2
Vomiting	Additional description: Vomiting		
subjects affected / exposed	12 / 27 (44.44%)	6 / 17 (35.29%)	1 / 6 (16.67%)
occurrences (all)	24	9	1
Hepatobiliary disorders			
Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		
subjects affected / exposed	8 / 27 (29.63%)	2 / 17 (11.76%)	4 / 6 (66.67%)
occurrences (all)	8	2	10
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dermatitis	Additional description: Dermatitis		

subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Dermatitis contact	Additional description: Dermatitis contact		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dry skin	Additional description: Dry skin		
subjects affected / exposed	2 / 27 (7.41%)	5 / 17 (29.41%)	1 / 6 (16.67%)
occurrences (all)	2	6	1
Eczema	Additional description: Eczema		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Erythema	Additional description: Erythema		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Henoch-Schonlein purpura	Additional description: Henoch-Schonlein purpura		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Nail dystrophy	Additional description: Nail dystrophy		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nail growth abnormal	Additional description: Nail growth abnormal		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nail ridging	Additional description: Nail ridging		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Onychoclasis	Additional description: Onychoclasis		

subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Onycholysis	Additional description: Onycholysis		
subjects affected / exposed	3 / 27 (11.11%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Onychomadesis	Additional description: Onychomadesis		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome	Additional description: Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pigmentation disorder	Additional description: Pigmentation disorder		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	3 / 27 (11.11%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Rash	Additional description: Rash		
subjects affected / exposed	8 / 27 (29.63%)	4 / 17 (23.53%)	1 / 6 (16.67%)
occurrences (all)	26	8	2
Rash macular	Additional description: Rash macular		
subjects affected / exposed	6 / 27 (22.22%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	14	4	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash vesicular	Additional description: Rash vesicular		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Skin induration	Additional description: Skin induration		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin irritation	Additional description: Skin irritation		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin ulcer	Additional description: Skin ulcer		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Stasis dermatitis	Additional description: Stasis dermatitis		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Haematuria	Additional description: Haematuria		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence	Additional description: Urinary incontinence		
subjects affected / exposed	1 / 27 (3.70%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	2 / 6 (33.33%)
occurrences (all)	2	1	2
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Groin pain	Additional description: Groin pain		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	2 / 27 (7.41%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Limb discomfort	Additional description: Limb discomfort		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	4 / 27 (14.81%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	5	2	0
Muscle twitching	Additional description: Muscle twitching		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	1 / 27 (3.70%)	3 / 17 (17.65%)	0 / 6 (0.00%)
occurrences (all)	1	5	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 27 (0.00%)	3 / 17 (17.65%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	2 / 6 (33.33%)
occurrences (all)	0	4	2
Musculoskeletal stiffness	Additional description: Musculoskeletal stiffness		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myalgia	Additional description: Myalgia		
subjects affected / exposed	3 / 27 (11.11%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	5	1	0

Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Spinal pain	Additional description: Spinal pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tendonitis	Additional description: Tendonitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Angular cheilitis	Additional description: Angular cheilitis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site cellulitis	Additional description: Catheter site cellulitis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Dermatitis infected	Additional description: Dermatitis infected		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Device related sepsis	Additional description: Device related sepsis		

subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear infection fungal	Additional description: Ear infection fungal		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Genital herpes	Additional description: Genital herpes		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Herpes virus infection	Additional description: Herpes virus infection		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	3 / 27 (11.11%)	5 / 17 (29.41%)	1 / 6 (16.67%)
occurrences (all)	3	5	1
Lung infection	Additional description: Lung infection		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nail infection	Additional description: Nail infection		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	2 / 27 (7.41%)	5 / 17 (29.41%)	0 / 6 (0.00%)
occurrences (all)	2	5	0
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis	Additional description: Oropharyngeal candidiasis		

subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Paronychia	Additional description: Paronychia		
subjects affected / exposed	1 / 27 (3.70%)	2 / 17 (11.76%)	2 / 6 (33.33%)
occurrences (all)	1	2	3
Periorbital cellulitis	Additional description: Periorbital cellulitis		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pustular	Additional description: Rash pustular		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Tinea pedis	Additional description: Tinea pedis		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	4 / 27 (14.81%)	2 / 17 (11.76%)	2 / 6 (33.33%)
occurrences (all)	7	2	2
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	9 / 27 (33.33%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	17	1	0
Varicella zoster virus infection	Additional description: Varicella zoster virus infection		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection	Additional description: Viral upper respiratory tract infection		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Vulvovaginal candidiasis	Additional description: Vulvovaginal candidiasis		

subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	5 / 27 (18.52%)	9 / 17 (52.94%)	3 / 6 (50.00%)
occurrences (all)	6	17	3
Glucose tolerance impaired	Additional description: Glucose tolerance impaired		
subjects affected / exposed	0 / 27 (0.00%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 27 (0.00%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	2 / 27 (7.41%)	3 / 17 (17.65%)	1 / 6 (16.67%)
occurrences (all)	6	7	1
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	2 / 27 (7.41%)	1 / 17 (5.88%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	4 / 27 (14.81%)	2 / 17 (11.76%)	0 / 6 (0.00%)
occurrences (all)	8	3	0
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	5 / 27 (18.52%)	0 / 17 (0.00%)	2 / 6 (33.33%)
occurrences (all)	8	0	3
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	1 / 27 (3.70%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypophagia	Additional description: Hypophagia		
subjects affected / exposed	0 / 27 (0.00%)	0 / 17 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 27 (3.70%)	2 / 17 (11.76%)	2 / 6 (33.33%)
occurrences (all)	4	2	2

Non-serious adverse events	Escalation 3/4 25mg	Lung expansion 25mg	Escalation 2/5 100mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	24 / 24 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acral lentiginous melanoma	Additional description: Acral lentiginous melanoma		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Post thrombotic syndrome	Additional description: Post thrombotic syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Dry skin prophylaxis	Additional description: Dry skin prophylaxis		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Device related infection	Additional description: Device related infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Early satiety	Additional description: Early satiety		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Extravasation	Additional description: Extravasation		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Face oedema	Additional description: Face oedema		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	3 / 3 (100.00%)	11 / 24 (45.83%)	3 / 3 (100.00%)
occurrences (all)	4	27	7
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Localised oedema	Additional description: Localised oedema		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Malaise	Additional description: Malaise		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mass	Additional description: Mass		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	1 / 3 (33.33%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	9	0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 3 (0.00%)	5 / 24 (20.83%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Suprapubic pain	Additional description: Suprapubic pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thirst	Additional description: Thirst		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Breast haemorrhage	Additional description: Breast haemorrhage		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Perineal pain	Additional description: Perineal pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal inflammation	Additional description: Vaginal inflammation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Vulvovaginal discomfort	Additional description: Vulvovaginal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cough	Additional description: Cough		
subjects affected / exposed	0 / 3 (0.00%)	7 / 24 (29.17%)	2 / 3 (66.67%)
occurrences (all)	0	7	4
Dry throat	Additional description: Dry throat		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 3 (33.33%)	8 / 24 (33.33%)	3 / 3 (100.00%)
occurrences (all)	1	15	8
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	1 / 3 (33.33%)	5 / 24 (20.83%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Laryngospasm	Additional description: Laryngospasm		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort	Additional description: Nasal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Productive cough	Additional description: Productive cough		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	2 / 3 (66.67%)
occurrences (all)	0	1	2

Stridor	Additional description: Stridor		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome	Additional description: Upper-airway cough syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion	Additional description: Upper respiratory tract congestion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression	Additional description: Depression		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hallucination	Additional description: Hallucination		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Nightmare	Additional description: Nightmare		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		

subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased	Additional description: Blood sodium decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased	Additional description: Blood triglycerides increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
CD4 lymphocytes decreased	Additional description: CD4 lymphocytes decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase	Additional description: Gamma-glutamyltransferase increased		

increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Liver function test abnormal	Additional description: Liver function test abnormal		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Neutrophil count increased	Additional description: Neutrophil count increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Weight increased	Additional description: Weight increased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	17	0
White blood cell count increased	Additional description: White blood cell count increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Cystitis radiation	Additional description: Cystitis radiation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fall	Additional description: Fall		

subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonitis chemical	Additional description: Pneumonitis chemical		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin injury	Additional description: Skin injury		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wound	Additional description: Wound		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Congenital, familial and genetic disorders			
Hand-foot-genital syndrome	Additional description: Hand-foot-genital syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrial tachycardia	Additional description: Atrial tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia	Additional description: Sinus tachycardia		

subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia	Additional description: Amnesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aphasia	Additional description: Aphasia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ataxia	Additional description: Ataxia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cluster headache	Additional description: Cluster headache		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder	Additional description: Cognitive disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state	Additional description: Confusional state		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness	Additional description: Dizziness		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dizziness postural	Additional description: Dizziness postural		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Headache	Additional description: Headache		
subjects affected / exposed	0 / 3 (0.00%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokinesia	Additional description: Hypokinesia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lethargy	Additional description: Lethargy		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Migraine	Additional description: Migraine		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	2 / 3 (66.67%)	9 / 24 (37.50%)	2 / 3 (66.67%)
occurrences (all)	2	11	2
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Peripheral motor neuropathy	Additional description: Peripheral motor neuropathy		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Presyncope	Additional description: Presyncope		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Somnolence	Additional description: Somnolence		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trigeminal nerve disorder	Additional description: Trigeminal nerve disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	3 / 3 (100.00%)	14 / 24 (58.33%)	1 / 3 (33.33%)
occurrences (all)	9	26	2
Blood disorder	Additional description: Blood disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone marrow failure	Additional description: Bone marrow failure		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	0	7	1
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Blepharitis	Additional description: Blepharitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye discharge	Additional description: Eye discharge		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pain	Additional description: Eye pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Foreign body sensation in eyes	Additional description: Foreign body sensation in eyes		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal mass	Additional description: Abdominal mass		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		

subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Anorectal discomfort	Additional description: Anorectal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	1	1	7
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 3 (66.67%)	9 / 24 (37.50%)	2 / 3 (66.67%)
occurrences (all)	3	17	15
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Duodenogastric reflux	Additional description: Duodenogastric reflux		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	0 / 3 (0.00%)	5 / 24 (20.83%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Epigastric discomfort	Additional description: Epigastric discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation	Additional description: Eructation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flatulence	Additional description: Flatulence		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		

subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration	Additional description: Mouth ulceration		
subjects affected / exposed	0 / 3 (0.00%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Nausea	Additional description: Nausea		
subjects affected / exposed	3 / 3 (100.00%)	11 / 24 (45.83%)	2 / 3 (66.67%)
occurrences (all)	4	20	14
Oral pain	Additional description: Oral pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral	Additional description: Paraesthesia oral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sensitivity of teeth	Additional description: Sensitivity of teeth		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	1 / 3 (33.33%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	5	13
Hepatobiliary disorders			
Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		

subjects affected / exposed	1 / 3 (33.33%)	14 / 24 (58.33%)	0 / 3 (0.00%)
occurrences (all)	2	21	0
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dermatitis	Additional description: Dermatitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact	Additional description: Dermatitis contact		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin	Additional description: Dry skin		
subjects affected / exposed	1 / 3 (33.33%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	5	0
Eczema	Additional description: Eczema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema	Additional description: Erythema		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Henoch-Schonlein purpura	Additional description: Henoch-Schonlein purpura		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	0 / 3 (0.00%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail dystrophy	Additional description: Nail dystrophy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail growth abnormal	Additional description: Nail growth abnormal		

subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nail ridging	Additional description: Nail ridging		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onychoclasis	Additional description: Onychoclasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onycholysis	Additional description: Onycholysis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onychomadesis	Additional description: Onychomadesis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome	Additional description: Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder	Additional description: Pigmentation disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 3 (33.33%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Rash	Additional description: Rash		
subjects affected / exposed	0 / 3 (0.00%)	6 / 24 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	8	2
Rash macular	Additional description: Rash macular		
subjects affected / exposed	1 / 3 (33.33%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	2
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Rash vesicular	Additional description: Rash vesicular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin induration	Additional description: Skin induration		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin irritation	Additional description: Skin irritation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin ulcer	Additional description: Skin ulcer		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Stasis dermatitis	Additional description: Stasis dermatitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria	Additional description: Haematuria		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urinary incontinence	Additional description: Urinary incontinence		

subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 3 (0.00%)	4 / 24 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	5	5
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Groin pain	Additional description: Groin pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort	Additional description: Limb discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle twitching	Additional description: Muscle twitching		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		

subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Musculoskeletal stiffness	Additional description: Musculoskeletal stiffness		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Neck pain	Additional description: Neck pain		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Spinal pain	Additional description: Spinal pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tendonitis	Additional description: Tendonitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Angular cheilitis	Additional description: Angular cheilitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Catheter site cellulitis	Additional description: Catheter site cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Cystitis	Additional description: Cystitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis infected	Additional description: Dermatitis infected		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Device related sepsis	Additional description: Device related sepsis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection fungal	Additional description: Ear infection fungal		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Genital herpes	Additional description: Genital herpes		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection	Additional description: Herpes virus infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	10 / 24 (41.67%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Lung infection	Additional description: Lung infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail infection	Additional description: Nail infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	3 / 24 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis	Additional description: Oropharyngeal candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia	Additional description: Paronychia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital cellulitis	Additional description: Periorbital cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rash pustular	Additional description: Rash pustular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Tinea pedis	Additional description: Tinea pedis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	3

Varicella zoster virus infection	Additional description: Varicella zoster virus infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection	Additional description: Viral upper respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis	Additional description: Vulvovaginal candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	1 / 3 (33.33%)	6 / 24 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	9	1
Glucose tolerance impaired	Additional description: Glucose tolerance impaired		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	1 / 3 (33.33%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	2	1	2
Hyponatraemia	Additional description: Hyponatraemia		

subjects affected / exposed	1 / 3 (33.33%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Hypophagia	Additional description: Hypophagia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 3 (33.33%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	1	6	0

Non-serious adverse events	Escalation 3/4 75mg	Escalation 2/5 75mg	Escalation 2/5 50mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acral lentiginous melanoma	Additional description: Acral lentiginous melanoma		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypertension	Additional description: Hypertension		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Post thrombotic syndrome	Additional description: Post thrombotic syndrome		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Superior vena cava syndrome	Additional description: Superior vena cava syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dry skin prophylaxis	Additional description: Dry skin prophylaxis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Device related infection	Additional description: Device related infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Early satiety	Additional description: Early satiety		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Extravasation	Additional description: Extravasation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Face oedema	Additional description: Face oedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	3 / 3 (100.00%)	4 / 6 (66.67%)	1 / 1 (100.00%)
occurrences (all)	15	16	1
Influenza like illness	Additional description: Influenza like illness		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Localised oedema	Additional description: Localised oedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mass	Additional description: Mass		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Suprapubic pain	Additional description: Suprapubic pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thirst	Additional description: Thirst		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast haemorrhage	Additional description: Breast haemorrhage		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Perineal pain	Additional description: Perineal pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal inflammation	Additional description: Vaginal inflammation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort	Additional description: Vulvovaginal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cough	Additional description: Cough		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	2	2	0

Dry throat	Additional description: Dry throat		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Laryngospasm	Additional description: Laryngospasm		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort	Additional description: Nasal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Productive cough	Additional description: Productive cough		
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Stridor	Additional description: Stridor		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome	Additional description: Upper-airway cough syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion	Additional description: Upper respiratory tract congestion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Depression	Additional description: Depression		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hallucination	Additional description: Hallucination		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nightmare	Additional description: Nightmare		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Blood magnesium increased	Additional description: Blood magnesium increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased	Additional description: Blood sodium decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased	Additional description: Blood triglycerides increased		

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
CD4 lymphocytes decreased	Additional description: CD4 lymphocytes decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal	Additional description: Liver function test abnormal		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased	Additional description: Neutrophil count increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Weight increased	Additional description: Weight increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased	Additional description: White blood cell count increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cystitis radiation	Additional description: Cystitis radiation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fall	Additional description: Fall		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumonitis chemical	Additional description: Pneumonitis chemical		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin injury	Additional description: Skin injury		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound	Additional description: Wound		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Hand-foot-genital syndrome	Additional description: Hand-foot-genital syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Atrial tachycardia	Additional description: Atrial tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia	Additional description: Sinus tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Amnesia	Additional description: Amnesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aphasia	Additional description: Aphasia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ataxia	Additional description: Ataxia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cluster headache	Additional description: Cluster headache		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder	Additional description: Cognitive disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dizziness	Additional description: Dizziness		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dizziness postural	Additional description: Dizziness postural		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	1 / 3 (33.33%)	4 / 6 (66.67%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
Headache	Additional description: Headache		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypokinesia	Additional description: Hypokinesia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lethargy	Additional description: Lethargy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Migraine	Additional description: Migraine		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	0 / 1 (0.00%)
occurrences (all)	1	6	0
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy	Additional description: Peripheral motor neuropathy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Presyncope	Additional description: Presyncope		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Somnolence	Additional description: Somnolence		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Trigeminal nerve disorder	Additional description: Trigeminal nerve disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	4	5	0
Blood disorder	Additional description: Blood disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bone marrow failure	Additional description: Bone marrow failure		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	3 / 3 (100.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0

Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis	Additional description: Blepharitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye discharge	Additional description: Eye discharge		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye pain	Additional description: Eye pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes	Additional description: Foreign body sensation in eyes		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Abdominal mass	Additional description: Abdominal mass		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal pain	Additional description: Abdominal pain		

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 1 (100.00%)
occurrences (all)	0	1	4
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anorectal discomfort	Additional description: Anorectal discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 1 (100.00%)
occurrences (all)	1	1	1
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	0 / 1 (0.00%)
occurrences (all)	12	11	0
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Duodenogastric reflux	Additional description: Duodenogastric reflux		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Epigastric discomfort	Additional description: Epigastric discomfort		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eructation	Additional description: Eructation		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flatulence	Additional description: Flatulence		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration	Additional description: Mouth ulceration		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 3 (0.00%)	5 / 6 (83.33%)	1 / 1 (100.00%)
occurrences (all)	0	7	3
Oral pain	Additional description: Oral pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral	Additional description: Paraesthesia oral		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sensitivity of teeth	Additional description: Sensitivity of teeth		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	7	1	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	1 / 1 (100.00%)
occurrences (all)	1	2	5
Hepatobiliary disorders			

Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Dermatitis	Additional description: Dermatitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact	Additional description: Dermatitis contact		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry skin	Additional description: Dry skin		
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Eczema	Additional description: Eczema		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Erythema	Additional description: Erythema		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Henoch-Schonlein purpura	Additional description: Henoch-Schonlein purpura		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nail disorder	Additional description: Nail disorder		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nail dystrophy	Additional description: Nail dystrophy		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nail growth abnormal	Additional description: Nail growth abnormal		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nail ridging	Additional description: Nail ridging		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Onychoclasis	Additional description: Onychoclasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Onycholysis	Additional description: Onycholysis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Onychomadesis	Additional description: Onychomadesis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome	Additional description: Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder	Additional description: Pigmentation disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	6	0
Rash	Additional description: Rash		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Rash macular	Additional description: Rash macular		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash vesicular	Additional description: Rash vesicular		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin discolouration	Additional description: Skin discolouration		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin induration	Additional description: Skin induration		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin irritation	Additional description: Skin irritation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin ulcer	Additional description: Skin ulcer		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Stasis dermatitis	Additional description: Stasis dermatitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematuria	Additional description: Haematuria		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence	Additional description: Urinary incontinence		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Groin pain	Additional description: Groin pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Limb discomfort	Additional description: Limb discomfort		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle twitching	Additional description: Muscle twitching		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscular weakness	Additional description: Muscular weakness		

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness	Additional description: Musculoskeletal stiffness		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Spinal pain	Additional description: Spinal pain		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tendonitis	Additional description: Tendonitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Angular cheilitis	Additional description: Angular cheilitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site cellulitis	Additional description: Catheter site cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cystitis	Additional description: Cystitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Dermatitis infected	Additional description: Dermatitis infected		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Device related sepsis	Additional description: Device related sepsis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ear infection fungal	Additional description: Ear infection fungal		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Genital herpes	Additional description: Genital herpes		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection	Additional description: Herpes virus infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Lung infection	Additional description: Lung infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Nail infection	Additional description: Nail infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal candidiasis	Additional description: Oropharyngeal candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paronychia	Additional description: Paronychia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Periorbital cellulitis	Additional description: Periorbital cellulitis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rash pustular	Additional description: Rash pustular		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tinea pedis	Additional description: Tinea pedis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Varicella zoster virus infection	Additional description: Varicella zoster virus infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection	Additional description: Viral upper respiratory tract infection		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis	Additional description: Vulvovaginal candidiasis		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	1 / 1 (100.00%)
occurrences (all)	2	2	1
Glucose tolerance impaired	Additional description: Glucose tolerance impaired		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypophagia	Additional description: Hypophagia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	3 / 3 (100.00%)	0 / 6 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2013	Am. 01: Changes to Protocol 7.2, 8.2.3 {10 ovarian pts / schedule for EXP}
10 December 2013	Am.02: change to schedules, 4.1.2.2, 5.5.1, {increase EXP ovarian on 3on/4off 10 +15}
06 June 2014	Am.03: added Guys 104, added 15 sq. lung, exclusion with CYP, 7.2 haem and biochem test, screening SAEs exempt {EXP 3on/4off = 10 ovarian + 15 lung, 2on/5off = 15 lung}
18 December 2014	Am.04: added 105, 106, 107, 108, 109 - seq of circulating free DNA (5) (8.3), {incr EXP sq. lung on 3on/4off from 15 to 40}
16 April 2015	Am.05: added buccal swabs and 2nd base blood
02 November 2015	Am.06: description of tumour inclusion increased, contraception inclusion removed in error AZD interruptions for pneumonitis
05 February 2016	Am.07: 4.1.1.5 contraception returned

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported