



## Clinical trial results:

### First-In-Human, Dose Escalating Safety Study of Tissue Factor Specific Antibody-Drug Conjugate Tisotumab Vedotin (Humax®-TF-ADC) in Patients with Locally Advanced and/or Metastatic Solid Tumors Known to Express Tissue Factor

#### Summary

EudraCT number	2013-001074-15
Trial protocol	GB
Global end of trial date	02 May 2019

#### Results information

Result version number	v1 (current)
This version publication date	28 April 2021
First version publication date	28 April 2021

#### Trial information

##### Trial identification

Sponsor protocol code	GEN701
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02001623
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Genmab A/S
Sponsor organisation address	Kalvebod Brygge 43, Copenhagen, Denmark, DK-1560
Public contact	Clinical Trial Information, Genmab A/S, +45 70202728, clinicaltrials@genmab.com
Scientific contact	Clinical Trial Information, Genmab A/S, +45 70202728, clinicaltrials@genmab.com

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 May 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 May 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to establish the tolerability of tisotumab vedotin in a mixed population of participants with specified solid tumors.

Protection of trial subjects:

The trial was conducted in accordance with the protocol and amendments, the International Council for Harmonisation E6 guideline for Good Clinical Practice, applicable local regulations, and ethical principles that have their origins in the Declaration of Helsinki. In addition, the trial was conducted in accordance with FDA 21 Code of Federal Regulations parts 312, 50, and 56, and the directive 2001/20/EC of the European Parliament.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Belgium: 35
Country: Number of subjects enrolled	Denmark: 29
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	United Kingdom: 92
Worldwide total number of subjects	195
EEA total number of subjects	70

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)	138
From 65 to 84 years	57
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

In the dose escalation part of the study, 40 participants were screened and 27 were enrolled and received treatment. In the dose expansion part of the study, 294 participants were screened and 168 were enrolled and received treatment.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Dose Escalation Part

Arm description:

Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).

Arm type	Experimental
Investigational medicinal product name	Tisotumab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tisotumab vedotin was administered as an intravenous (IV) infusion at doses 0.3, 0.6, 0.9, 1.2, 1.5, 1.8, 2.0 and 2.2 mg/kg.

<b>Arm title</b>	Dose Expansion Part
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Arm description:

Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).

Arm type	Experimental
Investigational medicinal product name	Tisotumab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tisotumab vedotin was administered as an IV infusion at a dose of 2.0 mg/kg.

<b>Number of subjects in period 1</b>	Dose Escalation Part	Dose Expansion Part
Started	27	168
Completed 4 cycles of treatment	9	81
Completed 12 cycles of treatment	2	5
Completed	2	5
Not completed	25	163
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	16
Physician decision	-	18
Adverse event, non-fatal	3	35
Dose limiting toxicity	1	-
Other - miscellaneous	-	1
Lost to follow-up	-	1
Disease Progression	19	92

## Baseline characteristics

### Reporting groups

Reporting group title	Dose Escalation Part
Reporting group description:	
Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).	
Reporting group title	Dose Expansion Part
Reporting group description:	
Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).	

Reporting group values	Dose Escalation Part	Dose Expansion Part	Total
Number of subjects	27	168	195
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	118	138
From 65-84 years	7	50	57
85 years and over	0	0	0
Age continuous			
Units: years			
median	62	58	
full range (min-max)	43 to 73	21 to 79	-
Gender categorical			
Units: Subjects			
Female	18	122	140
Male	9	46	55
Race			
Units: Subjects			
White	27	155	182
Black or African American	0	2	2
Asian	0	5	5
Native Hawaiian or other Pacific Islander	0	1	1
Other	0	2	2
Missing	0	3	3
Ethnicity			
Units: Subjects			

Hispanic or Latino	0	2	2
Not Hispanic or Latino	27	164	191
Missing	0	2	2

## End points

### End points reporting groups

Reporting group title	Dose Escalation Part
Reporting group description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).	
Reporting group title	Dose Expansion Part
Reporting group description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days; 1Q3W) for four cycles (12 weeks total). After four cycles, if there was evidence of the participant benefiting from treatment, at the discretion of the treating physician, there was an option to continue in the study for up to a maximum of eight additional cycles (24 weeks) or until unacceptable toxicity was observed (maximum treatment duration: 36 weeks total).	
Subject analysis set title	Dose Escalation Part: 0.3 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 0.3 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 0.6 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 0.6 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 0.9 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 0.9 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 1.2 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 1.2 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 1.5 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 1.5 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 1.8 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 1.8 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 2.0 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.	
Subject analysis set title	Dose Escalation Part: 2.2 mg/kg
Subject analysis set type	Sub-group analysis



Subject analysis set description:

Participants received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.2 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Bladder Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with bladder cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Cervical Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with cervical cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Endometrial Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with endometrial cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Esophageal Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with esophageal cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with NSCLC received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Ovarian Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ovarian cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Prostate Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with prostate cancer received tisotumab vedotin on Day 1 of each cycle (each treatment cycle was 21 days) as an IV infusion at a dose of 2.0 mg/kg of body weight.

Subject analysis set title	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK analysis set includes all participants in the dose expansion who had been exposed to tisotumab vedotin and had at least one PK assessment after the first dose.

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### **Primary: Dose Escalation Part: Evaluation of Treatment-Emergent Adverse Events**

End point title	Dose Escalation Part: Evaluation of Treatment-Emergent Adverse Events <sup>[1]</sup>
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End point description:

Evaluation of treatment-emergent adverse events (AEs) includes number of participants with at least one:

AE

Serious adverse event (SAE)

Infusion-related AE

Common Terminology Criteria for Adverse Events (CTCAE) grade  $\geq 3$

Treatment-related AE

End point type	Primary
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End point timeframe:

Treatment emergent adverse events are reported from Day 1 to 30 days after dosing. The exposure ranged from 1 to 249 days in the escalation part.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants				
AEs	3	3	3	3
SAEs	2	1	0	2
Infusion-Related AEs	1	0	0	0
CTCAE Grade $\geq 3$ AEs	2	3	1	1
AEs Related to Study Drug	3	3	2	3

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Participants				
AEs	3	3	3	6
SAEs	2	2	2	4
Infusion-Related AEs	0	0	0	0
CTCAE Grade $\geq 3$ AEs	2	3	2	4
AEs Related to Study Drug	3	3	3	6

## Statistical analyses

No statistical analyses for this end point

## Primary: Dose Expansion Part: Evaluation of Treatment-Emergent Adverse Events

End point title	Dose Expansion Part: Evaluation of Treatment-Emergent Adverse Events <sup>[2]</sup>
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End point description:

Evaluation of treatment-emergent adverse events (AEs) includes number of participants with at least one:

AE

Serious adverse event (SAE)

Infusion-related AE

Common terminology criteria for adverse events (CTCAE) grade  $\geq 3$

Treatment-related AE

End point type	Primary
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End point timeframe:

Treatment emergent adverse events are reported from Day 1 to 30 days after dosing. The exposure ranged from 1 to 325 days in the expansion part.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Participants				
AEs	15	55	14	15
SAEs	7	26	5	8
Infusion-Related AEs	1	1	1	1
CTCAE Grade $\geq 3$ AEs	9	30	8	8
AEs Related to Study Drug	15	54	13	14

End point values	Dose Expansion Part: Non- Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Participants				
AEs	15	36	18	
SAEs	6	13	6	
Infusion-Related AEs	2	0	0	
CTCAE Grade $\geq 3$ AEs	10	16	11	
AEs Related to Study Drug	14	36	18	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Number of Participants with Markedly Abnormal Hematology Values

End point title	Dose Escalation and Expansion Part: Number of Participants with Markedly Abnormal Hematology Values
End point description:	
Number of participants with markedly abnormal hematology results were defined as all participants who experienced at least 1 CTCAE grade $\geq 3$ hematology value.	
End point type	Secondary
End point timeframe:	
Day 1 to end of follow-up, up to a maximum of 60 weeks	

<b>End point values</b>	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: participants	2	1	1	0

<b>End point values</b>	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: participants	2	2	0	1

<b>End point values</b>	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: participants	0	23	0	3

<b>End point values</b>	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: participants	1	5	3	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Escalation and Expansion Parts: Number of Participants with Markedly Abnormal Coagulation Values

End point title	Dose Escalation and Expansion Parts: Number of Participants with Markedly Abnormal Coagulation Values
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End point description:

Number of participants with markedly abnormal coagulation results were defined as all participants who experienced at least 1 CTCAE grade  $\geq 3$  coagulation value.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: participants	0	0	0	0

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: participants	0	0	0	1

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: participants	1	7	2	0

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: participants	2	5	4	

## Statistical analyses

**Secondary: Dose Escalation and Expansion Part: Number of Participants with Markedly Abnormal Biochemistry Values**

End point title	Dose Escalation and Expansion Part: Number of Participants with Markedly Abnormal Biochemistry Values
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End point description:

Number of participants with markedly abnormal biochemistry results were defined as all participants who experienced at least 1 CTCAE grade  $\geq 3$  biochemistry value.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: participants	2	1	3	0

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: participants	1	0	1	2

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: participants	4	8	4	6

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: participants	2	9	4	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Escalation and Expansion Parts: Number of Participants Who Experienced a Skin Rash

End point title	Dose Escalation and Expansion Parts: Number of Participants Who Experienced a Skin Rash
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants	1	0	0	2

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Participants	0	2	2	4

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Participants	3	6	2	2

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Participants	2	8	5	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Parts: Number of Participants Who Experienced a Bleeding Event

End point title	Dose Escalation and Expansion Parts: Number of Participants Who Experienced a Bleeding Event
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End point description:

Bleeding adverse events of special interest included treatment emergent adverse events with preferred terms within the following standardised MedDRA queries: Haemorrhage terms, excluding laboratory terms SMQ [20000039] (Broad) and Haemorrhage, laboratory terms SMQ [20000040] (Narrow).

Bleeding adverse events of special interest were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) and were graded from 1 to 5, where 1 indicated a mild event and 5 indicated a fatal event. Bleeding events of all grades are included in the numbers below.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants	0	1	0	3

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Participants	3	3	2	5



End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Participants	10	31	10	7

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Participants	9	27	10	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Escalation and Expansion Part: Number of Participants Who Experienced a Neuropathy Event

End point title	Dose Escalation and Expansion Part: Number of Participants Who Experienced a Neuropathy Event
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End point description:

Peripheral neuropathy events of special interest were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) and were graded from 1 to 5, where 1 indicated a mild event and 5 indicated a fatal event. Peripheral neuropathy events of all grades are included in the numbers below.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants	0	1	1	1

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Participants	0	1	0	1

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Participants	5	17	6	3

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Participants	5	17	7	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: Clearance of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation Part: Clearance of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study. Data was not planned to be collected for the clearance of tisotumab vedotin and total HuMax-TF. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[3]</sup>	3 <sup>[4]</sup>	3	3
Units: mL/hr/kg				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	()	1.61 (± 7.79)	1.46 (± 15.23)	1.07 (± 11.60)
Tisotumab Vedotin: Cycle 2	()	1.72 (± 4.98)	1.44 (± 6.32)	1.07 (± 10.45)
Total HuMax-TF: Cycle 1	()	1.02 (± 0.20)	0.98 (± 16.90)	0.69 (± 12.61)
Total HuMax-TF: Cycle 2	()	1.05 (± 9.95)	0.98 (± 6.52)	0.71 (± 13.41)

Notes:

[3] - No evaluable PK assessments

[4] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 1 N = 2

Total HuMax-TF Cycle 2 N = 2

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3 <sup>[5]</sup>	3 <sup>[6]</sup>	5 <sup>[7]</sup>
Units: mL/hr/kg				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	1.84 (± 20.59)	1.17 (± 60.05)	1.56 (± 34.12)	0.87 (± 8.93)
Tisotumab Vedotin: Cycle 2	2.05 (± 26.80)	0.93 (± 24.03)	1.30 (± 19.06)	1.03 (± 11.34)
Total HuMax-TF: Cycle 1	1.26 (± 31.29)	0.81 (± 69.72)	0.87 (± 33.85)	0.56 (± 14.13)
Total HuMax-TF: Cycle 2	1.40 (± 31.39)	0.53 (± 12.41)	0.82 (± 26.45)	0.61 (± 9.72)

Notes:

[5] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[6] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[7] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: Volume of Distribution of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation Part: Volume of Distribution of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study. Data was not planned to be collected for the volume of distribution of tisotumab vedotin and total HuMax-TF for the dose expansion part. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[8]</sup>	3 <sup>[9]</sup>	3	3
Units: mL/kg				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	()	68.40 (± 11.84)	70.80 (± 14.54)	63.46 (± 16.87)
Tisotumab Vedotin: Cycle 2	()	76.69 (± 9.53)	69.74 (± 7.99)	62.61 (± 6.03)
Total HuMax-TF: Cycle 1	()	51.55 (± 1.61)	60.27 (± 17.79)	57.38 (± 8.65)
Total HuMax-TF: Cycle 2	()	55.75 (± 10.80)	57.13 (± 8.90)	58.48 (± 12.66)

Notes:

[8] - Not calculated where the percentage of the AUC that is due to the extrapolation is more than 20%.

[9] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 1 N = 2

Total HuMax-TF Cycle 2 N = 2

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3 <sup>[10]</sup>	3 <sup>[11]</sup>	5 <sup>[12]</sup>
Units: mL/kg				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	86.10 (± 12.38)	81.13 (± 35.60)	92.04 (± 21.62)	61.46 (± 18.07)
Tisotumab Vedotin: Cycle 2	99.20 (± 20.82)	70.21 (± 42.93)	74.82 (± 4.19)	72.74 (± 5.79)
Total HuMax-TF: Cycle 1	77.55 (± 10.74)	67.26 (± 50.61)	68.69 (± 30.52)	50.69 (± 7.20)
Total HuMax-TF: Cycle 2	84.98 (± 22.85)	50.62 (± 36.02)	60.40 (± 17.48)	58.10 (± 12.31)

Notes:

[10] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[11] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[12] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Area Under the Curve from Time Zero to the Last Measurable Concentration (AUC0-t) of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation and Expansion Part: Area Under the Curve from Time Zero to the Last Measurable Concentration (AUC0-t) of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	2.5 (± 3.1)	15.4 (± 8.2)	25.1 (± 16.9)	45.2 (± 9.3)
Tisotumab Vedotin: Cycle 2	2.0 (± 15.7)	9.9 (± 49.1)	25.6 (± 7.1)	45.2 (± 10.1)
Total HuMax-TF: Cycle 1	2.9 (± 0.5)	15.4 (± 53.1)	35.0 (± 18.9)	60.4 (± 13.4)
Total HuMax-TF: Cycle 2	2.4 (± 12.3)	14.4 (± 55.4)	35.7 (± 7.1)	58.8 (± 15.5)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[13]</sup>	6 <sup>[14]</sup>
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	33.1 (± 19.0)	63.0 (± 49.3)	52.3 (± 33.1)	84.9 (± 33.7)
Tisotumab Vedotin: Cycle 2	29.8 (± 25.1)	42.7 (± 72.7)	62.7 (± 21.5)	86.3 (± 14.4)
Total HuMax-TF: Cycle 1	44.9 (± 27.8)	86.7 (± 54.3)	85.9 (± 36.7)	123.0 (± 34.7)
Total HuMax-TF: Cycle 2	40.9 (± 26.2)	60.2 (± 76.6)	92.5 (± 33.4)	133.6 (± 13.9)

Notes:

[13] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[14] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[15]</sup>			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				

Tisotumab Vedotin: Cycle 1	79.31 (± 49.40)			
Tisotumab Vedotin: Cycle 2	68.54 (± 55.49)			
Total HuMax-TF: Cycle 1	112.70 (± 45.23)			
Total HuMax-TF: Cycle 2	114.54 (± 45.83)			

Notes:

[15] - Tisotumab Vedotin Cycle 1 N = 167

Tisotumab Vedotin Cycle 2 N = 146

HuMax-TF Cycle 2 N = 146

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: Area Under the Curve from Time Zero Extrapolated to Infinity (AUC0-inf) of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation Part: Area Under the Curve from Time Zero Extrapolated to Infinity (AUC0-inf) of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2. AUC0-inf was only analyzed in the dose escalation part of the study. Data was not planned to be collected for the AUC0-inf of tisotumab vedotin and total HuMax-TF for the dose expansion part. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[16]</sup>	3 <sup>[17]</sup>	3	3
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	( )	15.57 (± 7.81)	25.77 (± 15.70)	46.68 (± 10.99)
Tisotumab Vedotin: Cycle 2	( )	14.52 (± 4.98)	26.12 (± 6.44)	46.59 (± 9.98)
Total HuMax-TF: Cycle 1	( )	23.75 (± 0.20)	37.02 (± 16.39)	69.96 (± 13.26)
Total HuMax-TF: Cycle 2	( )	23.01 (± 9.95)	37.08 (± 6.37)	67.93 (± 14.25)

Notes:

[16] - Not calculated where the percentage of the AUC that is due to the extrapolation is more than 20%.

[17] - Total HuMax-TF Cycle 1 N = 2

Total HuMax-TF Cycle 2 N = 2

End point values	Dose Escalation Part:	Dose Escalation Part:	Dose Escalation Part:	Dose Escalation Part:
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	1.5 mg/kg	1.8 mg/kg	2.0 mg/kg	2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3 <sup>[18]</sup>	3 <sup>[19]</sup>	5 <sup>[20]</sup>
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	33.95 (± 20.93)	63.88 (± 48.61)	53.47 (± 30.88)	105.84 (± 8.68)
Tisotumab Vedotin: Cycle 2	30.56 (± 26.43)	80.59 (± 24.03)	64.10 (± 19.06)	88.95 (± 11.04)
Total HuMax-TF: Cycle 1	48.19 (± 35.67)	90.08 (± 52.74)	93.29 (± 30.45)	157.81 (± 12.70)
Total HuMax-TF: Cycle 2	43.41 (± 30.31)	136.08 (± 12.41)	98.59 (± 26.45)	145.82 (± 9.42)

Notes:

[18] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[19] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[20] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 1 N = 2

Total HuMax-TF Cycle 2 N = 3

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Maximum Observed Plasma Concentration (C<sub>max</sub>) of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation and Expansion Part: Maximum Observed Plasma Concentration (C <sub>max</sub> ) of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	4.78 (± 12.35)	12.20 (± 9.47)	19.81 (± 17.32)	34.67 (± 18.48)
Tisotumab Vedotin: Cycle 2	3.85 (± 27.65)	12.51 (± 11.51)	20.25 (± 5.14)	32.38 (± 7.11)
Total HuMax-TF: Cycle 1	4.90 (± 13.00)	11.84 (± 8.31)	17.98 (± 11.64)	29.30 (± 10.14)
Total HuMax-TF: Cycle 2	3.96 (± 21.83)	11.54 (± 8.83)	16.90 (± 1.57)	31.33 (± 8.13)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[21]</sup>	6 <sup>[22]</sup>
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	23.12 (± 21.10)	35.42 (± 39.20)	32.30 (± 22.08)	55.53 (± 10.31)
Tisotumab Vedotin: Cycle 2	21.84 (± 24.97)	35.92 (± 30.39)	44.30 (± 0.32)	48.79 (± 26.37)
Total HuMax-TF: Cycle 1	23.55 (± 25.16)	30.57 (± 37.42)	38.78 (± 21.77)	58.02 (± 12.77)
Total HuMax-TF: Cycle 2	22.11 (± 21.03)	37.71 (± 42.96)	43.40 (± 6.67)	53.67 (± 19.75)

Notes:

[21] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[22] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[23]</sup>			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	29.1 (± 34.1)			
Tisotumab Vedotin: Cycle 2	26.1 (± 41.2)			
Total HuMax-TF: Cycle 1	39.8 (± 31.1)			
Total HuMax-TF: Cycle 2	38.3 (± 33.3)			

Notes:

[23] - Tisotumab Vedotin Cycle 1 N = 167

Tisotumab Vedotin Cycle 1 N = 146

Total HuMax-TF Cycle 2 N = 146

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Time of Cmax (Tmax) of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation and Expansion Part: Time of Cmax (Tmax) of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: hours				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	1.47 (± 72.74)	1.18 (± 13.03)	1.34 (± 11.77)	1.15 (± 11.66)
Tisotumab Vedotin: Cycle 2	1.54 (± 63.29)	1.34 (± 6.27)	1.32 (± 5.96)	1.13 (± 11.18)
Total HuMax-TF: Cycle 1	2.20 (± 49.15)	1.18 (± 13.03)	1.34 (± 11.77)	1.15 (± 11.66)
Total HuMax-TF: Cycle 2	2.19 (± 46.56)	1.34 (± 6.27)	1.32 (± 5.96)	1.13 (± 11.18)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[24]</sup>	6 <sup>[25]</sup>
Units: hours				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	1.12 (± 9.55)	1.18 (± 14.30)	1.18 (± 7.45)	1.11 (± 12.52)
Tisotumab Vedotin: Cycle 2	1.21 (± 16.61)	2.44 (± 35.75)	1.14 (± 9.29)	1.29 (± 7.55)
Total HuMax-TF: Cycle 1	1.12 (± 9.55)	1.18 (± 14.30)	1.18 (± 7.45)	1.11 (± 12.52)
Total HuMax-TF: Cycle 2	1.21 (± 16.61)	1.76 (± 50.43)	1.14 (± 9.29)	1.29 (± 7.55)

Notes:

[24] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[25] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[26]</sup>			
Units: hours				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	1.21 (± 364.12)			
Tisotumab Vedotin: Cycle 2	1.44 (± 303.89)			
Total HuMax-TF: Cycle 1	1.10 (± 397.92)			

Total HuMax-TF: Cycle 2	1.15 ( $\pm$ 356.23)			
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Notes:

[26] - Tisotumab Vedotin Cycle 1 N = 167

Tisotumab Vedotin Cycle 2 N = 146

Total HuMax-TF Cycle 2 = 146

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: Half-life (t<sub>1/2</sub>) of Tisotumab Vedotin and Total HuMax-TF

End point title	Dose Escalation Part: Half-life (t <sub>1/2</sub> ) of Tisotumab Vedotin and Total HuMax-TF
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2. T<sub>1/2</sub> was determined only for the dose escalation part of the study. Data was not planned to be collected for t<sub>1/2</sub> of tisotumab vedotin and total HuMax-TF for the dose expansion part per the study protocol.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: hours				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	12.22 ( $\pm$ 11.61)	29.53 ( $\pm$ 4.08)	33.72 ( $\pm$ 6.26)	41.06 ( $\pm$ 6.85)
Tisotumab Vedotin: Cycle 2	13.54 ( $\pm$ 5.50)	23.50 ( $\pm$ 39.89)	33.68 ( $\pm$ 1.74)	40.44 ( $\pm$ 4.69)
Total HuMax-TF: Cycle 1	16.05 ( $\pm$ 27.93)	28.66 ( $\pm$ 30.64)	42.52 ( $\pm$ 7.48)	57.37 ( $\pm$ 8.65)
Total HuMax-TF: Cycle 2	18.34 ( $\pm$ 8.73)	30.71 ( $\pm$ 27.65)	40.37 ( $\pm$ 4.27)	56.77 ( $\pm$ 9.60)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[27]</sup>	6 <sup>[28]</sup>
Units: hours				
geometric mean (geometric coefficient of variation)				
Tisotumab Vedotin: Cycle 1	32.42 ( $\pm$ 20.05)	47.89 ( $\pm$ 25.82)	40.93 ( $\pm$ 11.48)	41.19 ( $\pm$ 34.02)

Tisotumab Vedotin: Cycle 2	33.62 (± 14.50)	32.15 (± 62.74)	39.89 (± 23.15)	48.93 (± 5.61)
Total HuMax-TF: Cycle 1	42.72 (± 34.62)	57.72 (± 17.47)	54.95 (± 5.32)	55.10 (± 27.36)
Total HuMax-TF: Cycle 2	42.18 (± 25.39)	46.24 (± 53.11)	51.06 (± 9.18)	66.05 (± 10.07)

Notes:

[27] - Tisotumab Vedotin Cycle 2 N = 2

Total HuMax-TF Cycle 2 N = 2

[28] - Tisotumab Vedotin Cycle 2 N = 3

Total HuMax-TF Cycle 2 N = 3

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: AUC0-t of Free Monomethyl Auristatin E (MMAE)

End point title	Dose Escalation and Expansion Part: AUC0-t of Free Monomethyl Auristatin E (MMAE)
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	6.20 (± 72.05)	12.61 (± 28.18)	12.22 (± 67.23)	11.63 (± 52.69)
Cycle 2	3.19 (± 140.85)	4.69 (± 87.27)	14.89 (± 66.97)	16.92 (± 58.12)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[29]</sup>	6 <sup>[30]</sup>
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	26.55 (± 44.24)	22.55 (± 57.26)	67.42 (± 59.98)	26.47 (± 59.35)
Cycle 2	21.51 (± 34.25)	18.97 (± 52.14)	36.20 (± 33.82)	37.50 (± 43.08)

Notes:

[29] - Cycle 2 N = 2

[30] - Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[31]</sup>			
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	25.80 (± 93.91)			
Cycle 2	23.48 (± 76.47)			

Notes:

[31] - Cycle 2 N = 145

### Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Escalation Part: AUC0-inf of Free MMAE

End point title	Dose Escalation Part: AUC0-inf of Free MMAE
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2. AUC0-inf was not planned to be collected for the dose expansion part. AUC0-inf is not calculated where the percentage of the AUC that is due to the extrapolation is more than 20%. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2 <sup>[32]</sup>	1 <sup>[33]</sup>	2	1
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	12.63 (± 12.44)	13.93 (± 99999)	16.32 (± 57.56)	20.39 (± 0)
Cycle 2	99999 (± 99999)	99999 (± 99999)	22.32 (± 43.62)	31.40 (± 99999)

Notes:

[32] - Cycle 2 N = 0

[33] - Cycle 2 N = 0

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2 <sup>[34]</sup>	1	1 <sup>[35]</sup>	1
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	27.08 (± 58.96)	25.29 (± 99999)	78.31 (± 99999)	63.03 (± 99999)
Cycle 2	31.43 (± 99999)	33.23 (± 99999)	99999 (± 99999)	58.95 (± 99999)

Notes:

[34] - Cycle 2 N = 1

[35] - Cycle 2 N = 0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Cmax of Free MMAE

End point title	Dose Escalation and Expansion Part: Cmax of Free MMAE
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End point description:

PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.

End point type	Secondary
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End point timeframe:

Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	0.760 (± 62.505)	1.673 (± 30.756)	1.524 (± 54.491)	1.410 (± 19.149)
Cycle 2	1.091 (± 74.293)	1.342 (± 24.320)	2.059 (± 51.470)	2.243 (± 50.367)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[36]</sup>	6 <sup>[37]</sup>
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	2.807 (± 39.398)	2.587 (± 29.172)	6.351 (± 61.505)	4.877 (± 31.350)
Cycle 2	2.718 (± 39.492)	2.035 (± 39.785)	3.369 (± 36.875)	4.704 (± 18.856)

Notes:

[36] - Cycle 2 N = 2

[37] - Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[38]</sup>			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	3.16 (± 88.30)			
Cycle 2	2.73 (± 78.69)			

Notes:

[38] - Cycle 2 N = 145

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Tmax of Free MMAE

End point title	Dose Escalation and Expansion Part: Tmax of Free MMAE
End point description:	
PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2 in each part of the study.	
End point type	Secondary
End point timeframe:	
Before infusion, Day 1 (pre-dose) and 0.25 to 336 hours post-dose of Cycle 1 and Cycle 2 (each cycle was 21 days)	

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	23.88 (± 4.41)	22.77 (± 16.56)	24.39 (± 7.72)	24.19 (± 5.52)

Cycle 2	23.73 (± 5.78)	24.05 (± 8.48)	23.92 (± 13.04)	24.94 (± 1.48)
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End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3 <sup>[39]</sup>	6 <sup>[40]</sup>
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	25.07 (± 0.68)	47.74 (± 114.28)	83.24 (± 67.57)	84.88 (± 61.54)
Cycle 2	25.26 (± 0.76)	46.24 (± 112.48)	65.15 (± 104.61)	47.12 (± 112.10)

Notes:

[39] - Cycle 2 N = 2

[40] - Cycle 2 N = 3

End point values	Dose Expansion Part: Pharmacokinetics (PK) Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	168 <sup>[41]</sup>			
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	154.28 (± 54.214)			
Cycle 2	125.38 (± 31.21)			

Notes:

[41] - Cycle 2 = 145

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: PK Parameters, T 1/2 of Free MMAE

End point title	Dose Escalation Part: PK Parameters, T 1/2 of Free MMAE
End point description:	
PK parameters in plasma were determined based on non-compartmental methods and calculated separately for Cycle 1 and Cycle 2. T1/2 was determined only for the dose escalation part of the study.	
End point type	Secondary
End point timeframe:	
Dose escalation part (Cycles 1 and 2): Screening, pre-dose Day 1 then 0.25, 2, 5, 12, 24, 168, 336 and 504 hours post-dose.	

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2 <sup>[42]</sup>	1 <sup>[43]</sup>	2	1
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	95.15 (± 25.74)	69.34 (± 99999)	63.98 (± 2.24)	62.58 (± 99999)
Cycle 2	99999 (± 99999)	99999 (± 99999)	69.65 (± 3.86)	60.71 (± 99999)

Notes:

[42] - Cycle 2 N = 0

[43] - Cycle 2 N = 0

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2 <sup>[44]</sup>	1	1 <sup>[45]</sup>	1
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	63.65 (± 7.86)	78.90 (± 99999)	57.74 (± 99999)	68.47 (± 99999)
Cycle 2	70.20 (± 99999)	78.94 (± 99999)	99999 (± 99999)	63.92 (± 99999)

Notes:

[44] - Cycle 2 N = 1

[45] - Cycle 2 N = 0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Number of Participants with Positive Anti-Drug Antibodies (ADAs) to Tisotumab Vedotin

End point title	Dose Escalation and Expansion Part: Number of Participants with Positive Anti-Drug Antibodies (ADAs) to Tisotumab Vedotin
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End point description:

Participants who met the criterion for positive ADAs on treatment were defined as participants who were negative at baseline and had at least one positive post-baseline result, or participants who were positive at baseline and had at least one post-baseline result with a titer higher than baseline.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks



End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	49	12	13
Units: Participants	1	3	0	0

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	33	18	
Units: Participants	1	0	1	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Part: Anti-Tumor Activity Measured by Number of Participants Who Experienced Tumor Shrinkage

End point title	Dose Escalation Part: Anti-Tumor Activity Measured by Number of Participants Who Experienced Tumor Shrinkage
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

<b>End point values</b>	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: participants	0	0	0	1

<b>End point values</b>	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: participants	0	2	1	3

### Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Expansion Part: Anti-Tumor Activity Measured by Maximum Reduction in the Sum of Lesion Measurements

End point title	Dose Expansion Part: Anti-Tumor Activity Measured by Maximum Reduction in the Sum of Lesion Measurements
End point description: The number of subjects analysed includes all participants with baseline and one post-baseline evaluable tumor assessment.	
End point type	Secondary
End point timeframe: Day 1 to end of follow-up, up to a maximum of 60 weeks	

<b>End point values</b>	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	50	12	11
Units: millimeter(s)				
median (full range (min-max))	6.00 (-127.0 to 41.0)	-8.50 (-64.0 to 50.0)	1.00 (-11.0 to 26.0)	-2.00 (-51.0 to 40.0)

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	33	12	
Units: millimeter(s)				
median (full range (min-max))	0.00 (-59.0 to 31.0)	-4.00 (-41.0 to 115.0)	-1.00 (-11.0 to 15.0)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Percentage Change from Baseline in Prostate Specific Antigen (PSA)

End point title	Dose Escalation and Expansion Part: Percentage Change from Baseline in Prostate Specific Antigen (PSA)
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End point description:

PSA was only assessed in participants with castrate-resistant prostate cancer. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

The 'number of subjects analysed' number includes all participants with baseline and end of study evaluable assessment.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[46]</sup>	1	0 <sup>[47]</sup>	1
Units: percentage change in PSA				
median (full range (min-max))	( to )	64.35 (64.35 to 64.35)	( to )	40.91 (40.91 to 40.91)

Notes:

[46] - No participants with castrate-resistant prostate cancer

[47] - No participants with castrate-resistant prostate cancer

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	0 <sup>[48]</sup>	0 <sup>[49]</sup>	0 <sup>[50]</sup>
Units: percentage change in PSA				
median (full range (min-max))	3.92 (3.92 to 3.92)	( to )	( to )	( to )

Notes:

[48] - No participants with castrate-resistant prostate cancer

[49] - No participants with castrate-resistant prostate cancer

[50] - No participants with castrate-resistant prostate cancer

End point values	Dose Expansion Part: Prostate Cancer			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percentage change in PSA				
median (full range (min-max))	60.07 (3.4 to 996.5)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Part: Percentage Change from Baseline in CA-125

End point title	Dose Escalation and Expansion Part: Percentage Change from Baseline in CA-125
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End point description:

In the dose escalation part, CA-125 was only assessed for participants with ovarian cancer. In the dose expansion part, CA-125 was intended to be assessed only for participants with ovarian and endometrium cancer, but was additionally assessed for some participants with NSCLC and cervical cancer. 99999 = no evaluable data. 99999 is presented when no participants had evaluable data or only 1 participant had evaluable data, so geometric coefficient of variation could not be calculated.

The 'number of subjects analysed' number includes all participants with baseline and end of study evaluable assessment.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[51]</sup>	0 <sup>[52]</sup>	0 <sup>[53]</sup>	1
Units: percentage change				
median (full range (min-max))	( to )	( to )	( to )	18.75 (18.75 to 18.75)

Notes:

[51] - No participants with ovarian cancer

[52] - No participants with ovarian cancer

[53] - No participants with ovarian cancer

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[54]</sup>	1	1	2
Units: percentage change				
median (full range (min-max))	( to )	-13.98 (-13.98 to -13.98)	113.71 (113.71 to 113.71)	11.62 (-22.7 to 45.9)

Notes:

[54] - No participants with ovarian cancer

End point values	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	10	3	25
Units: percentage change				
median (full range (min-max))	-25.17 (-88.7 to 240.5)	37.85 (-46.1 to 666.2)	180.94 (47.1 to 980.5)	73.19 (-89.0 to 1924.4)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Parts: Objective Response Rate

End point title	Dose Escalation and Expansion Parts: Objective Response Rate
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End point description:

Percentage of participants with either a best overall response of complete response (CR) or partial response (PR) as assessed by the investigator per RECIST v1.1. The best overall response is the best response recorded from the start of the treatment until disease progression.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Percentage of participants				
number (confidence interval 95%)	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)	33 (1 to 91)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Percentage of participants				
number (confidence interval 95%)	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Percentage of participants				
number (confidence interval 95%)	27 (8 to 55)	24 (13 to 37)	7 (0 to 34)	13 (2 to 40)

End point values	Dose Expansion Part: Non- Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Percentage of participants				
number (confidence interval 95%)	13 (2 to 40)	14 (5 to 29)	0 (0 to 19)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Expansion Parts: Disease Control Rate

End point title	Dose Escalation and Expansion Parts: Disease Control Rate
End point description:	
Disease control rate was defined as the percentage of participants with CR, PR or SD as per investigator assessment per RECIST version 1.1 after 6, 12, 24 and 36 weeks.	
End point type	Secondary
End point timeframe:	
At 6, 12, 24 and 36 weeks	

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: Percentage of participants				
number (confidence interval 95%)				
Week 6	0 (0 to 71)	33 (1 to 91)	33 (1 to 91)	67 (9 to 99)
Week 12	0 (0 to 71)	33 (1 to 91)	33 (1 to 91)	67 (9 to 99)
Week 24	0 (0 to 71)	33 (1 to 91)	0 (0 to 71)	33 (1 to 91)
Week 36	0 (0 to 71)	33 (1 to 91)	0 (0 to 71)	33 (1 to 91)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: Percentage of participants				
number (confidence interval 95%)				
Week 6	33 (1 to 91)	100 (29 to 100)	67 (9 to 99)	50 (12 to 88)
Week 12	0 (0 to 71)	67 (9 to 99)	33 (1 to 91)	0 (0 to 46)
Week 24	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)	0 (0 to 46)
Week 36	0 (0 to 71)	0 (0 to 71)	0 (0 to 71)	0 (0 to 46)

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: Percentage of participants				
number (confidence interval 95%)				
Week 6	47 (21 to 73)	60 (46 to 73)	64 (35 to 87)	40 (16 to 68)
Week 12	33 (12 to 62)	47 (34 to 61)	43 (18 to 71)	20 (4 to 48)
Week 24	20 (4 to 48)	18 (9 to 31)	21 (5 to 51)	7 (0 to 32)
Week 36	7 (0 to 32)	11 (4 to 22)	0 (0 to 23)	0 (0 to 22)

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: Percentage of participants				

number (confidence interval 95%)				
Week 6	60 (32 to 84)	72 (55 to 86)	61 (36 to 83)	
Week 12	13 (2 to 40)	42 (26 to 59)	28 (10 to 53)	
Week 24	13 (2 to 40)	14 (5 to 29)	6 (0 to 27)	
Week 36	7 (0 to 32)	3 (0 to 15)	6 (0 to 27)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Dose Escalation and Expansion Parts: Progression Free Survival (PFS)

End point title	Dose Escalation and Expansion Parts: Progression Free Survival (PFS)
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End point description:

PFS was defined as the median time in weeks from Day 1 in Cycle 1 to first disease progression or death as assessed by the investigator. Only deaths that occurred within 60 days of the last visit were considered in the analysis and result are presented based on Kaplan-Meier estimates. Any results that could not be estimated are indicated as 99999.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg	Dose Escalation Part: 1.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	3
Units: weeks				
median (confidence interval 95%)	5.1 (4.9 to 5.4)	6.0 (3.9 to 49.1)	6.1 (4.9 to 99999)	27.1 (6.0 to 99999)

End point values	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: weeks				
median (confidence interval 95%)	6.1 (5.3 to 10.4)	17.1 (11.3 to 99999)	12.3 (5.0 to 14.1)	11.3 (2.1 to 11.3)

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	55	14	15
Units: weeks				
median (confidence interval 95%)	11.0 (5.1 to 43.0)	18.1 (9.3 to 23.0)	99999 (5.1 to 99999)	10.1 (5.3 to 17.0)

End point values	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	36	18	
Units: weeks				
median (confidence interval 95%)	13.0 (5.1 to 17.3)	13.0 (12.1 to 18.3)	12.9 (7.1 to 23.7)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Expansion Parts: Duration of Response (DOR)

End point title	Dose Expansion Parts: Duration of Response (DOR)
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End point description:

DOR was defined as the median time in weeks from when confirmed response was first documented until the first documented disease progression, or death from any cause, whichever was earliest as assessed by the investigator. A responder was defined as any participant with a best overall response of confirmed CR or PR. The 'subjects analysed' number only includes participants considered a responder. Any results in the dose expansion part of the study that could not be estimated are indicated as 99999.

The duration of response could not be estimated for the dose escalation part of the study as all participants who responded did not have disease progression or died due to any cause.

End point type	Secondary
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End point timeframe:

Day 1 to end of follow-up, up to a maximum of 60 weeks

End point values	Dose Expansion Part: Bladder Cancer	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	13	1	2
Units: weeks				
median (confidence interval 95%)	32.0 (11.0 to 32.0)	18.4 (13.1 to 41.7)	99999 (99999 to 99999)	18.3 (11.6 to 25.0)

<b>End point values</b>	Dose Expansion Part: Non-Small Cell Lung Cancer (NSCLC)	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2	5	0 <sup>[55]</sup>	
Units: weeks				
median (confidence interval 95%)	99999 (12.0 to 99999)	21.4 (13.1 to 29.6)	( to )	

Notes:

[55] - No participants with confirmed CR or PR.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events are reported from Day 1 to 30 days after dosing. The exposure ranged from 1 to 249 days in the escalation part and from 1 to 325 days in the expansion part.

Adverse event reporting additional description:

Deaths from all causes are reported from day of enrollment to end of follow up (up to maximum of 60 weeks).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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### Reporting groups

Reporting group title	Dose Escalation Part: 0.3 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 0.6 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 0.9 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 1.2 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 1.5 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 1.8 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 2.0 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Escalation Part: 2.2 mg/kg
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Bladder Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Cervical Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Endometrial Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Esophageal Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Non-Small-Cell Lung Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Ovarian Cancer
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Reporting group description:	-
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Reporting group title	Dose Expansion Part: Prostate Cancer
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Reporting group description:	-
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<b>Serious adverse events</b>	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	2	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Vascular disorders			
Vascular disorders			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Product issues			
Stent malfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Investigations			

Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Stress fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Nervous system disorders			
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Headache			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 disorders			



Vomiting				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	
Abdominal pain				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	
Diarrhoea				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	
Dysphagia				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	
Colitis				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	
Nausea				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 ulcer haemorrhage				

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Oesophageal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Subileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ascites			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Bacterial sepsis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Kidney infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Micrococcus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cystitis escherichia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Klebsiella infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hyperglycaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

<b>Serious adverse events</b>	Dose Escalation Part: 1.2 mg/kg	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	2 / 3 (66.67%)
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)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Vascular disorders			
Vascular disorders			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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



Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	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
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Product issues			
Stent malfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Stress fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Nervous system disorders			
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Febrile neutropenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Colitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 ulcer haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Oesophageal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Subileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	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
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Sepsis subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Upper respiratory tract infection subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Bacterial sepsis subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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 subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Clostridium difficile colitis subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Device related infection subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Kidney infection subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Micrococcus infection			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cystitis escherichia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Klebsiella infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	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
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	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
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

<b>Serious adverse events</b>	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg	Dose Expansion Part: Bladder Cancer
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	4 / 6 (66.67%)	7 / 15 (46.67%)
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)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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

Oesophageal cancer metastatic subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 Vascular disorders subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 Malaise subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 physical health deterioration subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (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
Catheter site pain subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Mucosal inflammation subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (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
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 embolism			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Stent malfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
Stress fracture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
<b>Febrile neutropenia</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Neutropenia</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
<b>Ear and labyrinth disorders</b>			
<b>Hypoacusis</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
<b>Gastrointestinal disorders</b>			
<b>Vomiting</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
<b>Abdominal pain</b>			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 15 (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
<b>Constipation</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 ulcer haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Oesophageal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			



subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Subileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (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
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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 obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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

Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Bacterial sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Kidney infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Micrococcus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Cystitis escherichia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Klebsiella infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (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
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (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

<b>Serious adverse events</b>	Dose Expansion	Dose Expansion	Dose Expansion
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	Part: Cervical Cancer	Part: Endometrial Cancer	Part: Esophageal Cancer
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 55 (47.27%)	5 / 14 (35.71%)	8 / 15 (53.33%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	2	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tumour pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Vascular disorders			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Mucosal inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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			
Dyspnoea			

subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Epistaxis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Insomnia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Stent malfunction			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Investigations			



Blood creatinine increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Transaminases increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
Stress fracture			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Nervous system disorders			
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Headache			

subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Ischaemic stroke			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Lethargy			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
Anaemia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (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			

Vomiting				
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Abdominal pain				
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (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	
Constipation				
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Diarrhoea				
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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	
Dysphagia				
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Colitis				
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Nausea				
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (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	
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (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 ulcer haemorrhage				

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Oesophageal perforation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Subileus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Ascites			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Gastritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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 obstruction			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Acute kidney injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Muscular weakness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (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

Pain in extremity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Myalgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
Urinary tract infection			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Bacterial sepsis			

subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Kidney infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Micrococcus infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Staphylococcal infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Urosepsis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (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
Cystitis escherichia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Klebsiella infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			



subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Hypoglycaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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
Diabetes mellitus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (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

<b>Serious adverse events</b>	Dose Expansion Part: Non-Small-Cell Lung Cancer	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)	13 / 36 (36.11%)	6 / 18 (33.33%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Vascular disorders			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Malaise			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 physical health deterioration			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Catheter site pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Mucosal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (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

Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Female genital tract fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 embolism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Stent malfunction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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			
Stress fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Ischaemic stroke			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Lethargy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Febrile neutropenia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (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
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Colitis			

subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (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
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 ulcer haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Oesophageal perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Subileus			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Intestinal obstruction			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Ascites			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0



Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Muscular weakness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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			
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (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
Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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

Lower respiratory tract infection subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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 subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Clostridium difficile colitis subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Kidney infection subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (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
Micrococcus infection			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (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 tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (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
Staphylococcal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Urosepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Cystitis escherichia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Klebsiella infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (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
Hyperglycaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (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
Hypoglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Dose Escalation Part: 0.3 mg/kg	Dose Escalation Part: 0.6 mg/kg	Dose Escalation Part: 0.9 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cancer pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	3	3	1
Pyrexia			

subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	2
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contrast media allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balanoposthitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Testicular pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Sleep disorder subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Vital dye staining cornea present subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Platelet count decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival staining			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Serum ferritin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time			

prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fibrin d dimer increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival scar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eyelid contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharynx radiation injury			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Chemical burns of eye subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Bradycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders			
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2	1 / 3 (33.33%) 1
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Headache			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brain oedema			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Central pain syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amputation stump pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	0	3	2
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0



Lymph node pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Neutrophilia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders			
Ear congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hypoacusis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blepharitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctival ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meibomianitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Noninfective conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Symblepharon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chorioretinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Entropion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Open angle glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trichiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye irritation			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	4
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophageal mucosal hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail ridging			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toxic skin eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin lesion			



subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthralgia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthritis climacteric			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Dose Escalation Part: 1.2 mg/kg	Dose Escalation Part: 1.5 mg/kg	Dose Escalation Part: 1.8 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypotension			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 3 (100.00%)
occurrences (all)	1	0	3
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infusion site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			



subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contrast media allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Balanoposthitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Testicular pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	3 / 3 (100.00%)
occurrences (all)	4	3	4
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hiccups			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vital dye staining cornea present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival staining			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Serum ferritin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fibrin d dimer increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival scar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eyelid contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharynx radiation injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sunburn			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chemical burns of eye			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			



subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Central pain syndrome			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amputation stump pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lymph node pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Neutrophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Conjunctival ulcer			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meibomianitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Noninfective conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Symblepharon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chorioretinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Entropion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Open angle glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trichiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1

Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	3
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Oesophageal mucosal hyperplasia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oesophagitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oral pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Proctalgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Tongue ulceration subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hepatobiliary disorders Bile duct obstruction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hepatitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	2 / 3 (66.67%) 2
Pruritus subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Rash			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail ridging			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toxic skin eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthritis climacteric			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tendonitis			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Urethritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Dose Escalation Part: 2.0 mg/kg	Dose Escalation Part: 2.2 mg/kg	Dose Expansion Part: Bladder Cancer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	3
Hot flush			



subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Intermittent claudication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	4 / 6 (66.67%)	8 / 15 (53.33%)
occurrences (all)	0	4	10
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 6 (66.67%)	2 / 15 (13.33%)
occurrences (all)	0	4	2
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Asthenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Contrast media allergy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Reproductive system and breast disorders			
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Balanoposthitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Metrorrhagia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Testicular pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Vulvovaginal dryness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	4 / 6 (66.67%) 5	13 / 15 (86.67%) 13
Dyspnoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	3 / 15 (20.00%) 3
Cough subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Nasal congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Dysphonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Nasal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasal crusting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	4 / 15 (26.67%)
occurrences (all)	0	1	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vital dye staining cornea present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Conjunctival staining			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Serum ferritin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood urea decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fibrin d dimer increased			



subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	0 / 15 (0.00%) 0
White blood cell count increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	0 / 15 (0.00%) 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Conjunctival scar			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Contusion			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Eyelid contusion			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Pharynx radiation injury			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Skin laceration			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Sunburn			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Chemical burns of eye			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	6 / 15 (40.00%)
occurrences (all)	0	0	7
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Peripheral motor neuropathy			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Central pain syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mental impairment			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Amputation stump pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lymph node pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neutrophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1

Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Lacrimation increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Conjunctival ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Meibomianitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Noninfective conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Symblepharon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Conjunctival disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Conjunctival haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	3 / 6 (50.00%)	0 / 15 (0.00%)
occurrences (all)	0	4	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Punctate keratitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chorioretinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Entropion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Open angle glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Trichiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye irritation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 6 (66.67%)	7 / 15 (46.67%)
occurrences (all)	1	4	7
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	6 / 15 (40.00%)
occurrences (all)	2	3	7
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3

Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0



Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oesophageal mucosal hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 3 (66.67%)	4 / 6 (66.67%)	3 / 15 (20.00%)
occurrences (all)	2	4	3
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	5
Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	2
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	3
Rash maculo-papular			

subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nail ridging			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pain of skin			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Toxic skin eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Urine flow decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 15 (20.00%)
occurrences (all)	0	2	3
Proteinuria			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Urinary hesitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Arthralgia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 15 (6.67%)
occurrences (all)	0	2	3
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Arthritis climacteric			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	7 / 15 (46.67%)
occurrences (all)	0	1	9

Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	2 / 15 (13.33%)
occurrences (all)	0	3	3
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Conjunctivitis bacterial subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Eye infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Gingivitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 15 (6.67%) 1
Haemophilus infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Tooth abscess subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Urethritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 15 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite			



subjects affected / exposed	1 / 3 (33.33%)	5 / 6 (83.33%)	3 / 15 (20.00%)
occurrences (all)	1	5	3
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	2 / 15 (13.33%)
occurrences (all)	1	2	2
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0

<b>Non-serious adverse events</b>	Dose Expansion Part: Cervical Cancer	Dose Expansion Part: Endometrial Cancer	Dose Expansion Part: Esophageal Cancer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 55 (100.00%)	14 / 14 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cancer pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Melanocytic naevus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	4 / 55 (7.27%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Hypertension			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lymphoedema			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	29 / 55 (52.73%)	10 / 14 (71.43%)	10 / 15 (66.67%)
occurrences (all)	34	12	10
Pyrexia			
subjects affected / exposed	11 / 55 (20.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	13	1	3
Mucosal inflammation			
subjects affected / exposed	5 / 55 (9.09%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	5	2	0
Oedema peripheral			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	3 / 55 (5.45%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	3	2	1
Malaise			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Chest pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			

subjects affected / exposed	3 / 55 (5.45%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
Pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Infusion site reaction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Contrast media allergy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	6 / 55 (10.91%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	7	0	0
Balanoposthitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	28 / 55 (50.91%)	11 / 14 (78.57%)	8 / 15 (53.33%)
occurrences (all)	40	13	10
Dyspnoea			
subjects affected / exposed	8 / 55 (14.55%)	3 / 14 (21.43%)	2 / 15 (13.33%)
occurrences (all)	8	3	2
Cough			
subjects affected / exposed	5 / 55 (9.09%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	8	1	3
Nasal congestion			
subjects affected / exposed	5 / 55 (9.09%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	5	1	0
Dysphonia			
subjects affected / exposed	3 / 55 (5.45%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	3	1	3
Rhinorrhoea			
subjects affected / exposed	0 / 55 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasal inflammation			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Nasal obstruction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sinus pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 55 (10.91%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	6	2	1
Depressed mood			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Confusional state			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Mood altered			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	9 / 55 (16.36%)	4 / 14 (28.57%)	2 / 15 (13.33%)
occurrences (all)	10	4	2
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 55 (10.91%)	3 / 14 (21.43%)	3 / 15 (20.00%)
occurrences (all)	9	5	3
Alanine aminotransferase increased			
subjects affected / exposed	7 / 55 (12.73%)	3 / 14 (21.43%)	3 / 15 (20.00%)
occurrences (all)	8	3	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	0	2	3
Blood creatinine increased			
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	5	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 55 (0.00%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	0	3	1
Vital dye staining cornea present			



subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Blood magnesium decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Conjunctival staining subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Blood fibrinogen increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Serum ferritin increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Blood urea decreased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Fibrin d dimer increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
White blood cell count increased subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	5	0	1
Conjunctival scar			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Contusion			
subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	1
Eyelid contusion			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pharynx radiation injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chemical burns of eye			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Bradycardia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	16 / 55 (29.09%)	5 / 14 (35.71%)	2 / 15 (13.33%)
occurrences (all)	19	5	2
Peripheral sensory neuropathy			
subjects affected / exposed	5 / 55 (9.09%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	5	3	0
Headache			
subjects affected / exposed	5 / 55 (9.09%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	7	3	1
Lethargy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Dysgeusia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Peripheral motor neuropathy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Migraine			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2

Paraesthesia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Carpal tunnel syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Central pain syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Mental impairment			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Myoclonus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Spinal cord compression subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Amputation stump pain subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	13 / 55 (23.64%) 17	2 / 14 (14.29%) 2	3 / 15 (20.00%) 4
Neutropenia subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Lymph node pain subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Neutrophilia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Ear and labyrinth disorders			
Ear congestion subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Hypoacusis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Vertigo			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	14 / 55 (25.45%)	6 / 14 (42.86%)	2 / 15 (13.33%)
occurrences (all)	14	6	2
Lacrimation increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	0	1	3
Blepharitis			
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Vision blurred			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Conjunctival ulcer			
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	4	0	1
Keratitis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	5	0	0
Meibomianitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Noninfective conjunctivitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Symblepharon			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Ocular hyperaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Conjunctival hyperaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Conjunctival disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Punctate keratitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chorioretinopathy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Entropion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Open angle glaucoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1



Periorbital oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Trichiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	25 / 55 (45.45%)	7 / 14 (50.00%)	7 / 15 (46.67%)
occurrences (all)	30	8	8
Constipation			
subjects affected / exposed	19 / 55 (34.55%)	3 / 14 (21.43%)	6 / 15 (40.00%)
occurrences (all)	21	3	8
Diarrhoea			
subjects affected / exposed	17 / 55 (30.91%)	6 / 14 (42.86%)	2 / 15 (13.33%)
occurrences (all)	26	8	4
Vomiting			
subjects affected / exposed	18 / 55 (32.73%)	4 / 14 (28.57%)	4 / 15 (26.67%)
occurrences (all)	23	6	5
Abdominal pain			
subjects affected / exposed	15 / 55 (27.27%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	17	1	1
Dyspepsia			
subjects affected / exposed	0 / 55 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Dry mouth			

subjects affected / exposed	3 / 55 (5.45%)	5 / 14 (35.71%)	0 / 15 (0.00%)
occurrences (all)	4	6	0
Stomatitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	3 / 55 (5.45%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	4	2	1
Rectal haemorrhage			
subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	5	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Dysphagia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	0	4
Abdominal distension			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 55 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Ascites			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cheilitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastritis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oesophageal mucosal hyperplasia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			

subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Hepatobiliary disorders Bile duct obstruction subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Hepatitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	22 / 55 (40.00%) 22	8 / 14 (57.14%) 8	4 / 15 (26.67%) 4
Pruritus subjects affected / exposed occurrences (all)	10 / 55 (18.18%) 11	2 / 14 (14.29%) 3	2 / 15 (13.33%) 3
Rash subjects affected / exposed occurrences (all)	7 / 55 (12.73%) 8	4 / 14 (28.57%) 4	1 / 15 (6.67%) 1
Dry skin subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	4 / 14 (28.57%) 5	0 / 15 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	0 / 14 (0.00%) 0	2 / 15 (13.33%) 2
Nail disorder subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Acne			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nail ridging			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Skin ulcer			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Toxic skin eruption			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	5 / 55 (9.09%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	7	2	0
Proteinuria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Urinary hesitation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Renal impairment			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hydronephrosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	5 / 55 (9.09%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	6	0	2
Arthralgia			
subjects affected / exposed	6 / 55 (10.91%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	6	2	0
Back pain			
subjects affected / exposed	6 / 55 (10.91%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	7	2	1
Pain in extremity			
subjects affected / exposed	4 / 55 (7.27%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	7	0	1
Muscular weakness			
subjects affected / exposed	3 / 55 (5.45%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	3	1	2
Musculoskeletal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Bone pain			

subjects affected / exposed	0 / 55 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Flank pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Arthritis climacteric			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	23 / 55 (41.82%)	6 / 14 (42.86%)	4 / 15 (26.67%)
occurrences (all)	37	8	5
Urinary tract infection			
subjects affected / exposed	11 / 55 (20.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	16	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	3 / 55 (5.45%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0



Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	3 / 14 (21.43%) 3	0 / 15 (0.00%) 0
Oral candidiasis subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Rash pustular subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 14 (7.14%) 1	0 / 15 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Candida infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	1 / 15 (6.67%) 1
Catheter site infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Conjunctivitis bacterial subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 14 (7.14%) 1	0 / 15 (0.00%) 0
Eye infection subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 14 (0.00%) 0	0 / 15 (0.00%) 0

Gingivitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	20 / 55 (36.36%)	5 / 14 (35.71%)	6 / 15 (40.00%)
occurrences (all)	22	6	7
Hypokalaemia			
subjects affected / exposed	11 / 55 (20.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	14	2	2
Hypomagnesaemia			
subjects affected / exposed	6 / 55 (10.91%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	6	1	3
Dehydration			

subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Hyponatraemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hyperglycaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Dose Expansion Part: Non-Small-Cell Lung Cancer	Dose Expansion Part: Ovarian Cancer	Dose Expansion Part: Prostate Cancer
Total subjects affected by non-serious adverse events			

subjects affected / exposed	15 / 15 (100.00%)	36 / 36 (100.00%)	18 / 18 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	5 / 36 (13.89%)	0 / 18 (0.00%)
occurrences (all)	0	6	0
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 15 (53.33%)	15 / 36 (41.67%)	15 / 18 (83.33%)
occurrences (all)	11	18	16
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	4 / 36 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	5	0
Mucosal inflammation			
subjects affected / exposed	2 / 15 (13.33%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	2	2	0
Oedema peripheral			
subjects affected / exposed	2 / 15 (13.33%)	5 / 36 (13.89%)	1 / 18 (5.56%)
occurrences (all)	2	5	1
Chills			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 15 (0.00%)	5 / 36 (13.89%)	0 / 18 (0.00%)
occurrences (all)	0	7	0
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	5	0
Chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Peripheral swelling			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Chest discomfort			

subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Contrast media allergy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Balanoposthitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Testicular pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vulvovaginal dryness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	11 / 15 (73.33%)	30 / 36 (83.33%)	12 / 18 (66.67%)
occurrences (all)	15	34	12
Dyspnoea			
subjects affected / exposed	3 / 15 (20.00%)	6 / 36 (16.67%)	2 / 18 (11.11%)
occurrences (all)	3	7	2
Cough			
subjects affected / exposed	5 / 15 (33.33%)	3 / 36 (8.33%)	1 / 18 (5.56%)
occurrences (all)	5	3	1
Nasal congestion			
subjects affected / exposed	1 / 15 (6.67%)	4 / 36 (11.11%)	0 / 18 (0.00%)
occurrences (all)	1	6	0
Dysphonia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	2 / 15 (13.33%)	6 / 36 (16.67%)	0 / 18 (0.00%)
occurrences (all)	2	6	0
Oropharyngeal pain			
subjects affected / exposed	2 / 15 (13.33%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	5	3	0
Haemoptysis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nasal inflammation			

subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nasal obstruction			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Productive cough			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Catarrh			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dry throat			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Laryngeal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rales			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus pain			



subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 15 (26.67%)	6 / 36 (16.67%)	2 / 18 (11.11%)
occurrences (all)	4	7	2
Depressed mood			
subjects affected / exposed	3 / 15 (20.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Depression			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Panic attack subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Restlessness subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Sleep disorder subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	3 / 36 (8.33%) 3	6 / 18 (33.33%) 6
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	2 / 36 (5.56%) 2	2 / 18 (11.11%) 2
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 36 (0.00%) 0	2 / 18 (11.11%) 2
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	0 / 36 (0.00%) 0	1 / 18 (5.56%) 2
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	1 / 18 (5.56%) 2
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	1 / 18 (5.56%) 1
Vital dye staining cornea present subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctival staining			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Serum ferritin increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Fibrin d dimer increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Conjunctival scar			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Contusion			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eyelid contusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pharynx radiation injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chemical burns of eye			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy peripheral			

subjects affected / exposed	3 / 15 (20.00%)	10 / 36 (27.78%)	3 / 18 (16.67%)
occurrences (all)	3	12	3
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	9 / 36 (25.00%)	1 / 18 (5.56%)
occurrences (all)	1	9	1
Headache			
subjects affected / exposed	1 / 15 (6.67%)	5 / 36 (13.89%)	3 / 18 (16.67%)
occurrences (all)	2	6	3
Lethargy			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	1	2	2
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	1	3	1
Peripheral motor neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Polyneuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3
Tremor			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Taste disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Balance disorder			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Brain oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Central pain syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dysaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nerve compression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Spinal cord compression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Amputation stump pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	3 / 18 (16.67%)
occurrences (all)	2	0	6
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	3 / 36 (8.33%)	1 / 18 (5.56%)
occurrences (all)	1	3	1
Lymph node pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			



Dry eye			
subjects affected / exposed	6 / 15 (40.00%)	6 / 36 (16.67%)	2 / 18 (11.11%)
occurrences (all)	7	6	2
Lacrimation increased			
subjects affected / exposed	2 / 15 (13.33%)	5 / 36 (13.89%)	0 / 18 (0.00%)
occurrences (all)	3	5	0
Blepharitis			
subjects affected / exposed	0 / 15 (0.00%)	5 / 36 (13.89%)	1 / 18 (5.56%)
occurrences (all)	0	5	1
Vision blurred			
subjects affected / exposed	2 / 15 (13.33%)	6 / 36 (16.67%)	0 / 18 (0.00%)
occurrences (all)	2	6	0
Conjunctival ulcer			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Keratitis			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Meibomianitis			
subjects affected / exposed	0 / 15 (0.00%)	5 / 36 (13.89%)	0 / 18 (0.00%)
occurrences (all)	0	5	0
Noninfective conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Symblepharon			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Eye pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	3	0	0
Ocular hyperaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Cataract			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Conjunctival hyperaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Ulcerative keratitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctival disorder			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Chorioretinopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Entropion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Open angle glaucoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Trichiasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Eye inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 15 (66.67%)	20 / 36 (55.56%)	12 / 18 (66.67%)
occurrences (all)	16	30	14
Constipation			
subjects affected / exposed	5 / 15 (33.33%)	11 / 36 (30.56%)	9 / 18 (50.00%)
occurrences (all)	5	13	11
Diarrhoea			
subjects affected / exposed	4 / 15 (26.67%)	14 / 36 (38.89%)	5 / 18 (27.78%)
occurrences (all)	4	19	7
Vomiting			
subjects affected / exposed	6 / 15 (40.00%)	11 / 36 (30.56%)	6 / 18 (33.33%)
occurrences (all)	6	18	9
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)	8 / 36 (22.22%)	6 / 18 (33.33%)
occurrences (all)	2	9	8
Dyspepsia			
subjects affected / exposed	2 / 15 (13.33%)	4 / 36 (11.11%)	1 / 18 (5.56%)
occurrences (all)	2	4	1
Dry mouth			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	2
Stomatitis			
subjects affected / exposed	0 / 15 (0.00%)	6 / 36 (16.67%)	2 / 18 (11.11%)
occurrences (all)	0	7	2
Abdominal discomfort			

subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Colitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Gingival bleeding			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematemesis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oesophageal mucosal hyperplasia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tongue ulceration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Bile duct obstruction subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Hepatitis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	7 / 15 (46.67%) 7	19 / 36 (52.78%) 19	6 / 18 (33.33%) 6
Pruritus subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	6 / 36 (16.67%) 7	1 / 18 (5.56%) 1
Rash subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	6 / 36 (16.67%) 6	4 / 18 (22.22%) 5
Dry skin subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2	2 / 36 (5.56%) 2	1 / 18 (5.56%) 1
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	5 / 36 (13.89%) 6	1 / 18 (5.56%) 1
Nail disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	3 / 36 (8.33%) 3	0 / 18 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Acne subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	2 / 36 (5.56%) 2	0 / 18 (0.00%) 0
Skin hyperpigmentation subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Rash macular			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
<b>Dermatitis</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
<b>Dermatitis acneiform</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Erythema</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Hyperhidrosis</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Nail ridging</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
<b>Onycholysis</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Pain of skin</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Palmar-plantar erythrodysesthesia syndrome</b>			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
<b>Rash pruritic</b>			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
<b>Skin ulcer</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
<b>Toxic skin eruption</b>			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Urine flow decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	4
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			



subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 36 (0.00%) 0	0 / 18 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	9 / 36 (25.00%)	5 / 18 (27.78%)
occurrences (all)	1	9	5
Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	6 / 36 (16.67%)	4 / 18 (22.22%)
occurrences (all)	2	7	5
Back pain			
subjects affected / exposed	2 / 15 (13.33%)	3 / 36 (8.33%)	5 / 18 (27.78%)
occurrences (all)	2	3	5
Pain in extremity			
subjects affected / exposed	3 / 15 (20.00%)	4 / 36 (11.11%)	0 / 18 (0.00%)
occurrences (all)	4	5	0
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	2 / 18 (11.11%)
occurrences (all)	2	2	2
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Muscle spasms			
subjects affected / exposed	2 / 15 (13.33%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Bursitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Muscle atrophy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Arthritis climacteric			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	6 / 15 (40.00%)	15 / 36 (41.67%)	9 / 18 (50.00%)
occurrences (all)	7	19	9
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	4 / 36 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	6	1
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	3 / 36 (8.33%)	2 / 18 (11.11%)
occurrences (all)	1	3	2
Oral herpes			
subjects affected / exposed	0 / 15 (0.00%)	4 / 36 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	2 / 36 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Oral candidiasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1

Sinusitis			
subjects affected / exposed	1 / 15 (6.67%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Rash pustular			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Candida infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haemophilus infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Skin infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urethritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 15 (33.33%)	12 / 36 (33.33%)	10 / 18 (55.56%)
occurrences (all)	5	13	14
Hypokalaemia			
subjects affected / exposed	2 / 15 (13.33%)	5 / 36 (13.89%)	2 / 18 (11.11%)
occurrences (all)	2	6	3
Hypomagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)	4 / 36 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	4	1
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	1 / 15 (6.67%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2013	<p>The following updates were made:</p> <ul style="list-style-type: none"><li>• Revisions made in accordance with questions raised by the UK Medicines and Healthcare products Regulatory Agency and the United States FDA.</li><li>• Revised inclusion criterion to exclude subjects with platinum-sensitive ovarian cancer from the Expansion Part of the trial.</li><li>• Revised inclusion criterion to ensure that subjects with metastatic castration resistant prostate cancer had received abiraterone and/or enzalutamide prior to entering the Expansion Part.</li><li>• Specified plan for assessing human anti-human antibodies to both antibody-drug conjugate and total antibody and plan for evaluating the impact of immunogenicity on PK, activity and safety of tisotumab vedotin.</li><li>• Visual acuity assessment was added.</li><li>• Communication plan on how the assignment of subjects to a cohort was undertaken was added.</li><li>• Criteria for subject withdrawal from treatment were modified.</li><li>• A list of strong CYP3A4 inhibitors was added.</li><li>• Investigators were to consult an ophthalmologist for any subject experiencing clinical significant ophthalmologic AEs.</li><li>• Dose Escalation rules were updated.</li><li>• Dose level toxicity definitions were updated.</li><li>• Details on post-infusion monitoring were added.</li><li>• Clarified that the CTCAE grade of all bleeding AEs were to be reported.</li></ul>
28 January 2014	<p>The following update was made:</p> <ul style="list-style-type: none"><li>• Updated in response to the Danish Competent Authority request to specify the contraceptive measures, and comments from a US site Clinical Review Committee to clarify trial-related procedures and further define research endpoints.</li></ul>
03 April 2014	<p>The following update was made:</p> <ul style="list-style-type: none"><li>• Exclusion criterion modified such that subjects requiring IV treatment with antimicrobial therapy starting less than 4 weeks prior to first dose or oral treatment with antimicrobial therapy starting less than 2 weeks prior to first dose were excluded.</li></ul>
05 May 2014	<p>The following update was made:</p> <ul style="list-style-type: none"><li>• Modified due to an event of pharyngeal tumor hemorrhage with fatal outcome. The DMC recommended exclusion of subjects with squamous cell carcinoma of the head and neck from the Dose Escalation Part.</li></ul>
12 September 2014	<p>The following update was made:</p> <ul style="list-style-type: none"><li>• Revised inclusion criterion with respect to coagulation status.</li></ul>
29 May 2015	<p>The following updates were made:</p> <ul style="list-style-type: none"><li>• Trial phase changed from I to I/II to reflect that only the Dose Escalation Part was first-in-human, and the Expansion Part was phase II.</li><li>• Updated the Expansion Part of the trial including clarification of the approach for the types of cancers that were included, and an increase of subjects to be enrolled.</li></ul>
23 November 2015	<p>The following updates were made:</p> <ul style="list-style-type: none"><li>• Updated to encompass adaptive changes based on biomarker-derived data.</li><li>• Prespecified 2 of the trial cohorts for Expansion Part, endometrial and cervical cancer.</li><li>• Increased the planned number of subjects in the Expansion Part.</li><li>• Aligned the treatment guidelines in the US and EU.</li></ul>

17 March 2016	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• In order to better describe safety and preliminary biological activity signals, a cap on previous exposure to anticancer therapies for subjects to be included in the Expansion Part was introduced in this amendment.</li> <li>• Requirements for tumor biopsies in the Expansion Part were changed so archived samples, if available, could be used.</li> <li>• Pregnancy tests were added for women of childbearing potential in accordance with the "Recommendations related to contraception and pregnancy testing in clinical trials" of the Clinical Trial Facilitation Group.</li> </ul>
03 June 2016	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• Clarified that the sponsor made every effort to ensure that the principles of GCP will be set in place for the exploratory analysis of protein biomarkers.</li> <li>• Specified the defined limit for human exposure of tisotumab vedotin and free toxin MMAE.</li> <li>• Clarified that all investigators received the suspected unexpected serious adverse reaction reports.</li> <li>• Explained that in case of potential serious breach, these were reported to the competent authorities immediately.</li> </ul>
07 July 2016	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• Updated with safety information concerning ocular events (conjunctivitis).</li> <li>• Inclusion criterion on acceptable hematological status was modified.</li> <li>• A 40-day wash-out period combined with a requirement for no residual check point related symptoms of autoimmune toxicity was added.</li> </ul>
27 October 2016	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• Modified the evaluation and mitigation plan for ocular events.</li> <li>• Some inclusion and exclusion criteria were reworded for clarification and/or to adapt to current experience or standard practice.</li> <li>• In the Expansion Part the wording was modified regarding the number of subjects per cohort (fixed at 14 subjects) and the conditions to expand to 30 subjects to maintain flexibility to expand the cohorts with the most promising benefit/risk ratios.</li> <li>• The number of participating sites for the Expansion Part was increased.</li> </ul>
22 December 2016	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• One CTCAE grade 3 event of conjunctivitis had already been reported in the GEN702 trial. Following the cutoff date of 31 May 2016, 3 additional CTCAE grade 3 events of conjunctivitis and one CTCAE grade 4 event of keratitis had been reported. The purpose of the amendment was to update this information in the protocol and to modify the dose modification and mitigation plans for ocular events accordingly, including mandatory preventive eye therapy.</li> </ul>
26 September 2017	<p>The following updates were made:</p> <ul style="list-style-type: none"> <li>• Modified to allow recruitment of up to 25 additional subjects with cervical cancer for a maximum of approximately 55 subjects.</li> <li>• Updated the clinical experience and risks to human subjects based on relevant experience in ongoing trials.</li> <li>• Clarified the evaluation and mitigation plan for ocular events.</li> </ul>
05 October 2017	<p>The following update was made:</p> <ul style="list-style-type: none"> <li>• Modified the inclusion/exclusion criteria to allow subjects on stable doses of anticoagulation therapy for <math>\geq 8</math> weeks to enter the trial.</li> </ul>

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported

