



Clinical trial results:

A Phase II, Double-Blind, Randomised, Placebo-Controlled Study to Assess the Efficacy and Safety of Selumetinib (AZD6244; ARRY-142886) (Hyd-Sulfate) in Combination with Docetaxel, Compared with Placebo in Combination with Docetaxel, in Patients receiving second line treatment for Locally Advanced or Metastatic Non Small Cell Lung Cancer (Stage IIIB - IV) (SELECT-2)

Summary

EudraCT number	2012-003622-25
Trial protocol	HU DE NL BG
Global end of trial date	31 October 2022

Results information

Result version number	v1 (current)
This version publication date	19 August 2023
First version publication date	19 August 2023

Trial information

Trial identification

Sponsor protocol code	D1532C00064
-----------------------	-------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	132 Hills Rd, Cambridge, United Kingdom, CB2 1PG
Public contact	Dr Gabriella Mariani, AstraZeneca, +44 0207 6048000, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Dr Gabriella Mariani, AstraZeneca, +44 0207 6048000, ClinicalTrialTransparency@astrazeneca.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	27 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2016
Global end of trial reached?	Yes
Global end of trial date	31 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy in terms of Progression Free Survival (PFS) for each comparison of selumetinib in combination with docetaxel, compared to placebo in combination with docetaxel.

Protection of trial subjects:

A treatment discontinuation visit was conducted as soon as possible after the patient received the last dose of the last study drug (selumetinib/placebo or docetaxel). Collection of AEs/serious adverse events (SAEs) continued until 30 days after the last dose of study treatment for patient's withdrawal from study. Thirty days after permanent discontinuation of the last study treatment (selumetinib/placebo or docetaxel), a treatment discontinuation follow up contact was performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Hungary: 50
Country: Number of subjects enrolled	Brazil: 39
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Poland: 3
Worldwide total number of subjects	212
EEA total number of subjects	154

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)	132
From 65 to 84 years	80
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Initially the study protocol allowed patients with KRASSm (KRAS mutation positive), KRAS NMD (No mutation detected) and KRAS mutation status unknown. Recruitment was put on hold after the 77th patient was randomised in September 2013, to allow a protocol amendment to include only patients with centrally confirmed KRAS NMD NSCLC to be enrolled.

Pre-assignment

Screening details:

Of the 337 enrolled patients, 212 patients were randomised into the study. All 212 patients who were randomised into the study were included in the Full Analysis Set (FAS). A total of 211 patients received at least 1 dose of treatment and were included in the safety analysis set. Patients received selumetinib (AZD6244; ARRY-142886) or Placebo.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Docetaxel 75 mg/m ²
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo + Docetaxel 75 mg/m ²
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo in combination with docetaxel intravenous [iv] 75 mg/m²
(hereafter referred to as Doc 75 mg/m² alone)

Arm title	Selumetinib 75 mg BD + Docetaxel 60 mg/m ²
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Selumetinib 75 mg BD + Docetaxel 60 mg/m ²
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Selumetinib 75 mg twice daily in combination with docetaxel intravenous [iv] 60 mg/m² (hereafter referred to as Sel 75 mg + Doc 60 mg/m²)

Arm title	Selumetinib 75 mg BD + Docetaxel 75 mg/m ²
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Selumetinib 75 mg twice daily in combination with docetaxel intravenous [iv] 75 mg/m2 (hereafter referred to as Sel 75 mg + Doc 75 mg/m2)

Number of subjects in period 1	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Started	43	85	84
Received Treatment	43	84	84
Did not receive Treatment	0	1	0
Completed	0	0	0
Not completed	43	85	84
Ongoing Selumetinib/Pbo at data cut-off	6	7	9
Discontinued Selumetinib/Placebo	37	77	75
Did not receive treatment	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo + Docetaxel 75 mg/m2
Reporting group description: -	
Reporting group title	Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Reporting group description: -	
Reporting group title	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Reporting group description: -	

Reporting group values	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Number of subjects	43	85	84
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)	26	51	55
From 65-84 years	17	34	29
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	63.6	62.4	60.4
standard deviation	± 7.75	± 8.53	± 9.35
Gender, Male/Female Units: Participants			
Female	16	19	26
Male	27	66	58
Study Specific Characteristic			
KRAS Mutation Status at Baseline			
Units: Subjects			
KRAS no mutation detected (NMD)	30	62	54
KRAS mutation positive	10	15	19
KRAS mutation unknown	3	8	11

Reporting group values	Total		
Number of subjects	212		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	132		
From 65-84 years	80		
85 years and over	0		
Age Continuous Units: Years arithmetic mean standard deviation	-		
Gender, Male/Female Units: Participants			
Female	61		
Male	151		
Study Specific Characteristic			
KRAS Mutation Status at Baseline			
Units: Subjects			
KRAS no mutation detected (NMD)	146		
KRAS mutation positive	44		
KRAS mutation unknown	22		

End points

End points reporting groups

Reporting group title	Placebo + Docetaxel 75 mg/m2
Reporting group description: -	
Reporting group title	Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Reporting group description: -	
Reporting group title	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Reporting group description: -	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	Time from randomisation until the date of objective disease progression as defined by Response Evaluation Criteria In Solid Tumours (RECIST version 1.1) or death (by any cause in the absence of progression)
End point type	Primary
End point timeframe:	Baseline and then every 6 weeks after randomization until objective disease progression

End point values	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	85	84	
Units: Months				
median (full range (min-max))	4.3 (0 to 15)	3.0 (0 to 33)	4.2 (0 to 28.5)	

Statistical analyses

Statistical analysis title	PFS
Statistical analysis description:	Median time from randomisation until the date of objective disease progression as defined by Response Evaluation Criteria In Solid Tumours (RECIST version 1.1) or death (by any cause in the absence of progression)
Comparison groups	Placebo + Docetaxel 75 mg/m2 v Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.584
Method	Cox Proportional Hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8
upper limit	1.61

Statistical analysis title	PFS
-----------------------------------	-----

Statistical analysis description:

Median time from randomisation until the date of objective disease progression as defined by Response Evaluation Criteria In Solid Tumours (RECIST version 1.1) or death (by any cause in the absence of progression)

Comparison groups	Placebo + Docetaxel 75 mg/m2 v Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.69
Method	Cox Proportional Hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.65
upper limit	1.31

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
-----------------	-----------------------

End point description:

the time from randomisation until death due to any cause. Any subject not known to have died at the time of analysis will be censored based on the last recorded date on which the subject was known to be alive

End point type	Secondary
----------------	-----------

End point timeframe:

Following progression, survival status was collected every 8 weeks until death, withdrawal of consent, or end of study, whichever occurred first

End point values	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	85	84	
Units: Months				
median (full range (min-max))	11.5 (0 to 33.5)	5.7 (0 to 34)	7.7 (0 to 32)	

Statistical analyses

Statistical analysis title	OS
Statistical analysis description: the time from randomisation until death due to any cause. Any subject not known to have died at the time of analysis will be censored based on the last recorded date on which the subject was known to be alive	
Comparison groups	Placebo + Docetaxel 75 mg/m2 v Selumetinib 75 mg BD + Docetaxel 75 mg/m2
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.485
Method	Cox Proportional Hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8
upper limit	1.78

Statistical analysis title	OS
Statistical analysis description: the time from randomisation until death due to any cause. Any subject not known to have died at the time of analysis will be censored based on the last recorded date on which the subject was known to be alive	
Comparison groups	Placebo + Docetaxel 75 mg/m2 v Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.126
Method	Cox Proportional Hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.97
upper limit	2.13

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from informed consent, throughout the treatment period until 30 days after discontinuation of the study treatment

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	18.1
--------------------	------

Reporting groups

Reporting group title	Placebo + Docetaxel 75 mg/m2
-----------------------	------------------------------

Reporting group description: -

Reporting group title	Selumetinib 75 mg BD + Docetaxel 75 mg/m2
-----------------------	---

Reporting group description: -

Reporting group title	Selumetinib 75 mg BD + Docetaxel 60 mg/m2
-----------------------	---

Reporting group description: -

Serious adverse events	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 43 (37.21%)	38 / 84 (45.24%)	40 / 84 (47.62%)
number of deaths (all causes)	26	57	64
number of deaths resulting from adverse events	1	7	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Thrombosis			

subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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
Aortic thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
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			
Performance status decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (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
Fatigue			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (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
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumothorax spontaneous			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Pneumothorax			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	4 / 84 (4.76%)
occurrences causally related to treatment / all	0 / 1	2 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood urea increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Injury, poisoning and procedural complications			
Chemical peritonitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Fall			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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

Left ventricular dysfunction subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic right ventricular failure subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Embolic stroke subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Ischaemic stroke subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dizziness			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	3 / 43 (6.98%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 3	1 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Colitis ischaemic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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
Glossitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Large intestine perforation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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
Ileus			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Haematemesis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Rectal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Dermatitis bullous			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Pneumonia pseudomonal			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Lung infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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
Infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (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
Gastroenteritis salmonella			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	10 / 84 (11.90%)
occurrences causally related to treatment / all	0 / 1	1 / 4	3 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Septic shock			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (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
Dehydration			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 75 mg/m2	Selumetinib 75 mg BD + Docetaxel 60 mg/m2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 43 (90.70%)	83 / 84 (98.81%)	81 / 84 (96.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oncologic complication			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	4 / 84 (4.76%)
occurrences (all)	0	2	4
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Circulatory collapse			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Embolism			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	3 / 43 (6.98%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	3	0	0
Hot flush			
subjects affected / exposed	2 / 43 (4.65%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	2	0	0
Hypertension			

subjects affected / exposed	3 / 43 (6.98%)	10 / 84 (11.90%)	2 / 84 (2.38%)
occurrences (all)	4	11	2
Hypotension			
subjects affected / exposed	2 / 43 (4.65%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	2	2	1
Lymphoedema			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Orthostatic hypotension			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	2 / 43 (4.65%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	2	0	1
Superior vena cava syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Chest discomfort			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Extravasation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	4 / 84 (4.76%)
occurrences (all)	0	4	4
Fatigue			

subjects affected / exposed	13 / 43 (30.23%)	26 / 84 (30.95%)	17 / 84 (20.24%)
occurrences (all)	17	32	21
General physical health deterioration			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Generalised oedema			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	0 / 84 (0.00%)
occurrences (all)	0	3	0
Hyperthermia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	2 / 84 (2.38%)
occurrences (all)	1	3	2
Malaise			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			
subjects affected / exposed	1 / 43 (2.33%)	7 / 84 (8.33%)	1 / 84 (1.19%)
occurrences (all)	1	8	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Oedema			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	0 / 84 (0.00%)
occurrences (all)	0	4	0
Asthenia			
subjects affected / exposed	2 / 43 (4.65%)	13 / 84 (15.48%)	12 / 84 (14.29%)
occurrences (all)	2	14	12
Catheter site related reaction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Oedema peripheral			

subjects affected / exposed occurrences (all)	8 / 43 (18.60%) 10	28 / 84 (33.33%) 38	16 / 84 (19.05%) 22
Performance status decreased subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 5	11 / 84 (13.10%) 20	11 / 84 (13.10%) 15
Pain subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	1 / 84 (1.19%) 1
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	0 / 84 (0.00%) 0	0 / 84 (0.00%) 0
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 2	0 / 84 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	0 / 84 (0.00%) 0	0 / 84 (0.00%) 0
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Respiratory, thoracic and mediastinal disorders Emphysema subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Aspiration subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Atelectasis subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Bronchospasm			

subjects affected / exposed	2 / 43 (4.65%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	2	2	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	3 / 84 (3.57%)
occurrences (all)	1	0	3
Cough			
subjects affected / exposed	8 / 43 (18.60%)	10 / 84 (11.90%)	7 / 84 (8.33%)
occurrences (all)	8	10	7
Dysphonia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	2 / 84 (2.38%)
occurrences (all)	0	1	2
Dyspnoea			
subjects affected / exposed	4 / 43 (9.30%)	14 / 84 (16.67%)	12 / 84 (14.29%)
occurrences (all)	4	15	12
Dyspnoea exertional			
subjects affected / exposed	2 / 43 (4.65%)	4 / 84 (4.76%)	3 / 84 (3.57%)
occurrences (all)	2	4	3
Epistaxis			
subjects affected / exposed	2 / 43 (4.65%)	8 / 84 (9.52%)	6 / 84 (7.14%)
occurrences (all)	3	9	6
Pulmonary oedema			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Lung disorder			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Lung infiltration			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0

Nasal dryness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nasal inflammation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nasal polyps			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 43 (0.00%)	5 / 84 (5.95%)	3 / 84 (3.57%)
occurrences (all)	0	5	3
Pharyngeal inflammation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	3 / 84 (3.57%)
occurrences (all)	1	3	3
Pleuritic pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Pneumothorax			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Pulmonary haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1

Pulmonary hypertension			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	2 / 43 (4.65%)	7 / 84 (8.33%)	1 / 84 (1.19%)
occurrences (all)	2	8	1
Rales			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Sinus disorder			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	2	0	0
Sputum discoloured			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Rhinitis allergic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	3 / 84 (3.57%)
occurrences (all)	0	1	3
Delirium			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Disorientation			

subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	0 / 84 (0.00%) 0	0 / 84 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	3 / 84 (3.57%) 3	4 / 84 (4.76%) 5
Sleep disorder subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 3	1 / 84 (1.19%) 2	0 / 84 (0.00%) 0
Investigations International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	2 / 84 (2.38%) 2	4 / 84 (4.76%) 4
Blood calcium decreased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	1 / 84 (1.19%) 1
Blood creatine phosphokinase MB increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	5 / 84 (5.95%) 11	3 / 84 (3.57%) 11
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 84 (1.19%) 1	1 / 84 (1.19%) 1
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Blood magnesium decreased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	2 / 84 (2.38%) 2
Blood pressure systolic increased			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Ejection fraction decreased			
subjects affected / exposed	2 / 43 (4.65%)	2 / 84 (2.38%)	4 / 84 (4.76%)
occurrences (all)	2	2	4
Haemoglobin decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hepatic enzyme abnormal			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	4 / 84 (4.76%)
occurrences (all)	0	0	4
Prothrombin time prolonged			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Weight increased			

subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 4	6 / 84 (7.14%) 6	3 / 84 (3.57%) 3
Intraocular pressure increased subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Injury, poisoning and procedural complications			
Animal bite subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Bone contusion subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	3 / 84 (3.57%) 4	0 / 84 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	1 / 84 (1.19%) 1	2 / 84 (2.38%) 2
Head injury subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Laceration subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 84 (0.00%) 0	1 / 84 (1.19%) 1
Lumbar vertebral fracture subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	0 / 84 (0.00%) 0	0 / 84 (0.00%) 0
Overdose			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Seroma			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Spinal compression fracture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Tendon rupture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	3 / 84 (3.57%)
occurrences (all)	1	4	3
Atrial flutter			
subjects affected / exposed	2 / 43 (4.65%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	2	0	0
Atrial tachycardia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0

Bundle branch block left			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Cardiac failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Arrhythmia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Sinus tachycardia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	1	2	1
Mitral valve incompetence			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nodal rhythm			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Pericarditis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Right ventricular failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	2 / 84 (2.38%)
occurrences (all)	0	1	2
Nervous system disorders			
Ataxia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Depressed level of consciousness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	7 / 43 (16.28%)	5 / 84 (5.95%)	5 / 84 (5.95%)
occurrences (all)	7	5	5
Dizziness postural			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Dysarthria			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	3 / 43 (6.98%)	8 / 84 (9.52%)	6 / 84 (7.14%)
occurrences (all)	3	8	6
Head discomfort			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	5 / 43 (11.63%)	3 / 84 (3.57%)	6 / 84 (7.14%)
occurrences (all)	5	3	6
Hemiparesis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Hepatic encephalopathy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Hypokinesia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hypotonia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Ageusia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Amnesia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Neuropathy peripheral			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences (all)	1	4	1
Paraesthesia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	3 / 84 (3.57%)
occurrences (all)	0	3	4
Peripheral motor neuropathy			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 43 (4.65%)	4 / 84 (4.76%)	4 / 84 (4.76%)
occurrences (all)	2	4	4
Polyneuropathy			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	4 / 84 (4.76%)
occurrences (all)	1	4	4
Somnolence			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Tremor			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Vocal cord paralysis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 43 (9.30%)	18 / 84 (21.43%)	20 / 84 (23.81%)
occurrences (all)	4	21	22
Leukocytosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	1	0	2
Febrile neutropenia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	0	4	1
Eosinophilia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	2 / 43 (4.65%)	3 / 84 (3.57%)	2 / 84 (2.38%)
occurrences (all)	3	3	2
Lymphadenopathy			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	10 / 43 (23.26%)	17 / 84 (20.24%)	9 / 84 (10.71%)
occurrences (all)	12	19	26
Neutrophilia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	2 / 84 (2.38%)
occurrences (all)	1	3	2

Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Hearing impaired			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Middle ear inflammation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Otorrhoea			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Vertigo			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	2 / 84 (2.38%)
occurrences (all)	1	1	2
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Chorioretinal disorder			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	1	3	1
Eye discharge			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Eye disorder			

subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Eye oedema			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	5	1
Eyelid pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	2 / 43 (4.65%)	7 / 84 (8.33%)	2 / 84 (2.38%)
occurrences (all)	2	7	2
Noninfective conjunctivitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Periorbital oedema			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	0	4	1
Vision blurred			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	4 / 84 (4.76%)
occurrences (all)	0	3	4
Visual acuity reduced			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Eye irritation			

subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	1 / 84 (1.19%) 1	0 / 84 (0.00%) 0
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Abdominal distension			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	2 / 84 (2.38%)
occurrences (all)	0	1	3
Abdominal pain			
subjects affected / exposed	3 / 43 (6.98%)	6 / 84 (7.14%)	9 / 84 (10.71%)
occurrences (all)	4	6	12
Abdominal pain lower			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	4 / 43 (9.30%)	8 / 84 (9.52%)	3 / 84 (3.57%)
occurrences (all)	5	9	3
Abdominal rigidity			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Aphthous ulcer			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 43 (2.33%)	6 / 84 (7.14%)	0 / 84 (0.00%)
occurrences (all)	1	6	0
Buccal mucosal roughening			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Chapped lips			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0

Cheilitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	5 / 43 (11.63%)	11 / 84 (13.10%)	16 / 84 (19.05%)
occurrences (all)	5	13	18
Dental cyst			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	12 / 43 (27.91%)	37 / 84 (44.05%)	41 / 84 (48.81%)
occurrences (all)	21	65	78
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Diverticulum			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	3 / 84 (3.57%)
occurrences (all)	1	4	3
Dyspepsia			
subjects affected / exposed	4 / 43 (9.30%)	4 / 84 (4.76%)	6 / 84 (7.14%)
occurrences (all)	10	4	6
Dysphagia			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences (all)	0	4	1
Eructation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Gastric ulcer			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0

Gastritis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Breath odour			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Glossitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Retroperitoneal haematoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Intra-abdominal haematoma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0

Lip erosion			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences (all)	0	4	1
Nausea			
subjects affected / exposed	10 / 43 (23.26%)	23 / 84 (27.38%)	25 / 84 (29.76%)
occurrences (all)	22	36	33
Odynophagia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Oral mucosal eruption			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Glossodynia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Steatorrhoea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	2	0

Stomatitis			
subjects affected / exposed	5 / 43 (11.63%)	23 / 84 (27.38%)	11 / 84 (13.10%)
occurrences (all)	7	33	11
Tooth loss			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	2	1	0
Vomiting			
subjects affected / exposed	8 / 43 (18.60%)	22 / 84 (26.19%)	20 / 84 (23.81%)
occurrences (all)	13	27	28
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Liver disorder			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	0	3	1
Acne			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Alopecia			
subjects affected / exposed	8 / 43 (18.60%)	15 / 84 (17.86%)	11 / 84 (13.10%)
occurrences (all)	8	16	11
Dermatitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Dermatitis acneiform			
subjects affected / exposed	1 / 43 (2.33%)	7 / 84 (8.33%)	9 / 84 (10.71%)
occurrences (all)	1	9	18
Dermatitis exfoliative			

subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	2 / 43 (4.65%)	16 / 84 (19.05%)	9 / 84 (10.71%)
occurrences (all)	2	16	10
Eczema			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	1 / 43 (2.33%)	5 / 84 (5.95%)	4 / 84 (4.76%)
occurrences (all)	1	6	5
Erythema multiforme			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Madarosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	0 / 84 (0.00%)
occurrences (all)	0	3	0
Skin exfoliation			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Rash papular			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nail disorder			
subjects affected / exposed	2 / 43 (4.65%)	1 / 84 (1.19%)	3 / 84 (3.57%)
occurrences (all)	2	1	3
Nail growth abnormal			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nail ridging			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Onychalgia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Onychoclasia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Onycholysis			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	1	2	1
Onychomadesis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Petechiae			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	2 / 84 (2.38%)
occurrences (all)	0	3	2

Pruritus			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	4 / 84 (4.76%)
occurrences (all)	0	4	5
Rash			
subjects affected / exposed	9 / 43 (20.93%)	29 / 84 (34.52%)	23 / 84 (27.38%)
occurrences (all)	10	44	26
Rash erythematous			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Rash generalised			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	3
Rosacea			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Skin ulcer			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Swelling face			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	2
Xeroderma			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 43 (0.00%)	5 / 84 (5.95%)	1 / 84 (1.19%)
occurrences (all)	0	6	1
Acute kidney injury			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Bladder pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Costovertebral angle tenderness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Oliguria			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	1	1	1
Renal cyst			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Renal impairment			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Renal infarct			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Renal vein thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Urinary retention			

subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	2	0
Pollakiuria			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 43 (4.65%)	4 / 84 (4.76%)	6 / 84 (7.14%)
occurrences (all)	2	5	7
Back pain			
subjects affected / exposed	4 / 43 (9.30%)	7 / 84 (8.33%)	3 / 84 (3.57%)
occurrences (all)	4	7	3
Bone pain			
subjects affected / exposed	2 / 43 (4.65%)	3 / 84 (3.57%)	0 / 84 (0.00%)
occurrences (all)	2	3	0
Joint swelling			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	2 / 43 (4.65%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	2	1	0
Muscular weakness			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	4 / 84 (4.76%)
occurrences (all)	1	3	7
Musculoskeletal chest pain			
subjects affected / exposed	4 / 43 (9.30%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	4	1	1
Musculoskeletal discomfort			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	1	1	1
Myalgia			
subjects affected / exposed	5 / 43 (11.63%)	9 / 84 (10.71%)	6 / 84 (7.14%)
occurrences (all)	5	10	6
Myopathy			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 43 (0.00%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences (all)	0	4	1
Osteitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	6 / 43 (13.95%)	2 / 84 (2.38%)	4 / 84 (4.76%)
occurrences (all)	7	2	5
Spinal pain			
subjects affected / exposed	0 / 43 (0.00%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	0	3	1
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Angular cheilitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	1 / 84 (1.19%)
occurrences (all)	0	2	1
Bronchitis			
subjects affected / exposed	2 / 43 (4.65%)	6 / 84 (7.14%)	2 / 84 (2.38%)
occurrences (all)	2	6	2
Candida infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0

Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Clostridium colitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 43 (2.33%)	5 / 84 (5.95%)	1 / 84 (1.19%)
occurrences (all)	1	5	1
Diverticulitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Erysipelas			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Folliculitis			
subjects affected / exposed	2 / 43 (4.65%)	2 / 84 (2.38%)	2 / 84 (2.38%)
occurrences (all)	2	2	2
Fungal skin infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	2
Gingivitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	2	0
Lung infection			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	4 / 84 (4.76%)
occurrences (all)	0	2	4

Mastitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	3 / 43 (6.98%)	1 / 84 (1.19%)	4 / 84 (4.76%)
occurrences (all)	3	1	5
Nosocomial infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	3 / 43 (6.98%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	4	1	1
Oral fungal infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	4 / 84 (4.76%)
occurrences (all)	0	2	5
Oral infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	1 / 43 (2.33%)	7 / 84 (8.33%)	1 / 84 (1.19%)
occurrences (all)	1	9	1
Peritonitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 84 (3.57%)	4 / 84 (4.76%)
occurrences (all)	1	3	4
Rash pustular			
subjects affected / exposed	0 / 43 (0.00%)	5 / 84 (5.95%)	1 / 84 (1.19%)
occurrences (all)	0	7	1

Respiratory tract infection			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	1	1	1
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 43 (4.65%)	3 / 84 (3.57%)	1 / 84 (1.19%)
occurrences (all)	2	3	1
Septic shock			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 43 (2.33%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	2 / 43 (4.65%)	1 / 84 (1.19%)	5 / 84 (5.95%)
occurrences (all)	2	1	7
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Abnormal loss of weight			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Central obesity			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	0 / 84 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	10 / 43 (23.26%)	18 / 84 (21.43%)	21 / 84 (25.00%)
occurrences (all)	10	20	21
Dehydration			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	4 / 84 (4.76%)
occurrences (all)	1	4	4
Diabetes mellitus			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	0 / 84 (0.00%)
occurrences (all)	1	0	0
Fluid overload			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	2
Hypercalcaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	2 / 43 (4.65%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	2	1	1
Hyperkalaemia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 84 (2.38%)	0 / 84 (0.00%)
occurrences (all)	0	3	0
Hyperphosphataemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 43 (4.65%)	2 / 84 (2.38%)	3 / 84 (3.57%)
occurrences (all)	3	3	3
Hypocalcaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1
Hypoglycaemia			

subjects affected / exposed	0 / 43 (0.00%)	1 / 84 (1.19%)	1 / 84 (1.19%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	1 / 43 (2.33%)	4 / 84 (4.76%)	1 / 84 (1.19%)
occurrences (all)	1	4	1
Hypokalaemia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 84 (2.38%)	5 / 84 (5.95%)
occurrences (all)	1	2	5
Hypoproteinaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	1	0	1
Vitamin K deficiency			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	2 / 84 (2.38%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	3 / 43 (6.98%)	2 / 84 (2.38%)	3 / 84 (3.57%)
occurrences (all)	3	3	4
Hypophagia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 84 (0.00%)	1 / 84 (1.19%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2013	All participating patients were to receive primary prophylactic G CSF
10 December 2013	Prospective central KRAS testing was added
28 July 2014	Benefit/risk and ethical assessment amended

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported