



Clinical trial results:

A double-blind placebo controlled randomized trial of PF-804 in patients with incurable stage IIIB/IV non-small cell lung cancer after failure of standard therapy for advanced or metastatic disease.

Summary

EudraCT number	2009-016509-41
Trial protocol	IT
Global end of trial date	16 July 2015

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	BR.26
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01000025
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	WWCR WORLDWIDE CLINICAL RESEARCH
Sponsor organisation address	Duite 1010, Overland Park - KS66210 -, Lowell-US, United States, 10955
Public contact	Barbara GEIGER, WWCR WORLDWIDE CLINICAL RESEARCH, bgeiger@clinipace.com
Scientific contact	Barbara GEIGER, WWCR WORLDWIDE CLINICAL RESEARCH, bgeiger@clinipace.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	01 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2013
Global end of trial reached?	Yes
Global end of trial date	16 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) between the 2 arms

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 December 2009
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	Italy: 111
Country: Number of subjects enrolled	Canada: 308
Country: Number of subjects enrolled	Korea, Republic of: 71
Country: Number of subjects enrolled	Philippines: 31
Country: Number of subjects enrolled	Thailand: 42
Country: Number of subjects enrolled	Australia: 77
Country: Number of subjects enrolled	Brazil: 39
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Peru: 1
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	New Zealand: 11
Worldwide total number of subjects	720
EEA total number of subjects	111

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)	373
From 65 to 84 years	347
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

no text entered

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	PF-804
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Arm description:

Study treatment arm

Arm type	Experimental
Investigational medicinal product name	PF-00299804
Investigational medicinal product code	
Other name	Dacomitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

45 mg PO, daily, treatment repeats every 28 days in the absence of disease progression or unacceptable toxicity.

Arm title	Placebo
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Arm description:

Control Arm

Arm type	Placebo
Investigational medicinal product name	PF-00299804
Investigational medicinal product code	
Other name	Dacomitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

45 mg PO, daily, treatment repeats every 28 days in the absence of disease progression or unacceptable toxicity.

Number of subjects in period 1	PF-804	Placebo
Started	480	240
Completed	12	2
Not completed	468	238
Consent withdrawn by subject	13	8
Adverse event, non-fatal	43	2
Death	23	13
Intercurrent Illness	26	7
Lack of efficacy	363	208

Baseline characteristics

Reporting groups

Reporting group title	PF-804
Reporting group description:	
Study treatment arm	
Reporting group title	Placebo
Reporting group description:	
Control Arm	

Reporting group values	PF-804	Placebo	Total
Number of subjects	480	240	720
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	63.5	65.5	
full range (min-max)	32 to 86	34 to 90	-
Gender categorical			
Units: Subjects			
Female	236	120	356
Male	244	120	364
Race			
Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	172	87	259
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	4	1	5
White	288	144	432
More than one race	0	0	0
Unknown or Not Reported	13	8	21
Region of Enrollment			
Units: Subjects			
United States	1	1	2
Philippines	20	11	31
Taiwan	11	6	17
Canada	207	101	308
Thailand	28	14	42

Brazil	25	14	39
Peru	0	1	1
Australia	50	27	77
New Zealand	7	4	11
Italy	77	34	111
Korea, Republic of	47	24	71
Argentina	7	3	10

End points

End points reporting groups

Reporting group title	PF-804
Reporting group description:	
Study treatment arm	
Reporting group title	Placebo
Reporting group description:	
Control Arm	

Primary: Overall survival

End point title	Overall survival
End point description:	
ITT	
End point type	Primary
End point timeframe:	
42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	240		
Units: Months				
median (confidence interval 95%)	6.83 (6.08 to 7.49)	6.31 (5.32 to 7.52)		

Statistical analyses

Statistical analysis title	Overall Survival
Statistical analysis description:	
The trial was designed to detect a 25% deduction in risk of death with PF-804 with 90% power using a 1-sided 2.5% level significance test. The sample size was estimated as 720 patients.	
Comparison groups	PF-804 v Placebo
Number of subjects included in analysis	720
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.506
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1

Confidence interval	
level	95 %
sides	1-sided
upper limit	1.21

Secondary: Overall Survival in KRAS-WT Patients

End point title	Overall Survival in KRAS-WT Patients
End point description: Patients with K-Ras mutation wild type	
End point type	Secondary
End point timeframe: 42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	120		
Units: Months				
median (confidence interval 95%)	7 (6.01 to 8.21)	5.19 (4.53 to 7)		

Statistical analyses

Statistical analysis title	Overall Survival in KRAS-WT Patients
Comparison groups	PF-804 v Placebo
Number of subjects included in analysis	340
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	1-sided
upper limit	1.03

Secondary: Overall Survival in EGFR-mutant Patients

End point title	Overall Survival in EGFR-mutant Patients
End point description: Patients with EGFR mutation	

End point type	Secondary
End point timeframe:	
42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	68		
Units: Months				
median (confidence interval 95%)	7.23 (6.08 to 8.61)	7.52 (4.99 to 9.49)		

Statistical analyses

Statistical analysis title	Overall Survival in EGFR-mutant Patients
Comparison groups	PF-804 v Placebo
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	1-sided
upper limit	1.44

Secondary: Progression-free Survival

End point title	Progression-free Survival
End point description:	
ITT	
End point type	Secondary
End point timeframe:	
42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	240		
Units: Months				
median (confidence interval 95%)	2.66 (1.91 to 3.32)	1.58 (0.99 to 1.74)		

Statistical analyses

Statistical analysis title	Progression-free Survival
Comparison groups	PF-804 v Placebo
Number of subjects included in analysis	720
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Log hazard ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	1-sided
upper limit	0.79

Secondary: Objective Response Rate

End point title	Objective Response Rate
End point description:	
ITT	
End point type	Secondary
End point timeframe:	
42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	240		
Units: percentage of participants				
arithmetic mean (confidence interval 95%)	7.1 (4.8 to 9.4)	1.3 (0 to 2.7)		

Statistical analyses

Statistical analysis title	Objective Response Rate
Comparison groups	PF-804 v Placebo
Number of subjects included in analysis	720
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	6.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	20.3

Secondary: Number of Participants With Toxicity as Measured by NCI CTCAE Version 4.0

End point title	Number of Participants With Toxicity as Measured by NCI CTCAE Version 4.0
End point description: As treated population	
End point type	Secondary
End point timeframe: 42 months	

End point values	PF-804	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	477	239		
Units: Number of Participants	467	223		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

42 months

Assessment type	Systematic
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Dictionary used

Dictionary name	NCI CTCAE
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Dictionary version	4
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Reporting groups

Reporting group title	PF-804
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Reporting group description:

Study treatment arm

Reporting group title	Placebo
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Reporting group description:

Control Arm

Serious adverse events	PF-804	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	187 / 477 (39.20%)	86 / 239 (35.98%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	76 / 477 (15.93%)	42 / 239 (17.57%)	
occurrences causally related to treatment / all	0 / 77	0 / 42	
deaths causally related to treatment / all	0 / 72	0 / 37	
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	12 / 477 (2.52%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	3 / 12	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death NOS			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infusion site extravasation			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death NOS			
subjects affected / exposed	1 / 477 (0.21%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Extravasation			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	9 / 477 (1.89%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	2 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			
subjects affected / exposed	1 / 477 (0.21%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			

Aspiration			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary hemorrhage			
subjects affected / exposed	6 / 477 (1.26%)	4 / 239 (1.67%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnea			
subjects affected / exposed	27 / 477 (5.66%)	14 / 239 (5.86%)	
occurrences causally related to treatment / all	0 / 31	0 / 17	
deaths causally related to treatment / all	0 / 2	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	8 / 477 (1.68%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumotorax			

subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Edema			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory Failure			
subjects affected / exposed	6 / 477 (1.26%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	2 / 6	0 / 2	
deaths causally related to treatment / all	2 / 2	0 / 1	
Dysphonia			
subjects affected / exposed	27 / 477 (5.66%)	14 / 239 (5.86%)	
occurrences causally related to treatment / all	0 / 31	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal inflammation			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality change			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Neutrophil count decrease			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight Loss			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pericardial effusion			
subjects affected / exposed	1 / 477 (0.21%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cognitive Disturbance			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial hemorrhage			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischemia cerebrovascular			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresthesia			

subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizures			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus headache			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attacks			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 477 (0.42%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal cord compression			
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal ulcer			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	4 / 477 (0.84%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Hemorrhage			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	17 / 477 (3.56%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	18 / 20	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 477 (0.00%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophageal stenosis			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal pain			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	5 / 477 (1.05%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction Gastric			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Hemorrhage			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	8 / 477 (1.68%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	7 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	4 / 477 (0.84%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash acneiform			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 477 (1.26%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	4 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall pain			

subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized muscle weakness			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic osteoarthropathy			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchial Infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis Infectious			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Infection			
subjects affected / exposed	31 / 477 (6.50%)	12 / 239 (5.02%)	
occurrences causally related to treatment / all	2 / 35	0 / 14	
deaths causally related to treatment / all	0 / 4	0 / 3	
Lymph gland infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal Infection			

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other Infections and Infestation			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 477 (0.42%)	3 / 239 (1.26%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Folliculitis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	16 / 477 (3.35%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	9 / 16	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
hypercalcemia		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hyperglycemia		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypokalemia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
hyponatremia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

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

Non-serious adverse events	PF-804	Placebo
Total subjects affected by non-serious adverse events		
subjects affected / exposed	465 / 477 (97.48%)	219 / 239 (91.63%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Tumor Pain		
subjects affected / exposed	5 / 477 (1.05%)	3 / 239 (1.26%)
occurrences (all)	5	3
Vascular disorders		
Embolism		
subjects affected / exposed	10 / 477 (2.10%)	7 / 239 (2.93%)
occurrences (all)	10	7
Flushing		

subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 5	2 / 239 (0.84%) 2	
Haematoma subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Hot flush subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Hypertension subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	4 / 239 (1.67%) 4	
Hypotension subjects affected / exposed occurrences (all)	8 / 477 (1.68%) 8	2 / 239 (0.84%) 2	
Lymphoedema subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Peripheral coldness subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Phlebitis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Thrombophlebitis superficial subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	0 / 239 (0.00%) 0	
Surgical and medical procedures			
Ear operation subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Nail operation subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
General disorders and administration site conditions			

Chills		
subjects affected / exposed	20 / 477 (4.19%)	4 / 239 (1.67%)
occurrences (all)	20	4
Death		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Early satiety		
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)
occurrences (all)	2	1
Face oedema		
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)
occurrences (all)	4	0
Fatigue		
subjects affected / exposed	164 / 477 (34.38%)	62 / 239 (25.94%)
occurrences (all)	177	64
Gait disturbance		
subjects affected / exposed	4 / 477 (0.84%)	6 / 239 (2.51%)
occurrences (all)	4	6
Influenza like illness		
subjects affected / exposed	7 / 477 (1.47%)	9 / 239 (3.77%)
occurrences (all)	9	11
Localised oedema		
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)
occurrences (all)	2	2
Malaise		
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)
occurrences (all)	3	1
Mass		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Non-cardiac chest pain		
subjects affected / exposed	19 / 477 (3.98%)	8 / 239 (3.35%)
occurrences (all)	20	8
Oedema peripheral		
subjects affected / exposed	34 / 477 (7.13%)	21 / 239 (8.79%)
occurrences (all)	41	21

Pain			
subjects affected / exposed	33 / 477 (6.92%)	23 / 239 (9.62%)	
occurrences (all)	34	23	
Pyrexia			
subjects affected / exposed	38 / 477 (7.97%)	13 / 239 (5.44%)	
occurrences (all)	42	13	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Erectile dysfunction			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Menstruation irregular			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Pelvic pain			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Vaginal discharge			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Vaginal inflammation			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences (all)	4	0	
Vulvovaginal dryness			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pain			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Bronchial obstruction		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Cough		
subjects affected / exposed	69 / 477 (14.47%)	35 / 239 (14.64%)
occurrences (all)	71	35
Dysphonia		
subjects affected / exposed	20 / 477 (4.19%)	5 / 239 (2.09%)
occurrences (all)	21	5
Dyspnoea		
subjects affected / exposed	105 / 477 (22.01%)	53 / 239 (22.18%)
occurrences (all)	106	59
Haemoptysis		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Epistaxis		
subjects affected / exposed	71 / 477 (14.88%)	3 / 239 (1.26%)
occurrences (all)	79	6
Haemothorax		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Hiccups		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Hypoxia		
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)
occurrences (all)	3	0
Laryngeal haemorrhage		
subjects affected / exposed	5 / 477 (1.05%)	4 / 239 (1.67%)
occurrences (all)	5	5
Laryngeal inflammation		
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)
occurrences (all)	4	0
Laryngeal pain		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1

Nasal congestion		
subjects affected / exposed	13 / 477 (2.73%)	1 / 239 (0.42%)
occurrences (all)	13	1
Nasal dryness		
subjects affected / exposed	6 / 477 (1.26%)	1 / 239 (0.42%)
occurrences (all)	7	1
Nasal inflammation		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Oropharyngeal pain		
subjects affected / exposed	25 / 477 (5.24%)	3 / 239 (1.26%)
occurrences (all)	28	3
Pharyngeal haemorrhage		
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)
occurrences (all)	1	2
Pharyngeal inflammation		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Pleural effusion		
subjects affected / exposed	0 / 477 (0.00%)	2 / 239 (0.84%)
occurrences (all)	0	2
Pleuritic pain		
subjects affected / exposed	2 / 477 (0.42%)	4 / 239 (1.67%)
occurrences (all)	2	4
Pneumonitis		
subjects affected / exposed	4 / 477 (0.84%)	1 / 239 (0.42%)
occurrences (all)	8	1
Pneumothorax		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Productive cough		
subjects affected / exposed	25 / 477 (5.24%)	18 / 239 (7.53%)
occurrences (all)	29	20
Pulmonary haemorrhage		
subjects affected / exposed	20 / 477 (4.19%)	10 / 239 (4.18%)
occurrences (all)	21	11

Respiratory failure subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 4	0 / 239 (0.00%) 0	
Rhinitis allergic subjects affected / exposed occurrences (all)	9 / 477 (1.89%) 10	4 / 239 (1.67%) 4	
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 2	0 / 239 (0.00%) 0	
Sinus disorder subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Sneezing subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 4	0 / 239 (0.00%) 0	
Stridor subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Tracheal inflammation subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	18 / 477 (3.77%) 18	2 / 239 (0.84%) 3	
wheezing subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	2 / 239 (0.84%) 2	
Psychiatric disorders			
Abnormal dreams subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Agitation subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	1 / 239 (0.42%) 2	
Anxiety			

subjects affected / exposed occurrences (all)	12 / 477 (2.52%) 13	5 / 239 (2.09%) 5	
Confusional state subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 4	2 / 239 (0.84%) 2	
Delirium subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Depression subjects affected / exposed occurrences (all)	10 / 477 (2.10%) 10	5 / 239 (2.09%) 5	
Hallucination subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	33 / 477 (6.92%) 33	12 / 239 (5.02%) 13	
Irritability subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Personality change subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1	
Restlessness subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Suicidal ideation subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Investigations			
Amylase increased subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	

International normalised ratio increased			
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)	
occurrences (all)	3	1	
Prostatic specific antigen increased			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	62 / 477 (13.00%)	15 / 239 (6.28%)	
occurrences (all)	67	15	
Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Contusion			
subjects affected / exposed	6 / 477 (1.26%)	3 / 239 (1.26%)	
occurrences (all)	6	3	
Corneal abrasion			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Ear abrasion			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	7 / 477 (1.47%)	0 / 239 (0.00%)	
occurrences (all)	7	0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Fracture			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Ligament sprain			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Skin abrasion			

subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Thermal Burn subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Wound dehiscence subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 2	
Congenital, familial and genetic disorders			
Distichiasis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 2	0 / 239 (0.00%) 0	
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	1 / 239 (0.42%) 1	
Cardiac tamponade subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Myocardial infarction subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Pericardial Effusion subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1	
Sinus Tachycardia subjects affected / exposed occurrences (all)	7 / 477 (1.47%) 7	2 / 239 (0.84%) 2	
Supraventricular tachycardia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Ventricular arrhythmia			

subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Nervous system disorders			
Amnesia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Aphasia subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	5 / 239 (2.09%) 5	
Aphonia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Ataxia subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1	
Cerebral ischaemia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
cerebrovascular accident subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Cognitive disorder subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	2 / 239 (0.84%) 2	
Disturbance in attention subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	1 / 239 (0.42%) 1	
dizziness subjects affected / exposed occurrences (all)	44 / 477 (9.22%) 47	17 / 239 (7.11%) 19	
Dysarthria subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	2 / 239 (0.84%) 2	

Dysgeusia		
subjects affected / exposed	32 / 477 (6.71%)	3 / 239 (1.26%)
occurrences (all)	34	3
Dyskinesia		
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)
occurrences (all)	3	1
Encephalopathy		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
glossopharyngeal nerve disorder		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Haemorrhage intracranial		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	33 / 477 (6.92%)	16 / 239 (6.69%)
occurrences (all)	41	16
Hemiparesis		
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)
occurrences (all)	1	1
Hypoaesthesia		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Lethargy		
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)
occurrences (all)	2	2
Neuralgia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Paraesthesia		
subjects affected / exposed	12 / 477 (2.52%)	1 / 239 (0.42%)
occurrences (all)	12	1
Parosmia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0

Peripheral motor neuropathy subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	1 / 239 (0.42%) 1	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	23 / 477 (4.82%) 23	8 / 239 (3.35%) 8	
Presyncope subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Seizure subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 6	1 / 239 (0.42%) 1	
Somnolence subjects affected / exposed occurrences (all)	6 / 477 (1.26%) 6	3 / 239 (1.26%) 3	
Syncope subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 6	1 / 239 (0.42%) 1	
Tremor subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 4	2 / 239 (0.84%) 2	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Leukocytosis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Ear and labyrinth disorders			
Ear disorder subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1	
Ear pain subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	1 / 239 (0.42%) 1	
Hearing impaired			

subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	3 / 239 (1.26%) 3	
Middle ear inflammation subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Tinnitus subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	2 / 239 (0.84%) 2	
Vertigo subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	1 / 239 (0.42%) 1	
Vestibular disorder subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1	
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	37 / 477 (7.76%) 38	1 / 239 (0.42%) 1	
Blepharitis subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 3	0 / 239 (0.00%) 0	
Cataract subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Diplopia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 3	0 / 239 (0.00%) 0	
eye pain subjects affected / exposed occurrences (all)	10 / 477 (2.10%) 11	1 / 239 (0.42%) 1	
Eye pruritus subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	

Keratitis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	13 / 477 (2.73%)	1 / 239 (0.42%)	
occurrences (all)	14	1	
Periorbital oedema			
subjects affected / exposed	0 / 477 (0.00%)	3 / 239 (1.26%)	
occurrences (all)	0	3	
Photophobia			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Trichiasis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Ulcerative keratitis			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Vision blurred			
subjects affected / exposed	19 / 477 (3.98%)	0 / 239 (0.00%)	
occurrences (all)	21	0	
Visual acuity reduced			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Vitreous floaters			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	371 / 477 (77.78%)	41 / 239 (17.15%)	
occurrences (all)	576	54	
Dry mouth			
subjects affected / exposed	45 / 477 (9.43%)	7 / 239 (2.93%)	
occurrences (all)	49	8	
Dyspepsia			

subjects affected / exposed	20 / 477 (4.19%)	3 / 239 (1.26%)
occurrences (all)	20	3
Gastroesophageal reflux disease		
subjects affected / exposed	16 / 477 (3.35%)	8 / 239 (3.35%)
occurrences (all)	17	8
Abdominal pain		
subjects affected / exposed	43 / 477 (9.01%)	14 / 239 (5.86%)
occurrences (all)	47	14
Abdominal pain upper		
subjects affected / exposed	5 / 477 (1.05%)	3 / 239 (1.26%)
occurrences (all)	5	3
Aerophagia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Anal haemorrhage		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Ascites		
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)
occurrences (all)	2	1
Anal Inflammation		
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)
occurrences (all)	3	1
Chapped lips		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Cheilitis		
subjects affected / exposed	18 / 477 (3.77%)	0 / 239 (0.00%)
occurrences (all)	20	0
Constipation		
subjects affected / exposed	53 / 477 (11.11%)	38 / 239 (15.90%)
occurrences (all)	55	43
Dental Caries		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Duodenal ulcer		

subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Dysphagia		
subjects affected / exposed	13 / 477 (2.73%)	5 / 239 (2.09%)
occurrences (all)	14	5
Eructation		
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)
occurrences (all)	1	1
Flatulence		
subjects affected / exposed	5 / 477 (1.05%)	2 / 239 (0.84%)
occurrences (all)	5	2
Gastritis		
subjects affected / exposed	6 / 477 (1.26%)	1 / 239 (0.42%)
occurrences (all)	7	1
Gastrointestinal pain		
subjects affected / exposed	0 / 477 (0.00%)	2 / 239 (0.84%)
occurrences (all)	0	2
Gingival pain		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Haemorrhoidal haemorrhage		
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)
occurrences (all)	4	0
Haemorrhoids		
subjects affected / exposed	5 / 477 (1.05%)	0 / 239 (0.00%)
occurrences (all)	7	0
Hypoaesthesia oral		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Lip pain		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Lower gastrointestinal haemorrhage		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	3	0
Mouth haemorrhage		

subjects affected / exposed	5 / 477 (1.05%)	1 / 239 (0.42%)
occurrences (all)	5	1
Nausea		
subjects affected / exposed	139 / 477 (29.14%)	41 / 239 (17.15%)
occurrences (all)	169	51
Oesophageal pain		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Oesophagitis		
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)
occurrences (all)	3	0
Oral dysaesthesia		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Oral pain		
subjects affected / exposed	9 / 477 (1.89%)	3 / 239 (1.26%)
occurrences (all)	12	3
Periodontal disease		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Proctalgia		
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)
occurrences (all)	3	0
Rectal haemorrhage		
subjects affected / exposed	6 / 477 (1.26%)	0 / 239 (0.00%)
occurrences (all)	6	0
Salivary duct inflammation		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Salivary hypersecretion		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Stomatitis		
subjects affected / exposed	203 / 477 (42.56%)	7 / 239 (2.93%)
occurrences (all)	235	7
Tongue discolouration		

subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Tongue ulceration subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	1 / 239 (0.42%) 1	
Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	126 / 477 (26.42%) 180	29 / 239 (12.13%) 42	
Hepatobiliary disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 2	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	8 / 477 (1.68%) 8	3 / 239 (1.26%) 3	
Dermatitis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Dermatitis acneiform subjects affected / exposed occurrences (all)	270 / 477 (56.60%) 308	20 / 239 (8.37%) 23	
Dermatitis bullous subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0	
Dry skin subjects affected / exposed occurrences (all)	139 / 477 (29.14%) 155	16 / 239 (6.69%) 17	
Erythema multiforme			

subjects affected / exposed	13 / 477 (2.73%)	1 / 239 (0.42%)
occurrences (all)	14	1
Excessive granulation tissue		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Hair colour changes		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Hair growth abnormal		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Hair texture abnormal		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Hirsutism		
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)
occurrences (all)	4	0
Hyperhidrosis		
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)
occurrences (all)	2	1
Hypertrichosis		
subjects affected / exposed	3 / 477 (0.63%)	1 / 239 (0.42%)
occurrences (all)	3	1
Ingrowing nail		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Koilonychia		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Madarosis		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Nail discolouration		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Nail disorder		

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Nail ridging		
subjects affected / exposed	5 / 477 (1.05%)	0 / 239 (0.00%)
occurrences (all)	5	0
Onychoclasia		
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)
occurrences (all)	3	1
Onychomadesis		
subjects affected / exposed	4 / 477 (0.84%)	0 / 239 (0.00%)
occurrences (all)	4	0
Pain of skin		
subjects affected / exposed	7 / 477 (1.47%)	0 / 239 (0.00%)
occurrences (all)	8	0
Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	55 / 477 (11.53%)	2 / 239 (0.84%)
occurrences (all)	55	2
Pruritus		
subjects affected / exposed	79 / 477 (16.56%)	20 / 239 (8.37%)
occurrences (all)	97	25
Purpura		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Rash maculo-papular		
subjects affected / exposed	73 / 477 (15.30%)	14 / 239 (5.86%)
occurrences (all)	80	14
Scab		
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)
occurrences (all)	2	0
Skin atrophy		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	1	0
Skin disorder		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1

Skin exfoliation			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	16 / 477 (3.35%)	0 / 239 (0.00%)	
occurrences (all)	20	0	
Skin hyperpigmentation			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Skin induration			
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)	
occurrences (all)	2	2	
Skin ulcer			
subjects affected / exposed	21 / 477 (4.40%)	3 / 239 (1.26%)	
occurrences (all)	24	3	
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Telangiectasia			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 477 (0.63%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Chromaturia			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Cystitis noninfective			
subjects affected / exposed	2 / 477 (0.42%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Glycosuria			

subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 2	
Haematuria subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	0 / 239 (0.00%) 0	
Micturition urgency subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	2 / 239 (0.84%) 2	
Pollakiuria subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	2 / 239 (0.84%) 2	
proteinuria subjects affected / exposed occurrences (all)	7 / 477 (1.47%) 9	1 / 239 (0.42%) 1	
Urinary incontinence subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	2 / 239 (0.84%) 2	
Urinary retention subjects affected / exposed occurrences (all)	6 / 477 (1.26%) 6	0 / 239 (0.00%) 0	
Urinary tract pain subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	1 / 239 (0.42%) 1	
Endocrine disorders			
Adrenal insufficiency subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	1 / 239 (0.42%) 1	
Cushingoid subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Arthralgia		
subjects affected / exposed	1 / 477 (0.21%)	1 / 239 (0.42%)
occurrences (all)	1	1
Arthritis		
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)
occurrences (all)	3	2
Back pain		
subjects affected / exposed	32 / 477 (6.71%)	17 / 239 (7.11%)
occurrences (all)	35	17
Bone pain		
subjects affected / exposed	15 / 477 (3.14%)	10 / 239 (4.18%)
occurrences (all)	15	10
flank pain		
subjects affected / exposed	5 / 477 (1.05%)	3 / 239 (1.26%)
occurrences (all)	5	3
Groin pain		
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)
occurrences (all)	0	1
Hypertrophic osteoarthropathy		
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)
occurrences (all)	2	0
Joint range of motion decreased		
subjects affected / exposed	2 / 477 (0.42%)	2 / 239 (0.84%)
occurrences (all)	2	2
Muscular weakness		
subjects affected / exposed	25 / 477 (5.24%)	7 / 239 (2.93%)
occurrences (all)	25	7
Musculoskeletal pain		
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)
occurrences (all)	2	1
Myalgia		
subjects affected / exposed	10 / 477 (2.10%)	6 / 239 (2.51%)
occurrences (all)	12	7
Neck pain		
subjects affected / exposed	2 / 477 (0.42%)	7 / 239 (2.93%)
occurrences (all)	3	8

Pain in extremity subjects affected / exposed occurrences (all)	39 / 477 (8.18%) 43	19 / 239 (7.95%) 20	
Periarthritis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Infections and infestations			
Anorectal infection subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Bronchitis subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 4	1 / 239 (0.42%) 1	
Conjunctivitis subjects affected / exposed occurrences (all)	50 / 477 (10.48%) 59	0 / 239 (0.00%) 0	
Cystitis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Enterocolitis infectious subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Eye infection subjects affected / exposed occurrences (all)	5 / 477 (1.05%) 6	0 / 239 (0.00%) 0	
Eyelid infection subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 2	0 / 239 (0.00%) 0	
Furuncle subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Gingivitis subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0	
Herpes zoster			

subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0
Laryngitis		
subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0
Lip infection		
subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	0 / 239 (0.00%) 0
Lung infection		
subjects affected / exposed occurrences (all)	21 / 477 (4.40%) 22	5 / 239 (2.09%) 5
Mucosal infection		
subjects affected / exposed occurrences (all)	11 / 477 (2.31%) 11	4 / 239 (1.67%) 4
Nail infection		
subjects affected / exposed occurrences (all)	11 / 477 (2.31%) 12	0 / 239 (0.00%) 0
Otitis externa		
subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 2	0 / 239 (0.00%) 0
Otitis media		
subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	0 / 239 (0.00%) 0
Paronychia		
subjects affected / exposed occurrences (all)	138 / 477 (28.93%) 154	0 / 239 (0.00%) 0
Pharyngitis		
subjects affected / exposed occurrences (all)	2 / 477 (0.42%) 2	0 / 239 (0.00%) 0
Rash pustular		
subjects affected / exposed occurrences (all)	11 / 477 (2.31%) 15	1 / 239 (0.42%) 1
Rhinitis		
subjects affected / exposed occurrences (all)	5 / 477 (1.05%) 5	0 / 239 (0.00%) 0
Scrotal infection		

subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	22 / 477 (4.61%)	2 / 239 (0.84%)	
occurrences (all)	23	2	
Soft tissue infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Stoma site infection			
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Tooth Infection			
subjects affected / exposed	0 / 477 (0.00%)	2 / 239 (0.84%)	
occurrences (all)	0	2	
Tracheitis			
subjects affected / exposed	0 / 477 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	17 / 477 (3.56%)	6 / 239 (2.51%)	
occurrences (all)	19	7	
Urinary tract infection			
subjects affected / exposed	15 / 477 (3.14%)	8 / 239 (3.35%)	
occurrences (all)	21	8	
Vaginal infection			
subjects affected / exposed	2 / 477 (0.42%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Wound infection			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 477 (0.21%)	0 / 239 (0.00%)	
occurrences (all)	1	0	

Decreased appetite subjects affected / exposed occurrences (all)	147 / 477 (30.82%) 156	51 / 239 (21.34%) 54
Dehydration subjects affected / exposed occurrences (all)	16 / 477 (3.35%) 17	3 / 239 (1.26%) 3
Hypercalcaemia subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	1 / 239 (0.42%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	2 / 239 (0.84%) 2
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 477 (0.00%) 0	1 / 239 (0.42%) 1
Hypoglycaemia subjects affected / exposed occurrences (all)	3 / 477 (0.63%) 3	2 / 239 (0.84%) 3
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 477 (1.05%) 5	3 / 239 (1.26%) 3
Hypomagnesaemia subjects affected / exposed occurrences (all)	4 / 477 (0.84%) 4	3 / 239 (1.26%) 3
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	4 / 239 (1.67%) 4
Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 477 (0.21%) 1	0 / 239 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2011	AMENDMENT #1: 2011-JUL-21
23 April 2012	AMENDMENT #2: 2012-APR-23

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported