Clinical trial results:
A Phase II, Randomised, Double-blind, Parallel Group Study to Assess the Efficacy of Cediranib (AZD2171, RECENTIN) 45mg Versus Placebo following 12 Weeks of Treatment in Patients with Metastatic or Recurrent Renal Cell Carcinoma who have had no Previous Anti-VEGF Therapy

Summary

EudraCT number	2006-002455-33
Trial protocol	NL GB
Global end of trial date	18 October 2016

Results information

Result version number	v1 (current)
This version publication date	02 November 2017
First version publication date	02 November 2017

Trial information

Trial identification

Sponsor protocol code	D8480C00030

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 Road, Cambridge, United Kingdom, CB2 1PG
Public contact	Tsveta Milenkova, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Tsveta Milenkova, AstraZeneca, 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	16 May 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2008
Global end of trial reached?	Yes
Global end of trial date	18 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the efficacy of cediranib compared to the efficacy of placebo in patients with metastatic or recurrent renal cell carcinoma by comparing changes in tumour size after 12 weeks of therapy (or upon progression if this occurs before 12 weeks).

Protection of trial subjects:

If toxicity is encountered, the dose may be reduced (from 45mg to 30mg to 20mg) or treatment stopped until resolution of symptoms. At the discretion of the investigator, treatment may then be restarted. A maximum 14-day delay in dosing for cediranib is permitted. Only two dose level reductions will be allowed and re-escalations will not be permitted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 79
Country: Number of subjects enrolled	Netherlands: 26
Worldwide total number of subjects	105
EEA total number of subjects	105

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)	64
From 65 to 84 years	41

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

n=53 (Cediranib 45mg) and n=18 (Placebo) for both the full analysis set (ITT), and the safety set.

Pre-assignment

Screening details:

105 patients enrolled. 53 were randomised to Cediranib 45mg, 18 to Placebo, and 34 not randomised. All patients randomised received at least one dose of assigned treatment.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cediranib 45mg

Arm description:

Cediranib 45mg was be administered as a 30mg tablet and a 15mg tablet combination, taken orally once daily

Arm type	Experimental
Investigational medicinal product name	Cediranib
Investigational medicinal product code	AZD2171
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

45mg once daily, administered as a 30mg tablet and a 15mg tablet combination.

Arm title	Placebo

Arm description:

Cediranib placebo was be administered as a 30mg tablet and a 15mg tablet combination taken orally once daily.

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

Dosage and administration details:

45mg once daily, administered as a 30mg tablet and a 15mg tablet combination.

Number of subjects in period 1[1]	Cediranib 45mg	Placebo
Started	53	18
Completed	22	4
Not completed	31	14
Adverse event, non-fatal	6	5
Death	2	1
Other	21	6
Voluntary discontinuation by subject	2	1
Incorrect enrolment/eligib criteria not fulfilled	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number enrolled is not the same as number randomised onto the study baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Cediranib 45mg
Reporting group description:	
Cediranib 45mg was be administered as a 30mg tablet and a 15mg tablet combination, taken orally once daily	
Reporting group title	Placebo
Reporting group description:	
Cediranib placebo was be administered as a 30mg tablet and a 15mg tablet combination taken orally once daily.	

Reporting group values	Cediranib 45mg	Placebo	Total
Number of subjects	53	18	71
Age Categorical Units: Subjects			
≥18 years to <65 years	37	12	49
≥65 years to <75 years	14	5	19
≥75 years	2	1	3
Age Continuous Units: years			
arithmetic mean	60.7	62.4	
standard deviation	± 7.7	± 8.7	-
Gender Categorical Units: Subjects			
Female	13	3	16
Male	40	15	55
Race Units: Subjects			
Caucasian	52	18	70
Black	1	0	1
WHO performance status Units: Subjects			
Score of 0	38	10	48
Score of 1	13	7	20
Score of 2	2	1	3
Time from initial diagnosis to randomisation Units: Subjects			
<6 months	10	3	13
6 - <12 months	3	3	6
12 - <24 months	11	3	14
24 - <36 months	7	1	8
≥36 months	22	8	30
Histology type Units: Subjects			
Adenocarcinoma	3	2	5
Clear cell carcinoma	48	15	63
Other	2	1	3
Number of metastatic sites			

Units: Subjects			
0 sites	2	1	3
1 site	7	3	10
2 sites	19	7	26
3 sites	17	5	22
4 sites	6	2	8
5 sites	2	0	2
Memorial Sloane-Kettering Cancer Center risk group Units: Subjects			
Favourable risk	26	6	32
Intermediate risk	26	10	36
Poor risk	1	2	3
Tumour size at baseline Units: cm			
geometric mean	11.23	12.59	
standard deviation	± 73.7	± 117.7	-

End points

End points reporting groups

Reporting group title	Cediranib 45mg
Reporting group description:	
Cediranib 45mg was be administered as a 30mg tablet and a 15mg tablet combination, taken orally once daily	
Reporting group title	Placebo
Reporting group description:	
Cediranib placebo was be administered as a 30mg tablet and a 15mg tablet combination taken orally once daily.	

Primary: Change from baseline in tumour size at 12 weeks

End point title	Change from baseline in tumour size at 12 weeks
End point description:	
End point type	Primary
End point timeframe:	
Change from baseline in tumour size was assessed after 12 weeks of therapy (or upon progression if this occurred before 12 weeks).	

End point values	Cediranib 45mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	17		
Units: % change in tumour size				
least squares mean (inter-quartile range (Q1-Q3))	-20.48 (-27.2 to -13.2)	19.52 (7.7 to 32.6)		

Statistical analyses

Statistical analysis title	Change from baseline in tumour size at Week 12
Statistical analysis description:	
The change in tumour size at week 12 (or progression if prior to week 12) was assessed as a percentage change from baseline tumour size for each patient. The effect of AZD2171 on change in tumour size was estimated from an analysis of covariance (ANCOVA) model including terms for centre, treatment (AZD2171 or placebo) and Memorial Sloan-Kettering Cancer Centre (MSKCC) risk group as well as a covariate for baseline tumour size.	
Comparison groups	Cediranib 45mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Glsmeans ratio (converted to % change)
Point estimate	-33.5

Confidence interval	
level	90 %
sides	2-sided
lower limit	-40
upper limit	-26.3

Notes:

[1] - Glsmean = Geometric least squares mean

Secondary: Visit response at Week 12 or at progression if before Week 12

End point title	Visit response at Week 12 or at progression if before Week 12

End point description:

End point type	Secondary

End point timeframe:

Same as primary

End point values	Cediranib 45mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	18		
Units: Number of patients				
Responders	11	0		
Stable disease	32	4		
Progressive disease	8	13		
Non-evaluable	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Best change in tumour size during study

End point title	Best change in tumour size during study

End point description:

The best change from baseline in tumour size during the study for each patient was defined as the change in tumour size at the time when the smallest post-baseline tumour size was observed

End point type	Secondary

End point timeframe:

Till final database lock

End point values	Cediranib 45mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51[2]	17		
Units: Best change from baseline (%)				
arithmetic mean (standard deviation)	-26.90 (± 23.15)	1.09 (± 26.78)		

Notes:

[2] - Two patients known to progress but with missing target lesion data

Statistical analyses

No statistical analyses for this end point

Secondary: Best objective tumour response

End point title	Best objective tumour response

End point description:

The best change in tumour size is the smallest (most negative or least positive if none of the changes are negative) percentage change in tumour size from baseline. Patients who have no post-baseline target lesion size data during the study but are known to have progressed (i.e. patients with a best response of PD, patients who discontinue due to progression before their first scheduled RECIST assessment with no target lesion data entered at their discontinuation visit) had a 20% increase imputed as their best change in tumour size during the study.

End point type	Secondary

End point timeframe:

Till final database lock

End point values	Cediranib 45mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	18		
Units: Number of patients				
number (not applicable)				
Responders	18	1		
Stable disease	25	3		
Progressive disease	9	13		
Non-evaluable	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response[3]

End point description:

Response duration is measured from the time the criteria for CR/PR are first met (whichever is recorded first) until the patient progresses or dies, regardless of whether the patient is still taking study medication or starts taking another anti-cancer therapy (i.e. responses ongoing when a patient starts taking another anti-cancer therapy do not have to end in terms of duration of response if they have not

progressed but responses starting on new anti-cancer therapies will not be counted in the duration of response). Non-responders are excluded from the summary of response duration.

End point type	Secondary

End point timeframe:

Till final database lock

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only one patient responded in the placebo arm so it wasn't possible to calculate a median or other statistics therefore only the AZD2171 45mg arm has been reported.

End point values	Cediranib 45mg			
Subject group type	Reporting group			
Number of subjects analysed	18[4]			
Units: Months				
median (inter-quartile range (Q1-Q3))	18.6 (12.5 to 18.6)			

Notes:

[4] - 18 responders in Cediranib arm. Not possible calculate median in Placebo arm (n=1).

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

This is defined as the time from randomisation to the earlier date of objective progression (measured by RECIST) or death. Objective progression is assessed for all patients using the screening assessments as the baseline measurements. Patients who were still alive at the time of data cut-off, without a progression event, are censored at the date of their last evaluable objective tumour assessment.

End point type	Secondary

End point timeframe:

Till final database lock

End point values	Cediranib 45mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	18		
Units: Events				
median (inter-quartile range (Q1-Q3))	12.1 (5.62 to 21.4)	2.76 (2.27 to 3.48)		

Statistical analyses

Statistical analysis title	Cox proportional hazards model
Comparison groups	Cediranib 45mg v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.017
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.26
upper limit	0.78

Notes:

[5] - HR <1 favours cediranib

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose of study drug until last study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	PLACEBO
Reporting group description: PLACEBO	
Reporting group title	AZD2171 45 mg
Reporting group description: AZD2171 45 mg	

Serious adverse events	PLACEBO	AZD2171 45 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 18 (55.56%)	22 / 53 (41.51%)	
number of deaths (all causes)	1	5	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
INTRACRANIAL TUMOUR HAEMORRHAGE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC HYPOTENSION			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
FATIGUE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BARTHOLIN'S CYST			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURITIC PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

AGITATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONFUSIONAL STATE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CALCIUM INCREASED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
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			
CLAVICLE FRACTURE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER LIMB FRACTURE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			

alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
APHASIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL INFARCTION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
HEADACHE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOSS OF CONSCIOUSNESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
REVERSIBLE POSTERIOR LEUKOENCEPHALOPATHY SYNDROME			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	2 / 18 (11.11%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER HAEMORRHAGE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATIC FUNCTION ABNORMAL			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAUNDICE CHOLESTATIC			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (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			
DERMATITIS BULLOUS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN ULCER			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
HAEMATURIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROTIC SYNDROME			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROTEINURIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE ACUTE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BURSITIS			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULOSKELETAL CHEST PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
LOWER RESPIRATORY TRACT INFECTION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	0 / 18 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 4	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	PLACEBO	AZD2171 45 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 18 (88.89%)	53 / 53 (100.00%)	
Vascular disorders			
FLUSHING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
HOT FLUSH			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
HYPERTENSION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	10 / 18 (55.56%)	37 / 53 (69.81%)	
occurrences (all)	10	40	
HYPOTENSION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
LYMPHOEDEMA			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
PERIPHERAL COLDNESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
PHLEBITIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
ASTHENIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
CHILLS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	1	3	
FATIGUE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	12 / 18 (66.67%)	37 / 53 (69.81%)	
occurrences (all)	24	77	
FEELING COLD			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	6 / 53 (11.32%)	
occurrences (all)	0	6	
GAIT DISTURBANCE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	0 / 53 (0.00%)	
occurrences (all)	2	0	
INFLUENZA LIKE ILLNESS			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
INJECTION SITE INDURATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
IRRITABILITY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
LOCAL SWELLING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
MUCOSAL INFLAMMATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
NON-CARDIAC CHEST PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
OEDEMA PERIPHERAL			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	11 / 53 (20.75%)	
occurrences (all)	2	14	
PYREXIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
Reproductive system and breast disorders			
TESTICULAR CYST			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
COUGH			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	4 / 18 (22.22%)	9 / 53 (16.98%)	
occurrences (all)	5	15	
DYSPHONIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	9 / 18 (50.00%)	33 / 53 (62.26%)	
occurrences (all)	14	47	
DYSPNOEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	7 / 18 (38.89%)	11 / 53 (20.75%)	
occurrences (all)	8	19	
DYSPNOEA EXERTIONAL			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
EPISTAXIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	9 / 53 (16.98%)	
occurrences (all)	1	10	
HAEMOPTYSIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	6 / 53 (11.32%)	
occurrences (all)	0	6	
OROPHARYNGEAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	4 / 53 (7.55%)	
occurrences (all)	2	5	
PRODUCTIVE COUGH			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	4 / 53 (7.55%)	
occurrences (all)	1	5	
RALES			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	4 / 53 (7.55%)	
occurrences (all)	4	4	
RHINITIS ALLERGIC			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
RHINORRHOEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	5 / 53 (9.43%)	
occurrences (all)	0	5	
Psychiatric disorders			
ANXIETY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
APATHY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
CONFUSIONAL STATE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
DEPRESSED MOOD			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
DEPRESSION			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	4 / 18 (22.22%)	2 / 53 (3.77%)	
occurrences (all)	5	2	
EMOTIONAL DISORDER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
INSOMNIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	7 / 53 (13.21%)	
occurrences (all)	2	9	
LOSS OF LIBIDO			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
MOOD ALTERED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	3	
PERSONALITY CHANGE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Investigations			
BLOOD POTASSIUM INCREASED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
WEIGHT DECREASED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	5 / 18 (27.78%)	22 / 53 (41.51%)	
occurrences (all)	5	26	
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
POST PROCEDURAL COMPLICATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
PROCEDURAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
SUNBURN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
SPLINTER HAEMORRHAGES			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	1	4	
Nervous system disorders			
AGEUSIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
DIZZINESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	4 / 18 (22.22%)	9 / 53 (16.98%)	
occurrences (all)	5	13	
BALANCE DISORDER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
DYSGEUSIA			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	2 / 18 (11.11%)	9 / 53 (16.98%)	
occurrences (all)	2	12	
HEADACHE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	6 / 18 (33.33%)	30 / 53 (56.60%)	
occurrences (all)	10	46	
DYSKINESIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
HYPOAESTHESIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	3	
NEUROPATHY PERIPHERAL			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	2	
LETHARGY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	9 / 53 (16.98%)	
occurrences (all)	2	11	
PARAESTHESIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	5 / 53 (9.43%)	
occurrences (all)	2	5	
SOMNOLENCE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
SCIATICA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	0 / 53 (0.00%)	
occurrences (all)	2	0	

Ear and labyrinth disorders			
HYPOACUSIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
TINNITUS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	4 / 53 (7.55%)	
occurrences (all)	0	6	
Eye disorders			
CONJUNCTIVITIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
BLINDNESS TRANSIENT			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
VISION BLURRED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	3	
OCULAR HYPERAEMIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
ABDOMINAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	5 / 18 (27.78%)	14 / 53 (26.42%)	
occurrences (all)	6	18	
ABDOMINAL PAIN UPPER			

alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	9 / 53 (16.98%)	
occurrences (all)	0	10	
ANAL INFLAMMATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	5	
CONSTIPATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	8 / 18 (44.44%)	22 / 53 (41.51%)	
occurrences (all)	12	32	
DIARRHOEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	15 / 18 (83.33%)	46 / 53 (86.79%)	
occurrences (all)	30	124	
DRY MOUTH			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	7 / 53 (13.21%)	
occurrences (all)	1	7	
DYSPEPSIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	4 / 18 (22.22%)	9 / 53 (16.98%)	
occurrences (all)	5	13	
FLATULENCE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
GASTROOESOPHAGEAL REFLUX DISEASE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
GINGIVAL PAIN			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	2 / 18 (11.11%)	2 / 53 (3.77%)	
occurrences (all)	2	2	
GLOSSODYNIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	4 / 53 (7.55%)	
occurrences (all)	0	4	
HAEMORRHOIDS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	1	3	
LIP SWELLING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
MOUTH ULCERATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
NAUSEA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	8 / 18 (44.44%)	31 / 53 (58.49%)	
occurrences (all)	12	61	
ORAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	4 / 53 (7.55%)	
occurrences (all)	4	5	
RECTAL HAEMORRHAGE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	3	
STOMATITIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	7 / 18 (38.89%)	18 / 53 (33.96%)	
occurrences (all)	17	39	

TOOTHACHE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
VOMITING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	5 / 18 (27.78%)	16 / 53 (30.19%)	
occurrences (all)	7	31	
Hepatobiliary disorders			
JAUNDICE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
LIVER DISORDER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
ACTINIC KERATOSIS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
ALOPECIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	8 / 53 (15.09%)	
occurrences (all)	3	8	
BLISTER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
COLD SWEAT			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
DECUBITUS ULCER			

alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)		
occurrences (all)	1	0		
DRY SKIN				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	6 / 53 (11.32%)		
occurrences (all)	1	6		
ERYTHEMA				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	5 / 53 (9.43%)		
occurrences (all)	1	6		
HYPERKERATOSIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)		
occurrences (all)	1	3		
NIGHT SWEATS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)		
occurrences (all)	4	2		
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	4 / 18 (22.22%)	18 / 53 (33.96%)		
occurrences (all)	9	28		
PRURITUS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)		
occurrences (all)	1	3		
PSORIASIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)		
occurrences (all)	1	0		
RASH				
alternative dictionary used: MedDRA 17				

subjects affected / exposed	5 / 18 (27.78%)	13 / 53 (24.53%)	
occurrences (all)	6	20	
RASH ERYTHEMATOUS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
RASH GENERALISED			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
RASH MACULAR			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	3 / 53 (5.66%)	
occurrences (all)	3	5	
SCAR			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
SKIN EXFOLIATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	4	
SKIN INDURATION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
SKIN ULCER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	4	
XERODERMA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	

Renal and urinary disorders			
DYSURIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	1	1	
HAEMATURIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	2 / 53 (3.77%)	
occurrences (all)	1	2	
PROTEINURIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	5 / 53 (9.43%)	
occurrences (all)	1	6	
RENAL FAILURE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
HYPERTHYROIDISM			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
HYPOTHYROIDISM			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	7 / 53 (13.21%)	
occurrences (all)	2	7	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	4 / 18 (22.22%)	8 / 53 (15.09%)	
occurrences (all)	4	9	
ARTHROPATHY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	

BACK PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	6 / 18 (33.33%)	16 / 53 (30.19%)	
occurrences (all)	10	20	
BONE PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	3 / 53 (5.66%)	
occurrences (all)	2	3	
FLANK PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	2 / 53 (3.77%)	
occurrences (all)	4	2	
GROIN PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
JOINT STIFFNESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	4 / 53 (7.55%)	
occurrences (all)	0	5	
JOINT SWELLING			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	4 / 53 (7.55%)	
occurrences (all)	0	4	
MUSCLE RIGIDITY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
MUSCLE SPASMS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	7 / 53 (13.21%)	
occurrences (all)	2	9	
MUSCULAR WEAKNESS			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	5 / 53 (9.43%)	
occurrences (all)	1	8	
MUSCULOSKELETAL CHEST PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	5 / 53 (9.43%)	
occurrences (all)	1	6	
MUSCULOSKELETAL PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	9 / 53 (16.98%)	
occurrences (all)	2	12	
MUSCULOSKELETAL STIFFNESS			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	0 / 18 (0.00%)	6 / 53 (11.32%)	
occurrences (all)	0	6	
MYALGIA			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	3 / 18 (16.67%)	7 / 53 (13.21%)	
occurrences (all)	3	9	
MYOPATHY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	1 / 53 (1.89%)	
occurrences (all)	2	1	
NECK PAIN			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	5 / 53 (9.43%)	
occurrences (all)	2	7	
PAIN IN EXTREMITY			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	2 / 18 (11.11%)	10 / 53 (18.87%)	
occurrences (all)	2	13	
Infections and infestations			
INFLUENZA			
alternative dictionary used: MedDRA 17			

subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)		
occurrences (all)	1	4		
LOWER RESPIRATORY TRACT INFECTION				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	3 / 18 (16.67%)	10 / 53 (18.87%)		
occurrences (all)	6	12		
NASOPHARYNGITIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	4 / 18 (22.22%)	12 / 53 (22.64%)		
occurrences (all)	4	15		
ORAL CANDIDIASIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	2 / 18 (11.11%)	1 / 53 (1.89%)		
occurrences (all)	2	1		
ORAL HERPES				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	2 / 18 (11.11%)	0 / 53 (0.00%)		
occurrences (all)	3	0		
PHARYNGITIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)		
occurrences (all)	1	0		
PNEUMONIA				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)		
occurrences (all)	1	0		
SINUSITIS				
alternative dictionary used: MedDRA 17				
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)		
occurrences (all)	1	3		
UPPER RESPIRATORY TRACT INFECTION				
alternative dictionary used: MedDRA 17				

subjects affected / exposed	2 / 18 (11.11%)	6 / 53 (11.32%)	
occurrences (all)	2	6	
URINARY TRACT INFECTION			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	3 / 53 (5.66%)	
occurrences (all)	2	6	
Metabolism and nutrition disorders			
APPETITE DISORDER			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	1 / 18 (5.56%)	0 / 53 (0.00%)	
occurrences (all)	1	0	
DECREASED APPETITE			
alternative dictionary used: MedDRA 17			
subjects affected / exposed	7 / 18 (38.89%)	32 / 53 (60.38%)	
occurrences (all)	13	52	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported