Clinical trial results:
SAFETY AND TOLERABILITY OF ODM-201 IN PATIENTS WITH CASTRATE RESISTANT PROSTATE CANCER: OPEN, NON-RANDOMISED, UNCONTROLLED, MULTICENTRE, EXTENSION STUDY TO STUDY 3104001

Summary

EudraCT number	2010-022803-24
Trial protocol	GB FI CZ EE
Global end of trial date	21 October 2015

Results information

Result version number	v1 (current)
This version publication date	03 November 2016
First version publication date	03 November 2016

Trial information

Trial identification

Sponsor protocol code	3104002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01429064
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orion Corporation Orion Pharma
Sponsor organisation address	Orionintie 1, Espoo, Finland,
Public contact	clinicaltrials@orionpharma.com, Orion Corporation Orion Pharma, +358 104261,
Scientific contact	clinicaltrials@orionpharma.com, Orion Corporation Orion Pharma, +358 104261,

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	21 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2015
Global end of trial reached?	Yes
Global end of trial date	21 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this extension study is to gain more information about the long-term safety and tolerability of ODM-201.

Protection of trial subjects:

Tolerability and safety laboratory parameteres were followed once monthly for 6 months, and then every 3 months. Since the France-specific protocol amendment 5 (April 7th 2015), visit interval was every 4 months. Adverse events were recorded for the whole study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 2011
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: 32
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Finland: 27
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	76
EEA total number of subjects	69

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)	23
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 17 hospitals in Europe and USA.

Pre-assignment

Screening details:

Patients with response or stable disease at week 12 in ARADES 3104001 study as judged by the investigator were allowed to continue in the ARADES-EXT 3104002 extension study.

Period 1

Period 1 title	ODM-201 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1 (Dose Escalation)

Arm description:

ODM-201 200 mg/day, 400 mg/day, 600 mg/day, 1000 mg/day, 1400 mg/day, 1800 mg/day

Arm type	Experimental
Investigational medicinal product name	ODM-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Twice daily with food

Arm title	Phase 2 (200mg/Day)

Arm description:

Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor

Arm type	Experimental
Investigational medicinal product name	ODM-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Twice daily with food

Arm title	Phase 2 (400mg/Day)

Arm description:

Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor

Arm type	Experimental
Investigational medicinal product name	ODM-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Twice daily with food

Arm title	Phase 2 (1400mg/Day)

Arm description:

Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor

Arm type	Experimental
Investigational medicinal product name	ODM-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Twice daily with food

Number of subjects in period 1	Phase 1 (Dose Escalation)	Phase 2 (200mg/Day)	Phase 2 (400mg/Day)
Started	19	22	19
Completed	19	22	19

Number of subjects in period 1	Phase 2 (1400mg/Day)
Started	16
Completed	16

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1 (Dose Escalation)
Reporting group description:	
ODM-201 200 mg/day, 400 mg/day, 600 mg/day, 1000 mg/day, 1400 mg/day, 1800 mg/day	
Reporting group title	Phase 2 (200mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (400mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (1400mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	

Reporting group values	Phase 1 (Dose Escalation)	Phase 2 (200mg/Day)	Phase 2 (400mg/Day)
Number of subjects	19	22	19
Age categorical Units: Subjects			
Adults (18-64 years)	6	8	6
From 65-84 years	13	14	13
Gender categorical Units: Subjects			
Male	19	22	19

Reporting group values	Phase 2 (1400mg/Day)	Total	
Number of subjects	16	76	
Age categorical Units: Subjects			
Adults (18-64 years)	3	23	
From 65-84 years	13	53	
Gender categorical Units: Subjects			
Male	16	76	

End points

End points reporting groups

Reporting group title	Phase 1 (Dose Escalation)
Reporting group description:	
ODM-201 200 mg/day, 400 mg/day, 600 mg/day, 1000 mg/day, 1400 mg/day, 1800 mg/day	
Reporting group title	Phase 2 (200mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (400mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (1400mg/Day)
Reporting group description:	
Chemotherapy-naïve and CYP17 inhibitor-naïve, Post-chemotherapy and CYP17 inhibitor-naïve, Post-CYP17 inhibitor	

Primary: Frequency of adverse events

End point title	Frequency of adverse events[1]
End point description:	

End point type	Primary
End point timeframe:	
From the start of study treatment in the study 3104001 ARADES until the end-of-study visit of ARADES-EXTENSION study 3104002.	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics.	

End point values	Phase 1 (Dose Escalation)	Phase 2 (200mg/Day)	Phase 2 (400mg/Day)	Phase 2 (1400mg/Day)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	22	19	16
Units: Adverse events	19	22	19	16

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of study treatment administration until the end-of-study visit (4 weeks after the last study treatment dose).	
Adverse event reporting additional description:	
Adverse events were reported from the start of study 3104001 ARADES.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Phase 1
Reporting group description:	
200 mg day, 400 mg day, 600 mg day, 1000 mg day, 1400 mg day, 1800 mg day	
Reporting group title	Phase 2 (200mg/Day)
Reporting group description:	
Chemotherapy-naive and CYP17 inhibitor-naive, Post-chemotherapy and CYP17 inhibitor-naive, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (400 mg/Day)
Reporting group description:	
Chemotherapy-naive and CYP17 inhibitor-naive, Post-chemotherapy and CYP17 inhibitor-naive, Post-CYP17 inhibitor	
Reporting group title	Phase 2 (1400mg/Day)
Reporting group description:	
Chemotherapy-naive and CYP17 inhibitor-naive, Post-chemotherapy and CYP17 inhibitor-naive, Post-CYP17 inhibitor	

Serious adverse events	Phase 1	Phase 2 (200mg/Day)	Phase 2 (400 mg/Day)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 19 (26.32%)	7 / 22 (31.82%)	3 / 19 (15.79%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sleep apnoea syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Enterobacter test positive			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enterobacter infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenotrophomonas infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2 (1400mg/Day)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 16 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chills				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Sleep apnoea syndrome				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Insomnia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Enterobacter test positive				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Cervical vertebral fracture				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laceration			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				

subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethral stenosis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary incontinence				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Diverticulitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Enterobacter infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stenotrophomonas infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1	Phase 2 (200mg/Day)	Phase 2 (400 mg/Day)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 19 (100.00%)	22 / 22 (100.00%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Cancer pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Meningioma			

subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Metastases to liver			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Circulatory collapse			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	3 / 19 (15.79%)
occurrences (all)	1	1	4
Hypertension			
subjects affected / exposed	2 / 19 (10.53%)	2 / 22 (9.09%)	2 / 19 (10.53%)
occurrences (all)	2	2	3
Intermittent claudication			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lymphoedema			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Lymphostasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pelvic venous thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Poor peripheral circulation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Superficial vein prominence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 19 (26.32%)	1 / 22 (4.55%)	2 / 19 (10.53%)
occurrences (all)	5	1	2
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Face oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	5 / 19 (26.32%)	3 / 22 (13.64%)	5 / 19 (26.32%)
occurrences (all)	5	4	8
Influenza like illness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Localised oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Oedema peripheral			
subjects affected / exposed	3 / 19 (15.79%)	2 / 22 (9.09%)	1 / 19 (5.26%)
occurrences (all)	4	2	1
Pain			
subjects affected / exposed	4 / 19 (21.05%)	7 / 22 (31.82%)	1 / 19 (5.26%)
occurrences (all)	4	7	1
Peripheral swelling			

subjects affected / exposed	1 / 19 (5.26%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	3	2
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Erectile dysfunction			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Gynaecomastia			
subjects affected / exposed	3 / 19 (15.79%)	1 / 22 (4.55%)	2 / 19 (10.53%)
occurrences (all)	3	1	2
Pelvic pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Penile oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	3 / 19 (15.79%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Dyspnoea			
subjects affected / exposed	3 / 19 (15.79%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	3	2	0

Dyspnoea exertional			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	1	1	2
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Alcohol abuse			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Confusional state			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 22 (4.55%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
Sleep disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Blood creatinine increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Blood pressure increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Cardiac murmur			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			

subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Heart rate increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Liver palpable			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urine output increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Weight increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Foot fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Laceration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Coronary artery disease			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Mitral valve incompetence			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	1	1	0

Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Areflexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	2 / 19 (10.53%)	1 / 22 (4.55%)	3 / 19 (15.79%)
occurrences (all)	2	2	3
Headache			
subjects affected / exposed	4 / 19 (21.05%)	2 / 22 (9.09%)	1 / 19 (5.26%)
occurrences (all)	5	2	1
Hypoaesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hyporeflexia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Monoparesis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Paraplegia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Petit mal epilepsy			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	3 / 19 (15.79%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Somnolence			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	2 / 19 (10.53%)
occurrences (all)	0	1	3
Lymphadenopathy			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Motion sickness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eyelid oedema			

subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abnormal faeces			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Aphthous stomatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	3 / 19 (15.79%)	3 / 22 (13.64%)	3 / 19 (15.79%)
occurrences (all)	3	3	3

Diarrhoea			
subjects affected / exposed	9 / 19 (47.37%)	0 / 22 (0.00%)	2 / 19 (10.53%)
occurrences (all)	9	0	2
Dry mouth			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gingival pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	5 / 19 (26.32%)	2 / 22 (9.09%)	3 / 19 (15.79%)
occurrences (all)	6	5	4
Oesophagitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	2 / 19 (10.53%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Tongue discolouration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Vomiting			
subjects affected / exposed	3 / 19 (15.79%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	4	0	1
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Erythema			
subjects affected / exposed	2 / 19 (10.53%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Onychoclasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	2 / 19 (10.53%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Skin atrophy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin lesion			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bladder dilatation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
Haematuria			
subjects affected / exposed	1 / 19 (5.26%)	3 / 22 (13.64%)	1 / 19 (5.26%)
occurrences (all)	1	5	1
Haemorrhage urinary tract			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Lower urinary tract symptoms			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Micturition frequency decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Pollakiuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2

Urinary incontinence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Urinary retention			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urinary tract inflammation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 19 (31.58%)	7 / 22 (31.82%)	3 / 19 (15.79%)
occurrences (all)	7	10	6
Arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	7 / 19 (36.84%)	4 / 22 (18.18%)	5 / 19 (26.32%)
occurrences (all)	7	5	7
Bone pain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Bursitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dupuytren's contracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Exposed bone in jaw			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 19 (0.00%)	3 / 22 (13.64%)	0 / 19 (0.00%)
occurrences (all)	0	6	0
Groin pain			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Joint lock			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Joint swelling			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Muscular weakness			
subjects affected / exposed	1 / 19 (5.26%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Myalgia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	3
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 19 (5.26%)	2 / 22 (9.09%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
Pain in jaw			

subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pathological fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Lower respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 19 (21.05%)	2 / 22 (9.09%)	1 / 19 (5.26%)
occurrences (all)	4	2	1

Onychomycosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pyelonephritis acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Tinea cruris			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	2 / 22 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	3 / 19 (15.79%)	1 / 22 (4.55%)	1 / 19 (5.26%)
occurrences (all)	3	1	1
Viral infection			
subjects affected / exposed	1 / 19 (5.26%)	1 / 22 (4.55%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)	3 / 22 (13.64%)	5 / 19 (26.32%)
occurrences (all)	1	3	6
Hyperuricaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 22 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 (1400mg/Day)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Meningioma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metastases to liver			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Aortic arteriosclerosis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Circulatory collapse				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Deep vein thrombosis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Flushing				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Hot flush				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	3			
Hypertension				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Intermittent claudication				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lymphoedema				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lymphostasis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pelvic venous thrombosis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Poor peripheral circulation				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Superficial vein prominence				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	8 / 16 (50.00%)		
occurrences (all)	9		
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Peripheral swelling			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Erectile dysfunction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gynaecomastia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Penile oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		

Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Pharyngeal erythema subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0			
Pleural effusion subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Pulmonary embolism subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0			
Rales subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Wheezing subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0			
Psychiatric disorders Affective disorder subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Alcohol abuse subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0			
Confusional state subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Depression subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0			
Insomnia				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood urine present			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cardiac murmur			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Heart rate increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Liver palpable			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urine output increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Fall			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Foot fracture			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Ligament sprain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rib fracture			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Sunburn			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Coronary artery disease			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Mitral valve incompetence			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Supraventricular extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Ventricular extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Areflexia			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Dizziness				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hypoaesthesia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hyporeflexia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lethargy				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Monoparesis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Neuropathy peripheral				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Paraesthesia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Paraplegia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Petit mal epilepsy				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Presyncope				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Sciatica				

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Motion sickness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eyelid oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Periorbital oedema			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Abnormal faeces			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Anal fissure			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Aphthous stomatitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cheilitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Dyspepsia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Flatulence			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gingival pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Oesophagitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tongue discolouration			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Actinic keratosis			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nail discolouration			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Onychoclasis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin atrophy			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			

Bladder dilatation				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Dysuria				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Haematuria				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Haemorrhage urinary tract				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hydronephrosis				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Lower urinary tract symptoms				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Micturition frequency decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Micturition urgency				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Nocturia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pollakiuria				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Urinary incontinence				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Urinary retention				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			

Urinary tract inflammation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3		
Arthritis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	6 / 16 (37.50%) 7		
Bone pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Bursitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Dupuytren's contracture subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Exposed bone in jaw subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Flank pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Groin pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Joint lock subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Joint stiffness			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Joint swelling				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Muscle spasms				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Muscular weakness				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Musculoskeletal chest pain				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Musculoskeletal pain				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Myalgia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Neck pain				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Osteoarthritis				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Pain in extremity				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pain in jaw				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pathological fracture				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Spinal pain				

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Onychomycosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Pyelonephritis acute			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tinea cruris			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hyperuricaemia			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2012	Number of subjects and dose levels increased.
16 July 2012	Guidance on ODM-201 interruptions and dose decrease were added.
07 April 2015	100 MG CAPSULE CHANGED TO 300 MG TABLET FORMULATION. VISIT FREQUENCY CHANGED FROM 3 TO 4 MONTHS INTERVAL.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported