



Clinical trial results:

An Open-Label Study of Abiraterone Acetate in Subjects with Metastatic Castration- Resistant Prostate Cancer Who Have Progressed After Taxane-Based Chemotherapy

Summary

EudraCT number	2010-021425-13
Trial protocol	CZ HU ES IT LT DK GR
Global end of trial date	19 October 2015

Results information

Result version number	v1 (current)
This version publication date	23 September 2016
First version publication date	23 September 2016

Trial information

Trial identification

Sponsor protocol code	212082PCR3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01217697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development, LLC
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.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	19 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to collect additional safety data during treatment with abiraterone acetate plus prednisone or prednisolone among subjects with metastatic castration-resistant prostate cancer (CRPC) who had failed 1 or 2 chemotherapy regimens, 1 of which contains a taxane base such as docetaxel, who reside in areas in which abiraterone acetate was not yet available through local healthcare providers, and who were not eligible for enrollment into an available ongoing clinical study of abiraterone acetate.

Protection of trial subjects:

Safety evaluations included the collection of adverse events, evaluation of deaths, other serious adverse events and other significant adverse events, clinical laboratory tests, other safety observations (vital signs, physical examinations and Electrocardiograms).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2010
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	Australia: 312
Country: Number of subjects enrolled	Brazil: 73
Country: Number of subjects enrolled	Canada: 100
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Czech Republic: 107
Country: Number of subjects enrolled	Denmark: 57
Country: Number of subjects enrolled	Spain: 96
Country: Number of subjects enrolled	Greece: 61
Country: Number of subjects enrolled	Hong Kong: 17
Country: Number of subjects enrolled	Croatia: 20
Country: Number of subjects enrolled	Hungary: 84
Country: Number of subjects enrolled	Indonesia: 2
Country: Number of subjects enrolled	Italy: 550
Country: Number of subjects enrolled	Korea, Republic of: 45
Country: Number of subjects enrolled	Mexico: 63
Country: Number of subjects enrolled	Malaysia: 17
Country: Number of subjects enrolled	Poland: 50

Country: Number of subjects enrolled	Romania: 60
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	Singapore: 33
Country: Number of subjects enrolled	Thailand: 26
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	United States: 432
Worldwide total number of subjects	2316
EEA total number of subjects	1085

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)	595
From 65 to 84 years	1667
85 years and over	54

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 17 November 2010 to 19 October 2015.

Pre-assignment

Screening details:

2,316 Subjects were enrolled in the study.

Period 1

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

Arms

Arm title	Abiraterone Acetate
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Arm description:

Subjects received abiraterone acetate 1000 milligram (mg) daily as four tablets of 250 mg orally and 5 mg prednisone or prednisolone twice daily as oral dose.

Arm type	Experimental
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received prednisone 5 mg twice daily as oral tablet OR prednisolone 5 mg (if prednisone is not available).

Investigational medicinal product name	Abiraterone Acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received abiraterone acetate 1000 milligram (mg) daily as four tablets of 250 mg orally

Number of subjects in period 1	Abiraterone Acetate
Started	2316
Completed	0
Not completed	2316
Study Terminated by sponsor	59
Consent withdrawn by subject	153
Adverse Event	186
Market Authorization / Reimbursement	455
Death	178

Other	109
Lost to follow-up	18
Disease Progression	1142
Protocol deviation	16

Baseline characteristics

Reporting groups

Reporting group title	Abiraterone Acetate
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Reporting group description:

Subjects received abiraterone acetate 1000 milligram (mg) daily as four tablets of 250 mg orally and 5 mg prednisone or prednisolone twice daily as oral dose.

Reporting group values	Abiraterone Acetate	Total	
Number of subjects	2316	2316	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	595	595	
From 65 to 84 years	1667	1667	
85 years and over	54	54	
Title for AgeContinuous Units: years			
arithmetic mean	70		
standard deviation	± 8.07	-	
Title for Gender Units: subjects			
Male	2316	2316	

End points

End points reporting groups

Reporting group title	Abiraterone Acetate
Reporting group description: Subjects received abiraterone acetate 1000 milligram (mg) daily as four tablets of 250 mg orally and 5 mg prednisone or prednisolone twice daily as oral dose.	
Subject analysis set title	Safety Analysis Population
Subject analysis set type	Safety analysis
Subject analysis set description: Safety analysis set included all subjects who received at least one dose of primary study drug (Abiraterone acetate)	

Primary: Number of Subjects With Adverse Events (A.Es)

End point title	Number of Subjects With Adverse Events (A.Es) ^[1]
End point description: An adverse event is any untoward medical event that occurs in a participant administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product.	
End point type	Primary
End point timeframe: From the time of signing the informed consent to the time of the End-of-Study Visit (30 days after discontinuation of study drug)	
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: Statistical analysis was not reported for this endpoint as inferential analysis was not performed as planned.	

End point values	Abiraterone Acetate			
Subject group type	Reporting group			
Number of subjects analysed	2316 ^[2]			
Units: Subjects				
Treatment-emergent serious or clinically important	1166			
Grade 3-4 treatment emergent A.Es	980			
Treatment-emergent serious A.Es	682			
Treatment-emergent A.Es leading to treatment	385			
Treatment-emergent A.Es leading to death	248			

Notes:

[2] - Safety analysis population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of signing the informed consent to the time of the End-of-Study Visit (30 days after discontinuation of study drug)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	Abiraterone Acetate
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Reporting group description:

Subjects received abiraterone acetate 1000 milligram (mg) daily as four tablets of 250 mg orally and 5 mg prednisone or prednisolone twice daily as oral dose.

Serious adverse events	Abiraterone Acetate		
Total subjects affected by serious adverse events			
subjects affected / exposed	818 / 2316 (35.32%)		
number of deaths (all causes)	248		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer Pain			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Basal Cell Carcinoma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carcinoid Tumour of the Caecum			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric Cancer			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Colon Cancer			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung Adenocarcinoma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Neoplasm Malignant			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant Melanoma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Malignant Pleural Effusion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningeal Neoplasm			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to Bone Marrow			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metastases to Bone			

subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to Central Nervous System				
subjects affected / exposed	6 / 2316 (0.26%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
Metastases to Lung				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metastases to Liver				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Metastatic Pain				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Metastases to Meninges				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Neoplasm Malignant				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Pancreatic Carcinoma				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pancreatic Neoplasm				

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Prostate Cancer			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 4		
Prostate Cancer Metastatic			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Rectal Cancer			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour Flare			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour Pain			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial Occlusive Disease			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Circulatory Collapse			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Deep Vein Thrombosis			

subjects affected / exposed	8 / 2316 (0.35%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypertension			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	8 / 2316 (0.35%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 2		
Peripheral Ischaemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular Compression			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Venous Thrombosis Limb			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Aortic Valve Replacement			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary Angioplasty			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fasciectomy			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hernia Repair			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hospitalisation			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Photon Radiation Therapy to Brain			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Lobectomy			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiotherapy			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Decompression			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Fusion Surgery			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stent Removal			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	15 / 2316 (0.65%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 4		
Chest Discomfort			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest Pain			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Death			
subjects affected / exposed	12 / 2316 (0.52%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 12		
Device Failure			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Discomfort			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disease Progression			
subjects affected / exposed	25 / 2316 (1.08%)		
occurrences causally related to treatment / all	0 / 25		
deaths causally related to treatment / all	0 / 22		
Drug Interaction			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	15 / 2316 (0.65%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 4		
General Physical Health Deterioration			
subjects affected / exposed	39 / 2316 (1.68%)		
occurrences causally related to treatment / all	0 / 40		
deaths causally related to treatment / all	0 / 31		
Hernia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperpyrexia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Malaise			

subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multi-Organ Failure				
subjects affected / exposed	9 / 2316 (0.39%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 9			
Medical Device Complication				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-Cardiac Chest Pain				
subjects affected / exposed	5 / 2316 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Oedema				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oedema Peripheral				
subjects affected / exposed	10 / 2316 (0.43%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	20 / 2316 (0.86%)			
occurrences causally related to treatment / all	0 / 22			
deaths causally related to treatment / all	0 / 1			
Performance Status Decreased				
subjects affected / exposed	6 / 2316 (0.26%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
Sudden Death				

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pyrexia			
subjects affected / exposed	21 / 2316 (0.91%)		
occurrences causally related to treatment / all	0 / 29		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatic Obstruction			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute Interstitial Pneumonitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute Respiratory Failure			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Cough			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	15 / 2316 (0.65%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 2		
Epistaxis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Interstitial Lung Disease			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydrothorax			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal Oedema			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Disorder			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pleural Effusion			

subjects affected / exposed	9 / 2316 (0.39%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 1		
Pneumonia Aspiration			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary Congestion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Embolism			
subjects affected / exposed	12 / 2316 (0.52%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 2		
Pulmonary Microemboli			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Oedema			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Respiratory Arrest			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Respiratory Disorder			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory Failure			
subjects affected / exposed	10 / 2316 (0.43%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 10		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional State			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Disorientation			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Mental Status Changes			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal Ideation			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide Attempt			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Biopsy Liver			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood Creatinine Increased			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemoglobin Decreased			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
International Normalised Ratio Increased			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Liver Function Test Abnormal			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet Count Decreased			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatic Specific Antigen Increased			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urine Output Decreased			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Accidental Overdose			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Ankle Fracture			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Clavicle Fracture			

subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Cervical Vertebral Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Compression Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis Radiation			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Femoral Neck Fracture			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Femur Fracture			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Foot Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hand Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head Injury			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Humerus Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar Vertebral Fracture			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Open Wound			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Patella Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic Fracture			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post Procedural Haematuria			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius Fracture			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal Compression Fracture			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal Fracture			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Subdural Haematoma			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Subdural Haemorrhage			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Thoracic Vertebral Fracture			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Toxicity to Various Agents			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion Reaction			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic Brain Injury			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper Limb Fracture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound Secretion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 3		
Acute Myocardial Infarction			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Angina Pectoris			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina Unstable			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial Fibrillation			
subjects affected / exposed	8 / 2316 (0.35%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Atrial Flutter			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrioventricular Block			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bundle Branch Block Left			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Arrest			
subjects affected / exposed	8 / 2316 (0.35%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 8		
Cardiac Disorder			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure			
subjects affected / exposed	9 / 2316 (0.39%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 4		
Cardiac Failure Congestive			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 4		
Cardio-Respiratory Arrest			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Cardio-Respiratory Distress			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiovascular Disorder			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial Infarction			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Intracardiac Thrombus			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Ischaemia			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Palpitations			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial Effusion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular Tachycardia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular Tachycardia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Altered State of Consciousness			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Brain Oedema			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Central Nervous System Lesion			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cerebral Haemorrhage			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Cerebral Infarction			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cerebral Ischaemia			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cerebrovascular Accident			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 5		
Cognitive Disorder			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Coma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Convulsion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cranial Nerve Disorder			

subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Depressed Level of Consciousness				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diabetic Coma				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic Neuropathy				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Dysarthria				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Epilepsy				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Haemorrhage Intracranial				

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Hemiparesis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hemiplegia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Iiird Nerve Paralysis			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lethargy			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Loss of Consciousness			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic Encephalopathy			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nerve Root Compression			

subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Monoparesis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurological Symptom			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraparesis			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Paraplegia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sedation			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Cord Compression			
subjects affected / exposed	28 / 2316 (1.21%)		
occurrences causally related to treatment / all	0 / 28		
deaths causally related to treatment / all	0 / 2		
Syncope			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Trigeminal Neuralgia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient Ischaemic Attack			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	50 / 2316 (2.16%)		
occurrences causally related to treatment / all	0 / 53		
deaths causally related to treatment / all	0 / 12		
Anaemia Macrocytic			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bone Marrow Failure				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Disseminated Intravascular Coagulation				
subjects affected / exposed	4 / 2316 (0.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 3			
Febrile Neutropenia				
subjects affected / exposed	4 / 2316 (0.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Leukopenia				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Thrombocytopenia				
subjects affected / exposed	8 / 2316 (0.35%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 1			
Thrombotic Thrombocytopenic Purpura				

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ear and labyrinth disorders			
Vertigo Positional			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diplopia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Visual Impairment			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal Vein Occlusion			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Adhesions			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Abdominal Distension				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Abdominal Mass				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal Pain				
subjects affected / exposed	9 / 2316 (0.39%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 1			
Abdominal Pain Upper				
subjects affected / exposed	5 / 2316 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Anal Fistula				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal Haemorrhage				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Colonic Obstruction				
subjects affected / exposed	3 / 2316 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Colitis				

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
Diarrhoea			
subjects affected / exposed	11 / 2316 (0.47%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 1		
Diverticulum			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulum Intestinal Haemorrhagic			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal Ulcer			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Erosive Oesophagitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterovesical Fistula			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Hypomotility			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Haemorrhage			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Haematemesis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gingivitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hiatus Hernia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Impaired Gastric Emptying			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Obstruction			
subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Large Intestine Perforation			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
Mouth Haemorrhage			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proctalgia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obstruction Gastric			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal Haemorrhage			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Retroperitoneal Haemorrhage			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	13 / 2316 (0.56%)		
occurrences causally related to treatment / all	0 / 20		
deaths causally related to treatment / all	0 / 0		
Small Intestinal Obstruction			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis Acute			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cholecystitis			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic Function Abnormal			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic Failure			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 4		
Hepatitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatorenal Failure			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver Injury			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Bladder Obstruction			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysuria			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bladder Spasm			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	30 / 2316 (1.30%)		
occurrences causally related to treatment / all	0 / 41		
deaths causally related to treatment / all	0 / 2		
Hydronephrosis			
subjects affected / exposed	10 / 2316 (0.43%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 1		
Nephrolithiasis			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nephropathy Toxic			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obstructive Uropathy			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
Renal Impairment			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal Failure Acute			
subjects affected / exposed	16 / 2316 (0.69%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 5		
Ureteric Rupture			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urethral Stenosis			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Urinary Incontinence			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Retention			
subjects affected / exposed	12 / 2316 (0.52%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Obstruction			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal Insufficiency			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Arthralgia				
subjects affected / exposed	13 / 2316 (0.56%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 0			
Back Pain				
subjects affected / exposed	52 / 2316 (2.25%)			
occurrences causally related to treatment / all	0 / 58			
deaths causally related to treatment / all	0 / 3			
Bone Pain				
subjects affected / exposed	16 / 2316 (0.69%)			
occurrences causally related to treatment / all	0 / 16			
deaths causally related to treatment / all	0 / 3			
Bursitis				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Groin Pain				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemarthrosis				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar Spinal Stenosis				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle Spasms				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular Weakness				

subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal Chest Pain			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal Pain			
subjects affected / exposed	8 / 2316 (0.35%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neck Pain			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis of Jaw			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in Extremity			

subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Pathological Fracture			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Rhabdomyolysis			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Abscess Limb			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anal Abscess			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Alveolar Osteitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriovenous Fistula Site Infection			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis Infective			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bacterial Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary Tract Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary Sepsis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			

subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Clostridium Difficile Colitis			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cellulitis Orbital			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Device Related Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Enterocolitis Infectious			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia Bacteraemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia Sepsis			

subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye Infection				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	4 / 2316 (0.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal Infection				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Viral				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematoma Infection				
subjects affected / exposed	1 / 2316 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	4 / 2316 (0.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Infective Exacerbation of Chronic Obstructive Airways Disease				
subjects affected / exposed	2 / 2316 (0.09%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Laryngitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower Respiratory Tract Infection			
subjects affected / exposed	6 / 2316 (0.26%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Lobar Pneumonia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ludwig Angina			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Necrotising Fasciitis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia			
subjects affected / exposed	40 / 2316 (1.73%)		
occurrences causally related to treatment / all	0 / 44		
deaths causally related to treatment / all	0 / 8		
Osteomyelitis			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post Procedural Sepsis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psoas Abscess			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis Acute			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Salmonella Bacteraemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salmonella Sepsis			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salmonellosis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Scrotal Abscess			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	18 / 2316 (0.78%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 9		
Septic Shock			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Staphylococcal Sepsis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	34 / 2316 (1.47%)		
occurrences causally related to treatment / all	0 / 38		
deaths causally related to treatment / all	0 / 2		
Urinary Tract Infection Bacterial			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	25 / 2316 (1.08%)		
occurrences causally related to treatment / all	0 / 31		
deaths causally related to treatment / all	0 / 3		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound Sepsis			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Decreased Appetite			
subjects affected / exposed	5 / 2316 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	18 / 2316 (0.78%)		
occurrences causally related to treatment / all	0 / 19		
deaths causally related to treatment / all	0 / 2		
Diabetes Mellitus			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes Mellitus Inadequate Control			

subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Failure to Thrive			
subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Fluid Retention			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	4 / 2316 (0.17%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	3 / 2316 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	7 / 2316 (0.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			

subjects affected / exposed	2 / 2316 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 2316 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Abiraterone Acetate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	149 / 2316 (6.43%)		
Investigations			
Blood Alkaline Phosphatase Increased			
alternative assessment type: Systematic			
subjects affected / exposed	149 / 2316 (6.43%)		
occurrences (all)	172		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2010	Amendment clarified disease progression assessments in addition to other minor clarifications and corrections: Prostate-specific antigen (PSA) progression and clinical progression assessments were clarified, Key results from Study COU-AA-301 were summarized and included in the study design rationale as background for this early access protocol (EAP), Per the request from the United States (US) Food and Drug Administration, an exclusion criterion for prior systemic treatment with an azole drug, For example (e.g.), fluconazole, itraconazole, ketoconazole) within 1 month of study start was added. This was included because the safety of subjects with recent exposure to azoles and abiraterone had not been tested. Quality-of-Life (QoL) and medical resource utilization (MRU) assessments were expanded to be performed at non-European as well as European sites.
20 May 2011	Amendment added the following information in addition to the correction of minor errors: The end-of-study definition was revised with further clarification of the last assessment of the last subject. The dosage of abiraterone acetate was clarified to be once daily and not in divided doses Over the course of the day. References to sites in Europe for Patient-reported outcome/Medical resource utilization (PRO/MRU) assessments were removed as they may also be assessed at non-European sites. An attachment was added to clearly define PSA progression, to determine the eligibility of a subject for the study (referred to in the inclusion criteria). Concomitant therapy was added as an exclusion criterion. Location of recording clinically important signs and symptoms in the case report form (CRF) was specified. Clarification was made to inclusion criterion. Albumin was added to the serum chemistry panel to be consistent with other sections of the protocol. The definition of a serious adverse event (SAE) was updated, and the timeframe for case report form transmission to the sponsor was changed per company standards. Assessment of physical examination and measurement of blood pressure and weight were added to the CRF. Information on management of Grade 2 hypokalemia was added.
07 May 2012	Amendment added the following information in addition to the corrections of minor errors: Language for the reporting of all clinically important adverse events (AEs) to the sponsor was changed back to the wording in the original protocol. The timeframe for obtaining an electrocardiogram (ECG) in the screening period was changed to be consistent with the requirement associated with multiple gated acquisition (MUGA) scans. Assessment of serum testosterone level at screening was expanded to account for those areas where it was not the standard of care. The requirement for completion of the MRU questionnaire at Cycle 1 Day 1 was removed. An allowance for all study procedures to be conducted within a window of ± 2 days was added. Serum, magnesium, amylase, and lipase were added to the procedures required at the end of study visit. The term "investigator" was removed from "investigator prescribed" when referring to prednisone. The definition of uncontrolled hypertension in the exclusion criteria was clarified. Other azole drugs were added to list of prohibited medications. The upper limit of Grade 1 and the lower limit of Grade 2 increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) were amended from 2.5 x the upper limit of normal (ULN) to 3x ULN.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported