Clinical trial results:
A Randomized, Double-blind, Comparative Study of Abiraterone Acetate Plus Low dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Subjects With High Risk, Metastatic Hormone-Naive Prostate Cancer (mHNPC)

Summary

EudraCT number	2012-002940-26
Trial protocol	GB CZ FR SE HU PT FI ES IT SK DK DE BE PL BG NL
Global end of trial date	13 February 2022

Results information

Result version number	v1 (current)
This version publication date	26 February 2023
First version publication date	26 February 2023

Trial information

Trial identification

Sponsor protocol code	212082PCR3011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01715285
WHO universal trial number (UTN)	U1111-1135-7146

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 US Highway 202 South Raritan, New Jersey, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialDisclosure@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialDisclosure@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	13 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to determine whether abiraterone acetate plus low-dose prednisone (AA-P) in combination with ADT was superior to ADT alone in improving radiographic progression-free survival (rPFS) and overall survival (OS) in subjects with mHNPC who had high-risk prognostic factors.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	44 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 16
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Brazil: 56
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	China: 137
Country: Number of subjects enrolled	Colombia: 17
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	Hungary: 34

Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Italy: 39
Country: Number of subjects enrolled	Japan: 70
Country: Number of subjects enrolled	Korea, Republic of: 32
Country: Number of subjects enrolled	Mexico: 38
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Poland: 42
Country: Number of subjects enrolled	Portugal: 39
Country: Number of subjects enrolled	Romania: 43
Country: Number of subjects enrolled	Russian Federation: 184
Country: Number of subjects enrolled	Slovakia: 31
Country: Number of subjects enrolled	Sweden: 22
Country: Number of subjects enrolled	Turkey: 35
Country: Number of subjects enrolled	Ukraine: 79
Country: Number of subjects enrolled	South Africa: 20
Worldwide total number of subjects	1199
EEA total number of subjects	383

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)	454
From 65 to 84 years	728
85 years and over	17

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1209 subjects were enrolled and 1199 were randomised to treatment groups.10 subjects from Russian site were excluded from the analysis due to noncompliance with International Conference on Harmonisation Good Clinical Practice guidelines at site. The remaining 1199 randomised subjects comprised the intent-to-treat population.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Abiraterone Acetate+Prednisone+ADT

Arm description:

Subjects received abiraterone acetate tablet at a total dose of 1000 milligrams (mg) plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of androgen deprivation therapy (ADT) was administered.

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

Dosage and administration details:

Abiraterone acetate of 1000 mg (4 tablets of 250 mg) per day until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	Androgen deprivation therapy (ADT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Stable regimen of ADT, that is, lutenizing hormone releasing hormone (LHRH) agonists or surgical castration according to local guidelines until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Prednisone 5 mg once daily until disease progression, withdrawal of consent or unacceptable toxicity.

Arm title	Placebo + ADT

Arm description:

Subjects received placebo matched to abiraterone acetate plus prednisone orally once daily until disease

progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to abiraterone acetate)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to abiraterone acetate once daily until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	ADT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Stable regimen of ADT, that is, lutenizing hormone releasing hormone (LHRH) agonists or surgical castration according to local guidelines until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	Placebo (matched to prednisone)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to prednisone once daily until disease progression, withdrawal of consent or unacceptable toxicity.

Number of subjects in period 1	Abiraterone Acetate+Prednisone +ADT	Placebo + ADT
Started	597	602
Completed	0	72
Not completed	597	530
Adverse event, serious fatal	43	25
Physician decision	21	23
Consent withdrawn by subject	52	47
Non-compliance with Study Drug	4	2
Adverse event, non-fatal	53	31
Progressive Disease	254	388
Lost to follow-up	3	2
unspecified	167	12

Period 2

Period 2 title	Open-label (OL) Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	DB Period Placebo to OLE Abiraterone Acetate

Arm description:

Subjects who were originally randomised to the Placebo group were permitted to crossover to Abiraterone Acetate plus Prednisone treatment in open-label extension phase to receive abiraterone acetate tablet at a total dose of 1000 mg plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.

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

Dosage and administration details:

Abiraterone acetate of 1000 mg (4 tablets of 250 mg) per day until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	Androgen deprivation therapy (ADT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Stable regimen of ADT, that is, lutenizing hormone releasing hormone (LHRH) agonists or surgical castration according to local guidelines until disease progression, withdrawal of consent or unacceptable toxicity.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Prednisone 5 mg once daily until disease progression, withdrawal of consent or unacceptable toxicity.

Number of subjects in period 2	DB Period Placebo to OLE Abiraterone Acetate
Started	72
Completed	0
Not completed	72
Adverse event, serious fatal	4
Consent withdrawn by subject	6
Adverse event, non-fatal	1
Progressive Disease	1

unspecified	60

Baseline characteristics

Reporting groups	
Reporting group title	Abiraterone Acetate+Prednisone+ADT
Reporting group description:	
Subjects received abiraterone acetate tablet at a total dose of 1000 milligrams (mg) plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of androgen deprivation therapy (ADT) was administered.	
Reporting group title	Placebo + ADT
Reporting group description:	
Subjects received placebo matched to abiraterone acetate plus prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.	

Reporting group values	Abiraterone Acetate+Prednisone +ADT	Placebo + ADT	Total
Number of subjects	597	602	1199
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	221	233	454
From 65 to 84 years	367	361	728
85 years and over	9	8	17
Title for AgeContinuous Units: years			
arithmetic mean	67.3	66.8	
standard deviation	± 8.48	± 8.72	-
Title for Gender Units: subjects			
Male	597	602	1199

End points

End points reporting groups

Reporting group title	Abiraterone Acetate+Prednisone+ADT

Reporting group description:

Subjects received abiraterone acetate tablet at a total dose of 1000 milligrams (mg) plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of androgen deprivation therapy (ADT) was administered.

Reporting group title	Placebo + ADT

Reporting group description:

Subjects received placebo matched to abiraterone acetate plus prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.

Reporting group title	DB Period Placebo to OLE Abiraterone Acetate

Reporting group description:

Subjects who were originally randomised to the Placebo group were permitted to crossover to Abiraterone Acetate plus Prednisone treatment in open-label extension phase to receive abiraterone acetate tablet at a total dose of 1000 mg plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.

Primary: Radiographic Progression-Free Survival (rPFS)

End point title	Radiographic Progression-Free Survival (rPFS)

End point description:

rPFS: defined as time (in months) interval from randomisation to first date of radiographic progression or death. Radiographic progression included progression by bone scan (according to modified Prostate Cancer Working Group2 criteria), defined as at least 2 new lesions on bone scan and progression of soft tissue lesions by computed tomography or magnetic resonance imaging (according to Response Evaluation Criteria in Solid Tumors [RECIST]1.1 criteria). As per RECIST guideline, progression requires 20 percent increase in sum of diameters of all target lesions and minimum absolute increase of 5 millimeters (mm) in sum as compared to nadir sum of diameter. Intention to treat (ITT) analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that upper limit of 95%CI was not estimable due to lesser number of events.

End point type	Primary

End point timeframe:

Up to 44 months

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: Months				
median (confidence interval 95%)	33.02 (29.57 to 99999)	14.78 (14.69 to 18.27)		

Statistical analyses

Statistical analysis title	Abiraterone Acetate+Prednisone+ADT, Placebo + ADT
Comparison groups	Placebo + ADT v Abiraterone Acetate+Prednisone+ADT
Number of subjects included in analysis	1199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.466
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.394
upper limit	0.55

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival was defined as the time from randomisation to date of death from any cause. ITT analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that upper limit of 95% CI was not estimable due to lesser number of events.

End point type	Primary

End point timeframe:

Up to 66 months

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: months				
median (confidence interval 95%)	53.32 (48.23 to 99999)	36.53 (33.54 to 39.95)		

Statistical analyses

Statistical analysis title	Abiraterone Acetate+Prednisone+ADT, Placebo + ADT
Comparison groups	Abiraterone Acetate+Prednisone+ADT v Placebo + ADT

Number of subjects included in analysis	1199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.661
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.564
upper limit	0.775

Secondary: Time to Initiation of Chemotherapy

End point title	Time to Initiation of Chemotherapy

End point description:

Time to initiation of chemotherapy was defined as the time (in months) interval from the date of randomisation to the date of initiation of cytotoxic chemotherapy for prostate cancer. ITT analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that median and upper limit of 95% CI was not estimable due to lesser number of events.

End point type	Secondary

End point timeframe:

Up to 66 months

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: months				
median (confidence interval 95%)	99999 (62.62 to 99999)	57.59 (38.18 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Subsequent Therapy for Prostate Cancer

End point title	Time to Subsequent Therapy for Prostate Cancer

End point description:

Time to subsequent therapy was defined as the time interval from the date of randomisation to the date of initiation of subsequent therapy for prostate cancer. ITT analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that upper limit of 95% CI was not estimable due to lesser number of events.

End point type	Secondary
End point timeframe: Up to 66 months	

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: Months				
median (confidence interval 95%)	54.87 (46.42 to 99999)	21.22 (18.56 to 23.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Pain Progression

End point title	Time to Pain Progression

End point description:

Time to pain progression was defined as the time (in months) interval from randomisation to the first date a subject experienced a greater than or equal to (>=) 30 percent (%) increase in Brief Pain Inventory-Short Form (BPI-SF) from baseline in the BPI-SF worst pain intensity (Item 3) observed at 2 consecutive evaluations (>=4) weeks apart. BPI-SF was an 11-item questionnaire, designed to assess severity and impact of pain on daily functions. Total score ranged from 0 to 10 with 0 representing "no pain" and 10 representing" pain as bad as you can imagine. ITT analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that upper limit of 95% CI was not estimable due to lesser number of events.

End point type	Secondary
End point timeframe: Up to 66 months	

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: Months				
median (confidence interval 95%)	47.41 (33.15 to 99999)	16.62 (11.07 to 23.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Skeletal-Related Event

End point title	Time to Skeletal-Related Event

End point description:

Time to skeletal-related event was defined as the earliest of the following: clinical or pathological fracture, spinal cord compression, palliative radiation to bone, or surgery to bone. ITT analysis set included all subjects randomised into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received. Here, '99999' was used as a space filler which signifies that median upper limit and lower limit of 95% CI was not estimable due to lesser number of events.

End point type	Secondary

End point timeframe:

Up to 66 months

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Prostate-Specific Antigen (PSA) Progression

End point title	Time to Prostate-Specific Antigen (PSA) Progression

End point description:

Time to PSA progression was defined as the time (in months) interval from the date of randomisation to the date of PSA progression, according to PCWG2 criteria. PCWG2 defines PSA progression as the date that a 25 percent (%) or greater increase and an absolute increase of 2 nanogram per milliliters (ng/mL) or more from the nadir is documented, which is confirmed by a second value obtained 3 or more weeks later. ITT analysis set included all subjects randomized into the study and who were classified according to their assigned treatment group, regardless of the actual treatment received.

End point type	Secondary

End point timeframe:

Up to 66 months

End point values	Abiraterone Acetate+Prednisone+ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	602		
Units: Months				
median (confidence interval 95%)	33.31 (29.44 to 46.09)	7.43 (7.20 to 9.20)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to 30 days post last dose (that is, for DB period: up to 23 months and OLE period: up to 15.6 months), deaths were collected from baseline up to end of study (up to 66 months).

Adverse event reporting additional description:

Safety analysis set included all subjects randomised into the study and who received any part of study drugs. Only 72 deaths out of all cause mortalities contributed to discontinuation.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Abiraterone Acetate+Prednisone+ADT

Reporting group description:

Subjects received abiraterone acetate tablet at a total dose of 1000 milligram (mg) plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of androgen deprivation therapy (ADT) was administered.

Reporting group title	DB Period Placebo to OLE Abiraterone Acetate

Reporting group description:

Subjects who were originally randomised to the Placebo group were permitted to crossover to Abiraterone Acetate plus prednisone treatment in open-label extension phase to receive abiraterone acetate tablet at a total dose of 1000 mg plus 5 mg capsule of prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity.

Reporting group title	Placebo + ADT

Reporting group description:

Subjects received placebo matched to abiraterone acetate plus prednisone orally once daily until disease progression, withdrawal of consent or unacceptable toxicity. Stable regimen of ADT was administered.

Serious adverse events	Abiraterone Acetate+Prednisone +ADT	DB Period Placebo to OLE Abiraterone Acetate	Placebo + ADT
Total subjects affected by serious adverse events			
subjects affected / exposed	192 / 597 (32.16%)	4 / 72 (5.56%)	151 / 602 (25.08%)
number of deaths (all causes)	275	4	339
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Neoplasm			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of Colon			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-Cell Lymphoma			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer Pain			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Lymphocytic Leukaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Lymphocytic Leukaemia Stage 3			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Lung Adenocarcinoma			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon Cancer			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Colon Neoplasm			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lentigo Maligna			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Leukaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Chronic Myeloid Leukaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Malignant Melanoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Malignant Neoplasm of Renal Pelvis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Metastases to Meninges			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Neoplasm Malignant			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional Cell Carcinoma			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Neuroendocrine Tumour			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Carcinoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Plasma Cell Myeloma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Rectal Cancer			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Neoplasm of Thymus			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	4 / 597 (0.67%)	0 / 72 (0.00%)	4 / 602 (0.66%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Pressure Fluctuation			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Dissection			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angiopathy			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Aneurysm			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hypertension			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent Claudication			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Vascular Disorder			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Surgical and medical procedures			
Lipoma Excision			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Dislocation			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-Organ Failure			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema Peripheral			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hernia Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Swelling			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	6 / 597 (1.01%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatic Haemorrhage			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pelvic Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign Prostatic Hyperplasia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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

Prostatitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Bronchitis Chronic			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Bronchiectasis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal Pain			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Epistaxis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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

Dyspnoea			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphonia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pneumonia Aspiration			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pneumonitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pleural Effusion			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	4 / 602 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Mass			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Oedema			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
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 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental Disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biopsy Liver			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Blood Glucose Abnormal			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet Count Decreased			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood Testosterone Increased			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral Neck Fracture			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hip Fracture			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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

Ligament Sprain			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Lower Limb Fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney Rupture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal Burn			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic Fracture			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Traumatic Intracranial Haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Upper Limb Fracture			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Patella Fracture			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pneumothorax Traumatic			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post Procedural Haematoma			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis Fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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 Flutter			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Angina Pectoris			
subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Coronary Syndrome			
subjects affected / exposed	5 / 597 (0.84%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure			
subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Chronic			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Myocardial Ischaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral Valve Incompetence			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			

subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pericardial Effusion			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus Node Dysfunction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Nervous system disorders			
Balance Disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain Compression			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid Artery Stenosis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Haemorrhage			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Ischaemia			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cognitive Disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Cerebral Infarction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar Infarction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Loss of Consciousness			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia Gravis			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nerve Compression			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic Stroke			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Epilepsy			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre Syndrome			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Haemorrhagic Stroke			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Neuralgia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Optic Nerve Compression			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Paraparesis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraplegia			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech Disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Cord Compression			
subjects affected / exposed	11 / 597 (1.84%)	0 / 72 (0.00%)	11 / 602 (1.83%)
occurrences causally related to treatment / all	0 / 13	0 / 0	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			

subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular Encephalopathy			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	6 / 597 (1.01%)	1 / 72 (1.39%)	6 / 602 (1.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Cataract			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Glaucoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dental Caries			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Mass			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	4 / 602 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Duodenitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Perforation			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Intestinal Ischaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Gastrointestinal Haemorrhage			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal Hernia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Intestinal Haemorrhage			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 72 (1.39%)	0 / 602 (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
Intestinal Obstruction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Mouth Haemorrhage			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Nausea			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Polyp			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Peptic Ulcer			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hepatitis Toxic			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hepatocellular Injury			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Hepatobiliary Disease			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin Lesion			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	8 / 597 (1.34%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 11	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Bladder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Ureteric			

subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Kidney Disease			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Dysuria			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Outlet Obstruction			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
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	2 / 597 (0.34%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Urinary Tract Symptoms			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Micturition Urgency			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pollakiuria			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			

subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Injury			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Ureteric Obstruction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Urethral Haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral Stenosis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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 Tract Obstruction			
subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Retention			
subjects affected / exposed	10 / 597 (1.68%)	0 / 72 (0.00%)	11 / 602 (1.83%)
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Gouty Arthritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Arthralgia			

subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	4 / 602 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Back Pain			
subjects affected / exposed	5 / 597 (0.84%)	0 / 72 (0.00%)	10 / 602 (1.66%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of Jaw			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular Weakness			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	3 / 602 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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 Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Pain			
subjects affected / exposed	8 / 597 (1.34%)	0 / 72 (0.00%)	6 / 602 (1.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in Extremity			

subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in Jaw			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pathological Fracture			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Column Stenosis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trismus			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Spondylitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Bronchitis			
subjects affected / exposed	4 / 597 (0.67%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			

subjects affected / exposed	3 / 597 (0.50%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Cellulitis Orbital			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Device Related Infection			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Fungaemia			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Gastrointestinal Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Lung Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Herpes Zoster			

subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Osteomyelitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (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
Pyelonephritis Acute			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	12 / 597 (2.01%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	2 / 13	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis Acute			

subjects affected / exposed	0 / 597 (0.00%)	1 / 72 (1.39%)	0 / 602 (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
Pyelonephritis Chronic			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinusitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Sepsis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	8 / 597 (1.34%)	0 / 72 (0.00%)	5 / 602 (0.83%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Cord Infection			

subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	5 / 597 (0.84%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	4 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 597 (0.34%)	0 / 72 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes Mellitus			
subjects affected / exposed	0 / 597 (0.00%)	1 / 72 (1.39%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	4 / 597 (0.67%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic Syndrome			
subjects affected / exposed	0 / 597 (0.00%)	0 / 72 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Abiraterone Acetate+Prednisone +ADT	DB Period Placebo to OLE Abiraterone Acetate	Placebo + ADT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	533 / 597 (89.28%)	35 / 72 (48.61%)	515 / 602 (85.55%)
Investigations			
Alanine Aminotransferase Increased			

subjects affected / exposed	100 / 597 (16.75%)	5 / 72 (6.94%)	77 / 602 (12.79%)
occurrences (all)	239	14	135
Aspartate Aminotransferase Increased			
subjects affected / exposed	91 / 597 (15.24%)	5 / 72 (6.94%)	68 / 602 (11.30%)
occurrences (all)	196	12	141
Weight Increased			
subjects affected / exposed	54 / 597 (9.05%)	0 / 72 (0.00%)	51 / 602 (8.47%)
occurrences (all)	85	0	78
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	40 / 597 (6.70%)	1 / 72 (1.39%)	32 / 602 (5.32%)
occurrences (all)	68	1	48
Vascular disorders			
Hypertension			
subjects affected / exposed	229 / 597 (38.36%)	4 / 72 (5.56%)	133 / 602 (22.09%)
occurrences (all)	639	4	289
Hot Flush			
subjects affected / exposed	92 / 597 (15.41%)	1 / 72 (1.39%)	76 / 602 (12.62%)
occurrences (all)	126	1	88
Nervous system disorders			
Headache			
subjects affected / exposed	46 / 597 (7.71%)	2 / 72 (2.78%)	31 / 602 (5.15%)
occurrences (all)	80	31	60
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	58 / 597 (9.72%)	3 / 72 (4.17%)	89 / 602 (14.78%)
occurrences (all)	88	7	139
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	31 / 597 (5.19%)	0 / 72 (0.00%)	27 / 602 (4.49%)
occurrences (all)	48	0	36
Fatigue			
subjects affected / exposed	84 / 597 (14.07%)	1 / 72 (1.39%)	90 / 602 (14.95%)
occurrences (all)	132	1	115
Oedema Peripheral			

subjects affected / exposed	61 / 597 (10.22%)	2 / 72 (2.78%)	55 / 602 (9.14%)
occurrences (all)	85	4	75
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	39 / 597 (6.53%)	0 / 72 (0.00%)	35 / 602 (5.81%)
occurrences (all)	57	0	45
Nausea			
subjects affected / exposed	42 / 597 (7.04%)	1 / 72 (1.39%)	40 / 602 (6.64%)
occurrences (all)	53	1	52
Diarrhoea			
subjects affected / exposed	37 / 597 (6.20%)	0 / 72 (0.00%)	44 / 602 (7.31%)
occurrences (all)	47	0	56
Constipation			
subjects affected / exposed	68 / 597 (11.39%)	2 / 72 (2.78%)	67 / 602 (11.13%)
occurrences (all)	85	3	77
Abdominal Pain			
subjects affected / exposed	26 / 597 (4.36%)	0 / 72 (0.00%)	31 / 602 (5.15%)
occurrences (all)	41	0	41
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	41 / 597 (6.87%)	2 / 72 (2.78%)	18 / 602 (2.99%)
occurrences (all)	53	2	22
Psychiatric disorders			
Insomnia			
subjects affected / exposed	32 / 597 (5.36%)	1 / 72 (1.39%)	30 / 602 (4.98%)
occurrences (all)	36	2	31
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	96 / 597 (16.08%)	4 / 72 (5.56%)	86 / 602 (14.29%)
occurrences (all)	154	5	147
Back Pain			
subjects affected / exposed	120 / 597 (20.10%)	5 / 72 (6.94%)	122 / 602 (20.27%)
occurrences (all)	172	8	174
Bone Pain			
subjects affected / exposed	81 / 597 (13.57%)	0 / 72 (0.00%)	90 / 602 (14.95%)
occurrences (all)	109	0	113

Musculoskeletal Pain			
subjects affected / exposed	32 / 597 (5.36%)	2 / 72 (2.78%)	42 / 602 (6.98%)
occurrences (all)	42	2	58
Pain in Extremity			
subjects affected / exposed	72 / 597 (12.06%)	2 / 72 (2.78%)	69 / 602 (11.46%)
occurrences (all)	108	2	95
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	39 / 597 (6.53%)	3 / 72 (4.17%)	20 / 602 (3.32%)
occurrences (all)	53	3	23
Upper Respiratory Tract Infection			
subjects affected / exposed	42 / 597 (7.04%)	2 / 72 (2.78%)	29 / 602 (4.82%)
occurrences (all)	61	2	56
Nasopharyngitis			
subjects affected / exposed	47 / 597 (7.87%)	0 / 72 (0.00%)	36 / 602 (5.98%)
occurrences (all)	80	0	55
Influenza			
subjects affected / exposed	42 / 597 (7.04%)	3 / 72 (4.17%)	20 / 602 (3.32%)
occurrences (all)	53	3	26
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	143 / 597 (23.95%)	9 / 72 (12.50%)	23 / 602 (3.82%)
occurrences (all)	323	17	53
Hyperglycaemia			
subjects affected / exposed	83 / 597 (13.90%)	5 / 72 (6.94%)	72 / 602 (11.96%)
occurrences (all)	261	12	149
Decreased Appetite			
subjects affected / exposed	23 / 597 (3.85%)	0 / 72 (0.00%)	33 / 602 (5.48%)
occurrences (all)	27	0	35

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	The purpose of the amendment was to address requests and recommendations from health authorities (HA), Investigators, and Ethics Committees (ECs).
18 April 2014	The purpose of the amendment was to add radiographic progression-free survival (rPFS) as a co-primary endpoint with overall survival (OS).
15 February 2017	The purpose of the amendment was to provide clarifications to the open-label extension (OLE) Phase of the study including an outline of the open-label treatment criteria for crossover into the OLE Phase and the time and events schedules for study assessments. A Long-term Extension (LTE) Phase was added to the study. Updates were also made to the OLE Phase prednisone packaging description.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As per protocol the long-term extension (LTE) phase was planned but LTE phase is not included as part of this study hence no data was reported for LTE phase.

Notes: