



## Clinical trial results: Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy Summary

EudraCT number	2004-000193-31
Trial protocol	GB
Global end of trial date	

### Results information

Result version number	v2 (current)
This version publication date	13 August 2023
First version publication date	27 February 2021
Version creation reason	<ul style="list-style-type: none"><li>New data added to full data set</li></ul> Adding recently completed arms of the STAMPEDE trial

### Trial information

#### Trial identification

Sponsor protocol code	PR08
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#### Additional study identifiers

ISRCTN number	ISRCTN78818544
ClinicalTrials.gov id (NCT number)	NCT00268476
WHO universal trial number (UTN)	-
Other trial identifiers	CTA: 20363/0404/001, MREC: 04/MRE07/35, Previous IRAS (Minimal Data Set): 31586

Notes:

### Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E6BT
Public contact	STAMPEDE Trial Team, MRCCTU at UCL, mrcctu.stampede@ucl.ac.uk
Scientific contact	STAMPEDE Trial Team, MRCCTU at UCL, 44 20 7670 4938, laura.murphy@ucl.ac.uk

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	Interim
Date of interim/final analysis	19 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No
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Notes:

## General information about the trial

Main objective of the trial:

This study aims to look at how to improve the way in which prostate cancer is currently managed i.e. by adding new treatments to the standard of care, whether it can enable men to live longer or, by modifying the type of hormone therapy, live at least as long and enjoy a better quality of life. The principal research question for most arms is whether the treatment concerned improves overall survival; however some comparisons such as metformin are being looked at for other reasons.

Protection of trial subjects:

In routine care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Switzerland: 49
Country: Number of subjects enrolled	United Kingdom: 7052
Worldwide total number of subjects	7101
EEA total number of subjects	0

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)	2658
From 65 to 84 years	4439
85 years and over	4

## Subject disposition

### Recruitment

Recruitment details:

First patient randomised 17Oct2005

### Pre-assignment

Screening details:

Screening data not available centrally

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded
Blinding implementation details:	
Not blinded	

### Arms

Are arms mutually exclusive?	No
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<b>Arm title</b>	Arm A (SOC for B,C,E comparisons)
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Arm description:

Reference patients for A vs B, C , E

Arm type	No intervention
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No investigational medicinal product assigned in this arm

<b>Arm title</b>	Arm B
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Arm description:

Zoledronic acid

Arm type	Experimental
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Investigational medicinal product name	Zoledronic acid
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for infusion in administration system
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Routes of administration	Intravenous use
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Dosage and administration details:

4mg at six 3-weekly cycles, then 4-weekly until 2 years

<b>Arm title</b>	Arm C
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Arm description:

Docetaxel

Arm type	Experimental
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Investigational medicinal product name	Docetaxel
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for solution for infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

75mg/m2 for six 3-weekly cycles

<b>Arm title</b>	Arm E
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Arm description:

Zoledronic Acid and Docetaxel

Arm type	Experimental
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Investigational medicinal product name	Zoledronic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use
Dosage and administration details: 4mg at six 3-weekly cycles, then 4-weekly until 2 years	
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use
Dosage and administration details: 75mg/m2 for six 3-weekly cycles	
<b>Arm title</b>	Arm A (SOC for D,F comparisons)
Arm description: Reference patients for A vs D, F	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Arm D
Arm description: Celecoxib	
Arm type	Experimental
Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 400mg twice a day for 1 year	
<b>Arm title</b>	Arm F
Arm description: Zoledronic Acid and Celecoxib	
Arm type	Experimental
Investigational medicinal product name	Zoledronic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use
Dosage and administration details: 4mg at six 3-weekly cycles, then 4-weekly until 2 years	
Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 400mg twice a day for 1 year	
<b>Arm title</b>	Arm A (SOC - G comparison)

Arm description:	
Reference patients for arm G	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Arm G
Arm description:	
Abiraterone	
Arm type	Experimental
Investigational medicinal product name	Abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1000mg	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5mg	
<b>Arm title</b>	Arm A (SOC - J comparison)
Arm description:	
Reference patients for J comparison	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Arm J
Arm description:	
Enzalutamide and Abiraterone	
Arm type	Experimental
Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
160mg	
Investigational medicinal product name	Abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1000mg	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

<b>Number of subjects in period 1</b>	Arm A (SOC for B,C,E comparisons)	Arm B	Arm C
Started	1184	593	592
Completed	1184	593	592

<b>Number of subjects in period 1</b>	Arm E	Arm A (SOC for D,F comparisons)	Arm D
Started	593	622	312
Completed	593	622	312

<b>Number of subjects in period 1</b>	Arm F	Arm A (SOC - G comparison)	Arm G
Started	311	957	960
Completed	311	957	960

<b>Number of subjects in period 1</b>	Arm A (SOC - J comparison)	Arm J
Started	987	989
Completed	987	989

## Baseline characteristics

Reporting groups	
Reporting group title	Arm A (SOC for B,C,E comparisons)
Reporting group description:	
Reference patients for A vs B, C , E	
Reporting group title	Arm B
Reporting group description:	
Zoledronic acid	
Reporting group title	Arm C
Reporting group description:	
Docetaxel	
Reporting group title	Arm E
Reporting group description:	
Zoledronic Acid and Docetaxel	
Reporting group title	Arm A (SOC for D,F comparisons)
Reporting group description:	
Reference patients for A vs D, F	
Reporting group title	Arm D
Reporting group description:	
Celecoxib	
Reporting group title	Arm F
Reporting group description:	
Zoledronic Acid and Celecoxib	
Reporting group title	Arm A (SOC - G comparison)
Reporting group description:	
Reference patients for arm G	
Reporting group title	Arm G
Reporting group description:	
Abiraterone	
Reporting group title	Arm A (SOC - J comparison)
Reporting group description:	
Reference patients for J comparison	
Reporting group title	Arm J
Reporting group description:	
Enzalutamide and Abiraterone	

Reporting group values	Arm A (SOC for B,C,E comparisons)	Arm B	Arm C
Number of subjects	1184	593	592
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	521	265	270
From 65-84 years	663	328	322
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	1184	593	592

Reporting group values	Arm E	Arm A (SOC for D,F comparisons)	Arm D
Number of subjects	593	622	312
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	252	294	139
From 65-84 years	341	328	173
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	593	622	312

Reporting group values	Arm F	Arm A (SOC - G comparison)	Arm G
Number of subjects	311	957	960
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	146	322	326
From 65-84 years	164	635	633
85 years and over	1	0	1
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	311	957	960

Reporting group values	Arm A (SOC - J comparison)	Arm J	Total
Number of subjects	987	989	7101



Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	269	291	2658
From 65-84 years	717	697	4439
85 years and over	1	1	4
Gender categorical Units: Subjects			
Female	0	0	0
Male	987	989	7101

### Subject analysis sets

Subject analysis set title	Arm A (SOC for B,C,E comparisons)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Reference patients (ABCE comparison)	
Subject analysis set title	Arm B (ZA)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Experimental group, AB comparison	
Subject analysis set title	Arm C (doce)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Arm A vs C	
Subject analysis set title	Arm E (doce+ZA)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Docetaxel and Zoledronic acid	
Subject analysis set title	Arm A (SOC for D,F comparisons)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Reference patients (ADF comparisons)	
Subject analysis set title	Arm D (cel)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Arm A vs D	
Subject analysis set title	Arm F (cel+ZA)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Arm A vs F	
Subject analysis set title	Arm A (SOC G comparison)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Control arm for G comparison	

Subject analysis set title	Arm G
Subject analysis set type	Intention-to-treat
Subject analysis set description: Abiraterone + prednisolone	
Subject analysis set title	Arm A (SOC J comparison)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Reference patients for A vs J	
Subject analysis set title	Arm J
Subject analysis set type	Intention-to-treat
Subject analysis set description: Enzalutamide and Abiraterone	

Reporting group values	Arm A (SOC for B,C,E comparisons)	Arm B (ZA)	Arm C (doce)
Number of subjects	1184	593	592
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	521	265	270
From 65-84 years	663	328	322
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	1184	593	592

Reporting group values	Arm E (doce+ZA)	Arm A (SOC for D,F comparisons)	Arm D (cel)
Number of subjects	593	622	312
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	252	294	139
From 65-84 years	341	328	173
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	593	622	312

Reporting group values	Arm F (cel+ZA)	Arm A (SOC G comparison)	Arm G
Number of subjects	311	957	960
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	146	322	326
From 65-84 years	164	635	633
85 years and over	1		1
Gender categorical Units: Subjects			
Female	0	0	0
Male	311	957	960

Reporting group values	Arm A (SOC J comparison)	Arm J	
Number of subjects	987	989	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Gender categorical Units: Subjects			
Female			
Male			

## End points

### End points reporting groups

Reporting group title	Arm A (SOC for B,C,E comparisons)
Reporting group description: Reference patients for A vs B, C , E	
Reporting group title	Arm B
Reporting group description: Zoledronic acid	
Reporting group title	Arm C
Reporting group description: Docetaxel	
Reporting group title	Arm E
Reporting group description: Zoledronic Acid and Docetaxel	
Reporting group title	Arm A (SOC for D,F comparisons)
Reporting group description: Reference patients for A vs D, F	
Reporting group title	Arm D
Reporting group description: Celecoxib	
Reporting group title	Arm F
Reporting group description: Zoledronic Acid and Celecoxib	
Reporting group title	Arm A (SOC - G comparison)
Reporting group description: Reference patients for arm G	
Reporting group title	Arm G
Reporting group description: Abiraterone	
Reporting group title	Arm A (SOC - J comparison)
Reporting group description: Reference patients for J comparison	
Reporting group title	Arm J
Reporting group description: Enzalutamide and Abiraterone	
Subject analysis set title	Arm A (SOC for B,C,E comparisons)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Reference patients (ABCE comparison)	
Subject analysis set title	Arm B (ZA)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Experimental group, AB comparison	
Subject analysis set title	Arm C (doce)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Arm A vs C	
Subject analysis set title	Arm E (doce+ZA)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Docetaxel and Zoledronic acid

Subject analysis set title	Arm A (SOC for D,F comparisons)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Reference patients (ADF comparisons)

Subject analysis set title	Arm D (cel)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Arm A vs D

Subject analysis set title	Arm F (cel+ZA)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Arm A vs F

Subject analysis set title	Arm A (SOC G comparison)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Control arm for G comparison

Subject analysis set title	Arm G
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Abiraterone + prednisolone

Subject analysis set title	Arm A (SOC J comparison)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Reference patients for A vs J

Subject analysis set title	Arm J
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Enzalutamide and Abiraterone

### Primary: Overall survival

End point title	Overall survival
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End point description:

End point type	Primary
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End point timeframe:

Event driven analysis

End point values	Arm A (SOC for B,C,E comparisons)	Arm B (ZA)	Arm C (doce)	Arm E (doce+ZA)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1184	593	592	593
Units: Patients				
Died	415	201	175	187

End point values	Arm A (SOC for D,F comparisons)	Arm D (cel)	Arm F (cel+ZA)	Arm A (SOC G comparison)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	622	312	311	957
Units: Patients				
Died	303	143	138	522

End point values	Arm G	Arm A (SOC J comparison)	Arm J	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	960	987	989	
Units: Patients				
Died	396	391	290	

### Statistical analyses

<b>Statistical analysis title</b>	Zoledronic Acid vs SOC
Comparison groups	Arm A (SOC for B,C,E comparisons) v Arm B (ZA)
Number of subjects included in analysis	1777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.11

<b>Statistical analysis title</b>	Docetaxel vs SOC
Comparison groups	Arm A (SOC for B,C,E comparisons) v Arm C (doce)
Number of subjects included in analysis	1776
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.93

<b>Statistical analysis title</b>	Docetaxel+Zoledronic Acid vs SOC
Comparison groups	Arm A (SOC for B,C,E comparisons) v Arm E (doce+ZA)
Number of subjects included in analysis	1777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.97

<b>Statistical analysis title</b>	Celecoxib vs SOC
Comparison groups	Arm D (cel) v Arm A (SOC for D,F comparisons)
Number of subjects included in analysis	934
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.847
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.2

<b>Statistical analysis title</b>	Celecoxib + Zoledronic acid vs SOC
Comparison groups	Arm A (SOC for D,F comparisons) v Arm F (cel+ZA)

Number of subjects included in analysis	933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.05

<b>Statistical analysis title</b>	Abiraterone vs SOC
Comparison groups	Arm A (SOC G comparison) v Arm G
Number of subjects included in analysis	1917
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.71

<b>Statistical analysis title</b>	Enzalutamide and Abiraterone vs SOC
Comparison groups	Arm A (SOC J comparison) v Arm J
Number of subjects included in analysis	1976
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.74



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Events to March 4 2015 for A vs B,C,E comparisons

Events to December 15 2015 for A vs D,F comparisons

Events to July 3 2022 for A vs G/J comparisons

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.0
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### Reporting groups

Reporting group title	SOC (Arm A, ABCE comparison)
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Reporting group description:

Reference patients, Arm A, randomised between A,B,C,E

Reporting group title	ZA (Arm B)
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Reporting group description:

Experimental patients, AB comparison

Reporting group title	Doce (Arm C)
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Reporting group description:

Arm C docetaxel patients

Reporting group title	Doce+ZA (Arm E)
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Reporting group description:

Docetaxel plus Zoledronic acid

Reporting group title	SOC (Arm A, ADF comparison)
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Reporting group description:

Reference patients, Arm A, randomised between A,D,F

Reporting group title	Celecoxib (Arm D)
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Reporting group description:

Experimental arm, celecoxib comparison

Reporting group title	Celecoxib + ZA
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Reporting group description:

(Arm F)

Reporting group title	SOC (Arm A, G comparison)
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Reporting group description: -

Reporting group title	Abiraterone (Arm G)
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Reporting group description: -

Reporting group title	SOC (Arm A, J comparison)
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Reporting group description: -

Reporting group title	Enzalutamide + Abiraterone (Arm J)
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Reporting group description: -

Serious adverse events	SOC (Arm A, ABCE comparison)	ZA (Arm B)	Doce (Arm C)
Total subjects affected by serious adverse events			
subjects affected / exposed	117 / 1184 (9.88%)	80 / 593 (13.49%)	176 / 592 (29.73%)
number of deaths (all causes)	415	201	175
number of deaths resulting from	7	2	3

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	1 / 592 (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
Hypotension			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Surgical - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 1184 (0.17%)	0 / 593 (0.00%)	1 / 592 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			

subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	4 / 592 (0.68%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	3 / 1184 (0.25%)	2 / 593 (0.34%)	6 / 592 (1.01%)
occurrences causally related to treatment / all	0 / 3	0 / 2	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 1184 (0.00%)	1 / 593 (0.17%)	0 / 592 (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
Pain			
subjects affected / exposed	2 / 1184 (0.17%)	0 / 593 (0.00%)	0 / 592 (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
Headache			
subjects affected / exposed	2 / 1184 (0.17%)	0 / 593 (0.00%)	0 / 592 (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 - other			
subjects affected / exposed	10 / 1184 (0.84%)	11 / 593 (1.85%)	18 / 592 (3.04%)
occurrences causally related to treatment / all	0 / 10	0 / 11	5 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			

subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	8 / 592 (1.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Social - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	4 / 1184 (0.34%)	3 / 593 (0.51%)	5 / 592 (0.84%)
occurrences causally related to treatment / all	0 / 4	0 / 3	4 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory - other			
subjects affected / exposed	14 / 1184 (1.18%)	10 / 593 (1.69%)	22 / 592 (3.72%)
occurrences causally related to treatment / all	0 / 15	0 / 10	8 / 23
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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
Cognitive disorder			

subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric - other			
subjects affected / exposed	1 / 1184 (0.08%)	1 / 593 (0.17%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Thrombocytopenia			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	1 / 592 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations - other			
subjects affected / exposed	2 / 1184 (0.17%)	1 / 593 (0.17%)	5 / 592 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 1	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Bilirubin conjugated increased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	7 / 1184 (0.59%)	4 / 593 (0.67%)	4 / 592 (0.68%)
occurrences causally related to treatment / all	0 / 7	0 / 4	1 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
Arrhythmia			
subjects affected / exposed	2 / 1184 (0.17%)	1 / 593 (0.17%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart failure			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac - other			
subjects affected / exposed	7 / 1184 (0.59%)	7 / 593 (1.18%)	10 / 592 (1.69%)
occurrences causally related to treatment / all	0 / 7	0 / 7	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chest pain			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1184 (0.00%)	2 / 593 (0.34%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system - other			
subjects affected / exposed	12 / 1184 (1.01%)	5 / 593 (0.84%)	7 / 592 (1.18%)
occurrences causally related to treatment / all	0 / 14	0 / 5	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Seizure			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke			

subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 1184 (0.42%)	3 / 593 (0.51%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 8	0 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	7 / 1184 (0.59%)	3 / 593 (0.51%)	77 / 592 (13.01%)
occurrences causally related to treatment / all	0 / 7	0 / 4	79 / 83
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Neutrophil count decreased			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	3 / 592 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
ear - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye - other			
subjects affected / exposed	1 / 1184 (0.08%)	1 / 593 (0.17%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Conjunctivitis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 1184 (0.34%)	4 / 593 (0.67%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 4	0 / 4	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	3 / 1184 (0.25%)	1 / 593 (0.17%)	3 / 592 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	5 / 1184 (0.42%)	1 / 593 (0.17%)	8 / 592 (1.35%)
occurrences causally related to treatment / all	0 / 5	0 / 1	5 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 1184 (0.17%)	2 / 593 (0.34%)	3 / 592 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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
Haemorrhage			
subjects affected / exposed	2 / 1184 (0.17%)	1 / 593 (0.17%)	2 / 592 (0.34%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal - other			



subjects affected / exposed	11 / 1184 (0.93%)	5 / 593 (0.84%)	12 / 592 (2.03%)
occurrences causally related to treatment / all	0 / 12	0 / 5	2 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspepsia			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatobiliary - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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
Rash			
subjects affected / exposed	0 / 1184 (0.00%)	1 / 593 (0.17%)	1 / 592 (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
Skin - other			
subjects affected / exposed	1 / 1184 (0.08%)	1 / 593 (0.17%)	5 / 592 (0.84%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	4 / 1184 (0.34%)	2 / 593 (0.34%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 1184 (0.17%)	2 / 593 (0.34%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	4 / 1184 (0.34%)	3 / 593 (0.51%)	1 / 592 (0.17%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary - other			
subjects affected / exposed	18 / 1184 (1.52%)	9 / 593 (1.52%)	5 / 592 (0.84%)
occurrences causally related to treatment / all	0 / 20	0 / 9	0 / 5
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary frequency			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Bone pain			
subjects affected / exposed	3 / 1184 (0.25%)	2 / 593 (0.34%)	3 / 592 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 1184 (0.08%)	1 / 593 (0.17%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal - other			
subjects affected / exposed	13 / 1184 (1.10%)	15 / 593 (2.53%)	12 / 592 (2.03%)
occurrences causally related to treatment / all	0 / 13	10 / 15	3 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 1184 (0.42%)	2 / 593 (0.34%)	6 / 592 (1.01%)
occurrences causally related to treatment / all	0 / 6	0 / 2	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	1 / 592 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections - other			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			

subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Glucose tolerance decreased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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
Hypokalaemia			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	0 / 592 (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
Anorexia nervosa			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	1 / 1184 (0.08%)	0 / 593 (0.00%)	1 / 592 (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
Hypophosphataemia			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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
Diabetes mellitus			

subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	1 / 592 (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 - other			
subjects affected / exposed	0 / 1184 (0.00%)	2 / 593 (0.34%)	1 / 592 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Doce+ZA (Arm E)	SOC (Arm A, ADF comparison)	Celecoxib (Arm D)
Total subjects affected by serious adverse events			
subjects affected / exposed	209 / 593 (35.24%)	74 / 622 (11.90%)	40 / 312 (12.82%)
number of deaths (all causes)	187	303	143
number of deaths resulting from adverse events	8	6	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 593 (0.00%)	1 / 622 (0.16%)	0 / 312 (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
Hypotension			
subjects affected / exposed	4 / 593 (0.67%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	2 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			

subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Surgical - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 593 (0.34%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	17 / 593 (2.87%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	5 / 18	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 593 (0.17%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Headache			
subjects affected / exposed	2 / 593 (0.34%)	2 / 622 (0.32%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General - other			
subjects affected / exposed	17 / 593 (2.87%)	8 / 622 (1.29%)	6 / 312 (1.92%)
occurrences causally related to treatment / all	0 / 19	0 / 8	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	4 / 593 (0.67%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Social - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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	5 / 593 (0.84%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	2 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory - other			
subjects affected / exposed	22 / 593 (3.71%)	11 / 622 (1.77%)	7 / 312 (2.24%)
occurrences causally related to treatment / all	5 / 23	0 / 12	0 / 7
deaths causally related to treatment / all	1 / 3	0 / 1	0 / 2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	1 / 312 (0.32%)
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 - other			
subjects affected / exposed	0 / 593 (0.00%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depression			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Thrombocytopenia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations - other			



subjects affected / exposed	11 / 593 (1.85%)	1 / 622 (0.16%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	7 / 12	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	5 / 593 (0.84%)	5 / 622 (0.80%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Arrhythmia			
subjects affected / exposed	6 / 593 (1.01%)	0 / 622 (0.00%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	2 / 7	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart failure			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac - other			
subjects affected / exposed	9 / 593 (1.52%)	3 / 622 (0.48%)	3 / 312 (0.96%)
occurrences causally related to treatment / all	0 / 9	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chest pain			

subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Nervous system disorders</b>			
Dizziness			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system - other			
subjects affected / exposed	14 / 593 (2.36%)	8 / 622 (1.29%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 14	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
Anaemia			
subjects affected / exposed	2 / 593 (0.34%)	1 / 622 (0.16%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	65 / 593 (10.96%)	4 / 622 (0.64%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	66 / 73	0 / 4	0 / 0
deaths causally related to treatment / all	3 / 3	0 / 0	0 / 0
Neutrophil count decreased			

subjects affected / exposed	9 / 593 (1.52%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	9 / 9	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
ear - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye - other			
subjects affected / exposed	2 / 593 (0.34%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 593 (1.18%)	3 / 622 (0.48%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 7	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 593 (0.17%)	3 / 622 (0.48%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	10 / 593 (1.69%)	4 / 622 (0.64%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	5 / 11	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nausea			
subjects affected / exposed	6 / 593 (1.01%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	3 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	6 / 593 (1.01%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Haemorrhage			
subjects affected / exposed	5 / 593 (0.84%)	0 / 622 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 5	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal - other			
subjects affected / exposed	16 / 593 (2.70%)	5 / 622 (0.80%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	4 / 19	0 / 6	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatobiliary - other			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Nail discolouration			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Rash			
subjects affected / exposed	2 / 593 (0.34%)	0 / 622 (0.00%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin - other			
subjects affected / exposed	6 / 593 (1.01%)	1 / 622 (0.16%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 593 (0.34%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Haematuria			
subjects affected / exposed	3 / 593 (0.51%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	3 / 593 (0.51%)	2 / 622 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary - other			

subjects affected / exposed	8 / 593 (1.35%)	10 / 622 (1.61%)	5 / 312 (1.60%)
occurrences causally related to treatment / all	0 / 8	0 / 12	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Nephrolithiasis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary frequency			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 593 (0.17%)	3 / 622 (0.48%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Musculoskeletal - other			
subjects affected / exposed	38 / 593 (6.41%)	7 / 622 (1.13%)	6 / 312 (1.92%)
occurrences causally related to treatment / all	20 / 41	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			

subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Urinary tract infection			
subjects affected / exposed	4 / 593 (0.67%)	2 / 622 (0.32%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 593 (0.17%)	1 / 622 (0.16%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections - other			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Metabolism and nutrition disorders</b>			
Glucose tolerance decreased			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Hypokalaemia			

subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia nervosa			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Hypocalcaemia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 593 (0.17%)	0 / 622 (0.00%)	0 / 312 (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
Metabolism and nutrition - other			
subjects affected / exposed	4 / 593 (0.67%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Celecoxib + ZA	SOC (Arm A, G comparison)	Abiraterone (Arm G)
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 311 (20.58%)	144 / 957 (15.05%)	281 / 960 (29.27%)
number of deaths (all causes)	138	522	396
number of deaths resulting from adverse events	5	4	14



Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 311 (0.00%)	5 / 957 (0.52%)	3 / 960 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 311 (0.64%)	1 / 957 (0.10%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular - other			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Surgical and medical procedures			
Surgical - other			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			

subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	2 / 311 (0.64%)	4 / 957 (0.42%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	0 / 960 (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
Headache			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General - other			
subjects affected / exposed	4 / 311 (1.29%)	10 / 957 (1.04%)	27 / 960 (2.81%)
occurrences causally related to treatment / all	0 / 4	0 / 10	0 / 27
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Fall			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	6 / 960 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			

subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Social - other			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 311 (0.96%)	7 / 957 (0.73%)	11 / 960 (1.15%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory - other			
subjects affected / exposed	6 / 311 (1.93%)	15 / 957 (1.57%)	24 / 960 (2.50%)
occurrences causally related to treatment / all	0 / 6	0 / 17	0 / 28
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	1 / 311 (0.32%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric - other			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Thrombocytopenia			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations - other			
subjects affected / exposed	2 / 311 (0.64%)	1 / 957 (0.10%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	1 / 311 (0.32%)	7 / 957 (0.73%)	17 / 960 (1.77%)
occurrences causally related to treatment / all	0 / 1	0 / 7	1 / 17
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart failure			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac - other			
subjects affected / exposed	6 / 311 (1.93%)	8 / 957 (0.84%)	31 / 960 (3.23%)
occurrences causally related to treatment / all	1 / 6	0 / 8	3 / 33
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chest pain			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system - other			
subjects affected / exposed	6 / 311 (1.93%)	15 / 957 (1.57%)	23 / 960 (2.40%)
occurrences causally related to treatment / all	1 / 7	0 / 15	0 / 26
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
Seizure			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke			

subjects affected / exposed	0 / 311 (0.00%)	2 / 957 (0.21%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 311 (0.96%)	7 / 957 (0.73%)	6 / 960 (0.63%)
occurrences causally related to treatment / all	0 / 3	0 / 10	1 / 9
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	2 / 311 (0.64%)	2 / 957 (0.21%)	3 / 960 (0.31%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood - other			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
ear - other			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye - other			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Conjunctivitis			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 311 (1.93%)	8 / 957 (0.84%)	11 / 960 (1.15%)
occurrences causally related to treatment / all	0 / 6	0 / 8	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 311 (0.32%)	2 / 957 (0.21%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 311 (0.96%)	2 / 957 (0.21%)	12 / 960 (1.25%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 311 (0.00%)	2 / 957 (0.21%)	6 / 960 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	1 / 311 (0.32%)	7 / 957 (0.73%)	5 / 960 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 12	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal - other			

subjects affected / exposed	7 / 311 (2.25%)	19 / 957 (1.99%)	28 / 960 (2.92%)
occurrences causally related to treatment / all	1 / 7	0 / 19	0 / 30
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspepsia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatobiliary - other			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 311 (0.00%)	1 / 957 (0.10%)	3 / 960 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin - other			
subjects affected / exposed	2 / 311 (0.64%)	1 / 957 (0.10%)	11 / 960 (1.15%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			



Acute kidney injury			
subjects affected / exposed	2 / 311 (0.64%)	1 / 957 (0.10%)	6 / 960 (0.63%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 311 (0.32%)	7 / 957 (0.73%)	7 / 960 (0.73%)
occurrences causally related to treatment / all	0 / 1	0 / 13	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	2 / 311 (0.64%)	4 / 957 (0.42%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary - other			
subjects affected / exposed	5 / 311 (1.61%)	15 / 957 (1.57%)	24 / 960 (2.50%)
occurrences causally related to treatment / all	0 / 6	0 / 17	0 / 28
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary frequency			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction			
subjects affected / exposed	0 / 311 (0.00%)	5 / 957 (0.52%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Bone pain			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	4 / 960 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal - other			
subjects affected / exposed	9 / 311 (2.89%)	8 / 957 (0.84%)	22 / 960 (2.29%)
occurrences causally related to treatment / all	4 / 9	0 / 8	0 / 28
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 311 (0.64%)	8 / 957 (0.84%)	16 / 960 (1.67%)
occurrences causally related to treatment / all	0 / 2	0 / 9	1 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	3 / 311 (0.96%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections - other			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	6 / 960 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Abdominal infection			

subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 311 (0.00%)	3 / 957 (0.31%)	26 / 960 (2.71%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 34
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Sepsis			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	2 / 960 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Glucose tolerance decreased			
subjects affected / exposed	1 / 311 (0.32%)	0 / 957 (0.00%)	0 / 960 (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
Hypokalaemia			
subjects affected / exposed	1 / 311 (0.32%)	1 / 957 (0.10%)	5 / 960 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia nervosa			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 311 (0.00%)	2 / 957 (0.21%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	1 / 311 (0.32%)	1 / 957 (0.10%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition - other			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	1 / 960 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 311 (0.00%)	0 / 957 (0.00%)	0 / 960 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	SOC (Arm A, J comparison)	Enzalutamide + Abiraterone (Arm J)	
Total subjects affected by serious adverse events			
subjects affected / exposed	156 / 987 (15.81%)	302 / 989 (30.54%)	
number of deaths (all causes)	391	290	
number of deaths resulting from adverse events	1	16	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 987 (0.00%)	5 / 989 (0.51%)	
occurrences causally related to treatment / all	0 / 0	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 987 (0.10%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			

subjects affected / exposed	3 / 987 (0.30%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular - other			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Surgical - other			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	4 / 987 (0.41%)	9 / 989 (0.91%)	
occurrences causally related to treatment / all	0 / 4	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 987 (0.10%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Headache			
subjects affected / exposed	1 / 987 (0.10%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General - other			
subjects affected / exposed	8 / 987 (0.81%)	16 / 989 (1.62%)	
occurrences causally related to treatment / all	0 / 9	3 / 17	
deaths causally related to treatment / all	0 / 0	0 / 5	
Fall			
subjects affected / exposed	3 / 987 (0.30%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Social - other			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	1 / 987 (0.10%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	6 / 987 (0.61%)	5 / 989 (0.51%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory - other			
subjects affected / exposed	9 / 987 (0.91%)	12 / 989 (1.21%)	
occurrences causally related to treatment / all	0 / 9	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 987 (0.00%)	3 / 989 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric - other			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 987 (0.10%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Thrombocytopenia			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations - other			

subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	14 / 987 (1.42%)	23 / 989 (2.33%)	
occurrences causally related to treatment / all	0 / 14	4 / 25	
deaths causally related to treatment / all	0 / 0	0 / 4	
Arrhythmia			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
subjects affected / exposed	1 / 987 (0.10%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac - other			
subjects affected / exposed	12 / 987 (1.22%)	24 / 989 (2.43%)	
occurrences causally related to treatment / all	0 / 12	6 / 25	
deaths causally related to treatment / all	0 / 0	0 / 4	
Chest pain			



subjects affected / exposed	0 / 987 (0.00%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system - other			
subjects affected / exposed	7 / 987 (0.71%)	18 / 989 (1.82%)	
occurrences causally related to treatment / all	1 / 7	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 987 (0.10%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	0 / 1	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke			
subjects affected / exposed	2 / 987 (0.20%)	7 / 989 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 987 (0.41%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	14 / 987 (1.42%)	9 / 989 (0.91%)	
occurrences causally related to treatment / all	11 / 14	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			

subjects affected / exposed	1 / 987 (0.10%)	3 / 989 (0.30%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood - other			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
ear - other			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye - other			
subjects affected / exposed	0 / 987 (0.00%)	3 / 989 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 987 (0.41%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 987 (0.10%)	3 / 989 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 987 (0.20%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	1 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 987 (0.30%)	5 / 989 (0.51%)	
occurrences causally related to treatment / all	1 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	6 / 987 (0.61%)	9 / 989 (0.91%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal - other			
subjects affected / exposed	18 / 987 (1.82%)	17 / 989 (1.72%)	
occurrences causally related to treatment / all	0 / 23	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspepsia			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatobiliary - other			
subjects affected / exposed	2 / 987 (0.20%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 987 (0.10%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Nail discolouration			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	2 / 987 (0.20%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin - other			
subjects affected / exposed	2 / 987 (0.20%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 987 (0.10%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 987 (0.30%)	6 / 989 (0.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematuria			
subjects affected / exposed	4 / 987 (0.41%)	5 / 989 (0.51%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary - other			

subjects affected / exposed	9 / 987 (0.91%)	12 / 989 (1.21%)	
occurrences causally related to treatment / all	0 / 9	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary frequency			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction			
subjects affected / exposed	10 / 987 (1.01%)	3 / 989 (0.30%)	
occurrences causally related to treatment / all	0 / 11	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	2 / 987 (0.20%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 987 (0.10%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal - other			
subjects affected / exposed	11 / 987 (1.11%)	34 / 989 (3.44%)	
occurrences causally related to treatment / all	0 / 14	0 / 36	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 987 (0.20%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			

subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Urinary tract infection			
subjects affected / exposed	9 / 987 (0.91%)	20 / 989 (2.02%)	
occurrences causally related to treatment / all	0 / 9	1 / 24	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 987 (0.00%)	7 / 989 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections - other			
subjects affected / exposed	2 / 987 (0.20%)	5 / 989 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal infection			
subjects affected / exposed	0 / 987 (0.00%)	2 / 989 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	10 / 987 (1.01%)	21 / 989 (2.12%)	
occurrences causally related to treatment / all	0 / 12	0 / 29	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sepsis			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Metabolism and nutrition disorders</b>			
Glucose tolerance decreased			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 987 (0.00%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia nervosa			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 987 (0.10%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 987 (0.00%)	0 / 989 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition - other			
subjects affected / exposed	0 / 987 (0.00%)	4 / 989 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 987 (0.00%)	1 / 989 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	SOC (Arm A, ABCE comparison)	ZA (Arm B)	Doce (Arm C)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1152 / 1184 (97.30%)	579 / 593 (97.64%)	571 / 592 (96.45%)
Vascular disorders			
Hypertension			
subjects affected / exposed	84 / 1184 (7.09%)	50 / 593 (8.43%)	44 / 592 (7.43%)
occurrences (all)	129	90	74
Hot flush			
subjects affected / exposed	968 / 1184 (81.76%)	462 / 593 (77.91%)	454 / 592 (76.69%)
occurrences (all)	5324	2400	2425
General disorders and administration site conditions			
Fever			
subjects affected / exposed	29 / 1184 (2.45%)	38 / 593 (6.41%)	49 / 592 (8.28%)
occurrences (all)	39	51	58
Fatigue			
subjects affected / exposed	632 / 1184 (53.38%)	342 / 593 (57.67%)	431 / 592 (72.80%)
occurrences (all)	1999	1144	1616
Oedema			
subjects affected / exposed	164 / 1184 (13.85%)	72 / 593 (12.14%)	159 / 592 (26.86%)
occurrences (all)	350	124	354
Influenza like illness			
subjects affected / exposed	97 / 1184 (8.19%)	215 / 593 (36.26%)	87 / 592 (14.70%)
occurrences (all)	125	363	119
Pain			
subjects affected / exposed	363 / 1184 (30.66%)	240 / 593 (40.47%)	188 / 592 (31.76%)
occurrences (all)	720	485	384
General - other			
subjects affected / exposed	99 / 1184 (8.36%)	62 / 593 (10.46%)	86 / 592 (14.53%)
occurrences (all)	121	79	108
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	39 / 1184 (3.29%)	21 / 593 (3.54%)	58 / 592 (9.80%)
occurrences (all)	47	24	69
Reproductive system and breast disorders			



Erectile dysfunction subjects affected / exposed occurrences (all)	586 / 1184 (49.49%) 3230	296 / 593 (49.92%) 1587	277 / 592 (46.79%) 1545
Gynaecomastia subjects affected / exposed occurrences (all)	84 / 1184 (7.09%) 145	38 / 593 (6.41%) 57	29 / 592 (4.90%) 41
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	129 / 1184 (10.90%) 229	56 / 593 (9.44%) 73	95 / 592 (16.05%) 152
Dyspnoea subjects affected / exposed occurrences (all)	171 / 1184 (14.44%) 362	82 / 593 (13.83%) 154	122 / 592 (20.61%) 256
Rhinitis subjects affected / exposed occurrences (all)	62 / 1184 (5.24%) 102	32 / 593 (5.40%) 55	41 / 592 (6.93%) 71
Respiratory - other subjects affected / exposed occurrences (all)	95 / 1184 (8.02%) 150	58 / 593 (9.78%) 88	77 / 592 (13.01%) 115
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	291 / 1184 (24.58%) 784	152 / 593 (25.63%) 362	189 / 592 (31.93%) 457
Anxiety subjects affected / exposed occurrences (all)	0 / 1184 (0.00%) 0	0 / 593 (0.00%) 0	0 / 592 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 1184 (0.00%) 0	0 / 593 (0.00%) 0	0 / 592 (0.00%) 0
Libido decreased subjects affected / exposed occurrences (all)	0 / 1184 (0.00%) 0	0 / 593 (0.00%) 0	0 / 592 (0.00%) 0
Psychiatric - other subjects affected / exposed occurrences (all)	195 / 1184 (16.47%) 482	79 / 593 (13.32%) 171	100 / 592 (16.89%) 191

Investigations			
Neutrophil count			
subjects affected / exposed	46 / 1184 (3.89%)	25 / 593 (4.22%)	114 / 592 (19.26%)
occurrences (all)	82	37	160
Alkaline phosphatase increased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences (all)	0	0	0
cholesterol high			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences (all)	0	0	0
Investigations - other			
subjects affected / exposed	297 / 1184 (25.08%)	161 / 593 (27.15%)	160 / 592 (27.03%)
occurrences (all)	587	301	353
Aspartate aminotransferase increased			
subjects affected / exposed	32 / 1184 (2.70%)	17 / 593 (2.87%)	21 / 592 (3.55%)
occurrences (all)	58	31	39
Alanine aminotransferase increased			
subjects affected / exposed	110 / 1184 (9.29%)	55 / 593 (9.27%)	69 / 592 (11.66%)
occurrences (all)	218	102	139
Platelet count decreased			
subjects affected / exposed	28 / 1184 (2.36%)	21 / 593 (3.54%)	26 / 592 (4.39%)
occurrences (all)	60	38	60
Weight increased			
subjects affected / exposed	0 / 1184 (0.00%)	0 / 593 (0.00%)	0 / 592 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
cardiac - other			
subjects affected / exposed	60 / 1184 (5.07%)	24 / 593 (4.05%)	35 / 592 (5.91%)
occurrences (all)	133	37	59
Arrhythmia			
subjects affected / exposed	41 / 1184 (3.46%)	21 / 593 (3.54%)	21 / 592 (3.55%)
occurrences (all)	63	40	30
Nervous system disorders			
Dizziness			
subjects affected / exposed	141 / 1184 (11.91%)	75 / 593 (12.65%)	88 / 592 (14.86%)
occurrences (all)	252	152	141

Headache			
subjects affected / exposed	161 / 1184 (13.60%)	86 / 593 (14.50%)	95 / 592 (16.05%)
occurrences (all)	334	153	190
Nervous system - other			
subjects affected / exposed	106 / 1184 (8.95%)	64 / 593 (10.79%)	235 / 592 (39.70%)
occurrences (all)	163	97	597
Cognitive disorder			
subjects affected / exposed	21 / 1184 (1.77%)	16 / 593 (2.70%)	10 / 592 (1.69%)
occurrences (all)	26	21	12
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	322 / 1184 (27.20%)	212 / 593 (35.75%)	228 / 592 (38.51%)
occurrences (all)	931	653	691
Eye disorders			
Vision blurred			
subjects affected / exposed	54 / 1184 (4.56%)	27 / 593 (4.55%)	44 / 592 (7.43%)
occurrences (all)	85	54	73
Eye - other			
subjects affected / exposed	74 / 1184 (6.25%)	41 / 593 (6.91%)	91 / 592 (15.37%)
occurrences (all)	113	67	152
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	160 / 1184 (13.51%)	76 / 593 (12.82%)	114 / 592 (19.26%)
occurrences (all)	298	131	200
Constipation			
subjects affected / exposed	218 / 1184 (18.41%)	147 / 593 (24.79%)	207 / 592 (34.97%)
occurrences (all)	440	278	389
Diarrhoea			
subjects affected / exposed	251 / 1184 (21.20%)	139 / 593 (23.44%)	247 / 592 (41.72%)
occurrences (all)	495	250	499
Dyspepsia			
subjects affected / exposed	155 / 1184 (13.09%)	76 / 593 (12.82%)	137 / 592 (23.14%)
occurrences (all)	314	123	245
Flatulence			

subjects affected / exposed	167 / 1184 (14.10%)	79 / 593 (13.32%)	88 / 592 (14.86%)
occurrences (all)	395	160	158
Haemorrhage			
subjects affected / exposed	90 / 1184 (7.60%)	36 / 593 (6.07%)	44 / 592 (7.43%)
occurrences (all)	148	70	71
Nausea			
subjects affected / exposed	128 / 1184 (10.81%)	77 / 593 (12.98%)	151 / 592 (25.51%)
occurrences (all)	210	131	226
Vomiting			
subjects affected / exposed	61 / 1184 (5.15%)	30 / 593 (5.06%)	57 / 592 (9.63%)
occurrences (all)	81	39	73
Stomatitis			
subjects affected / exposed	36 / 1184 (3.04%)	25 / 593 (4.22%)	153 / 592 (25.84%)
occurrences (all)	57	31	210
Gastrointestinal - other			
subjects affected / exposed	181 / 1184 (15.29%)	75 / 593 (12.65%)	156 / 592 (26.35%)
occurrences (all)	294	108	260
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	65 / 1184 (5.49%)	35 / 593 (5.90%)	37 / 592 (6.25%)
occurrences (all)	105	69	71
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	61 / 1184 (5.15%)	37 / 593 (6.24%)	258 / 592 (43.58%)
occurrences (all)	109	51	583
Rash			
subjects affected / exposed	117 / 1184 (9.88%)	67 / 593 (11.30%)	73 / 592 (12.33%)
occurrences (all)	199	91	104
Alopecia			
subjects affected / exposed	7 / 1184 (0.59%)	2 / 593 (0.34%)	80 / 592 (13.51%)
occurrences (all)	7	3	136
Skin - other			
subjects affected / exposed	202 / 1184 (17.06%)	89 / 593 (15.01%)	238 / 592 (40.20%)
occurrences (all)	318	136	449
Renal and urinary disorders			

Urinary frequency subjects affected / exposed occurrences (all)	605 / 1184 (51.10%) 2125	308 / 593 (51.94%) 957	307 / 592 (51.86%) 969
Acute kidney injury subjects affected / exposed occurrences (all)	92 / 1184 (7.77%) 183	71 / 593 (11.97%) 232	49 / 592 (8.28%) 95
Haematuria subjects affected / exposed occurrences (all)	57 / 1184 (4.81%) 86	23 / 593 (3.88%) 34	22 / 592 (3.72%) 30
Chronic kidney disease subjects affected / exposed occurrences (all)	92 / 1184 (7.77%) 183	71 / 593 (11.97%) 232	49 / 592 (8.28%) 95
Renal - other subjects affected / exposed occurrences (all)	189 / 1184 (15.96%) 301	88 / 593 (14.84%) 132	97 / 592 (16.39%) 154
Urinary urgency subjects affected / exposed occurrences (all)	0 / 1184 (0.00%) 0	0 / 593 (0.00%) 0	0 / 592 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	144 / 1184 (12.16%) 246	69 / 593 (11.64%) 109	64 / 592 (10.81%) 107
Myalgia subjects affected / exposed occurrences (all)	184 / 1184 (15.54%) 316	109 / 593 (18.38%) 186	133 / 592 (22.47%) 226
Arthralgia subjects affected / exposed occurrences (all)	303 / 1184 (25.59%) 787	189 / 593 (31.87%) 426	202 / 592 (34.12%) 513
Bone pain subjects affected / exposed occurrences (all)	436 / 1184 (36.82%) 920	235 / 593 (39.63%) 531	190 / 592 (32.09%) 441
Musculoskeletal - other subjects affected / exposed occurrences (all)	437 / 1184 (36.91%) 922	245 / 593 (41.32%) 546	247 / 592 (41.72%) 549

<b>Infections and infestations</b> <b>Urinary tract infection</b> subjects affected / exposed occurrences (all)	94 / 1184 (7.94%) 119	57 / 593 (9.61%) 73	81 / 592 (13.68%) 108
<b>Sinusitis</b> subjects affected / exposed occurrences (all)	37 / 1184 (3.13%) 63	21 / 593 (3.54%) 29	21 / 592 (3.55%) 32
<b>Upper respiratory tract infection</b> subjects affected / exposed occurrences (all)	116 / 1184 (9.80%) 157	66 / 593 (11.13%) 85	97 / 592 (16.39%) 132
<b>Metabolism and nutrition disorders</b> <b>Hypocalcaemia</b> subjects affected / exposed occurrences (all)	39 / 1184 (3.29%) 55	64 / 593 (10.79%) 98	32 / 592 (5.41%) 42
<b>Anorexia nervosa</b> subjects affected / exposed occurrences (all)	91 / 1184 (7.69%) 120	49 / 593 (8.26%) 78	73 / 592 (12.33%) 85
<b>Glucose tolerance decreased</b> subjects affected / exposed occurrences (all)	37 / 1184 (3.13%) 49	21 / 593 (3.54%) 50	29 / 592 (4.90%) 53
<b>Metabolism - other</b> subjects affected / exposed occurrences (all)	104 / 1184 (8.78%) 152	29 / 593 (4.89%) 44	46 / 592 (7.77%) 56
<b>Hypokalaemia</b> subjects affected / exposed occurrences (all)	16 / 1184 (1.35%) 17	16 / 593 (2.70%) 19	20 / 592 (3.38%) 29

<b>Non-serious adverse events</b>	Doce+ZA (Arm E)	SOC (Arm A, ADF comparison)	Celecoxib (Arm D)
<b>Total subjects affected by non-serious adverse events</b> subjects affected / exposed	560 / 593 (94.44%)	605 / 622 (97.27%)	292 / 312 (93.59%)
<b>Vascular disorders</b> <b>Hypertension</b> subjects affected / exposed occurrences (all)	30 / 593 (5.06%) 42	35 / 622 (5.63%) 47	39 / 312 (12.50%) 63
<b>Hot flush</b> subjects affected / exposed occurrences (all)	442 / 593 (74.54%) 2356	495 / 622 (79.58%) 2877	229 / 312 (73.40%) 1321

General disorders and administration site conditions			
Fever			
subjects affected / exposed	70 / 593 (11.80%)	13 / 622 (2.09%)	6 / 312 (1.92%)
occurrences (all)	84	19	8
Fatigue			
subjects affected / exposed	427 / 593 (72.01%)	333 / 622 (53.54%)	151 / 312 (48.40%)
occurrences (all)	1607	1080	424
Oedema			
subjects affected / exposed	142 / 593 (23.95%)	97 / 622 (15.59%)	55 / 312 (17.63%)
occurrences (all)	283	207	100
Influenza like illness			
subjects affected / exposed	140 / 593 (23.61%)	63 / 622 (10.13%)	27 / 312 (8.65%)
occurrences (all)	210	84	36
Pain			
subjects affected / exposed	234 / 593 (39.46%)	187 / 622 (30.06%)	90 / 312 (28.85%)
occurrences (all)	501	364	162
General - other			
subjects affected / exposed	93 / 593 (15.68%)	70 / 622 (11.25%)	24 / 312 (7.69%)
occurrences (all)	132	82	24
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	42 / 593 (7.08%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences (all)	53	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	281 / 593 (47.39%)	308 / 622 (49.52%)	127 / 312 (40.71%)
occurrences (all)	1628	1851	740
Gynaecomastia			
subjects affected / exposed	37 / 593 (6.24%)	47 / 622 (7.56%)	19 / 312 (6.09%)
occurrences (all)	58	74	41
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	79 / 593 (13.32%)	59 / 622 (9.49%)	19 / 312 (6.09%)
occurrences (all)	136	103	31
Dyspnoea			

subjects affected / exposed occurrences (all)	117 / 593 (19.73%) 253	82 / 622 (13.18%) 169	45 / 312 (14.42%) 99
Rhinitis subjects affected / exposed occurrences (all)	39 / 593 (6.58%) 61	38 / 622 (6.11%) 65	17 / 312 (5.45%) 24
Respiratory - other subjects affected / exposed occurrences (all)	72 / 593 (12.14%) 103	64 / 622 (10.29%) 96	26 / 312 (8.33%) 38
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	170 / 593 (28.67%) 416	154 / 622 (24.76%) 389	69 / 312 (22.12%) 142
Anxiety subjects affected / exposed occurrences (all)	0 / 593 (0.00%) 0	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 593 (0.00%) 0	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
Libido decreased subjects affected / exposed occurrences (all)	0 / 593 (0.00%) 0	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
Psychiatric - other subjects affected / exposed occurrences (all)	95 / 593 (16.02%) 197	104 / 622 (16.72%) 274	48 / 312 (15.38%) 75
Investigations			
Neutrophil count subjects affected / exposed occurrences (all)	111 / 593 (18.72%) 148	28 / 622 (4.50%) 47	11 / 312 (3.53%) 26
Alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 593 (0.00%) 0	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
cholesterol high subjects affected / exposed occurrences (all)	0 / 593 (0.00%) 0	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
Investigations - other			



subjects affected / exposed	153 / 593 (25.80%)	173 / 622 (27.81%)	83 / 312 (26.60%)
occurrences (all)	317	361	180
Aspartate aminotransferase increased			
subjects affected / exposed	22 / 593 (3.71%)	16 / 622 (2.57%)	7 / 312 (2.24%)
occurrences (all)	28	34	11
Alanine aminotransferase increased			
subjects affected / exposed	63 / 593 (10.62%)	53 / 622 (8.52%)	29 / 312 (9.29%)
occurrences (all)	140	116	73
Platelet count decreased			
subjects affected / exposed	37 / 593 (6.24%)	15 / 622 (2.41%)	11 / 312 (3.53%)
occurrences (all)	74	40	29
Weight increased			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
cardiac - other			
subjects affected / exposed	24 / 593 (4.05%)	35 / 622 (5.63%)	18 / 312 (5.77%)
occurrences (all)	36	79	33
Arrhythmia			
subjects affected / exposed	18 / 593 (3.04%)	20 / 622 (3.22%)	17 / 312 (5.45%)
occurrences (all)	28	32	35
Nervous system disorders			
Dizziness			
subjects affected / exposed	93 / 593 (15.68%)	90 / 622 (14.47%)	40 / 312 (12.82%)
occurrences (all)	158	169	69
Headache			
subjects affected / exposed	98 / 593 (16.53%)	100 / 622 (16.08%)	35 / 312 (11.22%)
occurrences (all)	172	202	63
Nervous system - other			
subjects affected / exposed	206 / 593 (34.74%)	61 / 622 (9.81%)	42 / 312 (13.46%)
occurrences (all)	449	96	68
Cognitive disorder			
subjects affected / exposed	10 / 593 (1.69%)	12 / 622 (1.93%)	4 / 312 (1.28%)
occurrences (all)	16	15	6
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	252 / 593 (42.50%) 902	172 / 622 (27.65%) 495	78 / 312 (25.00%) 255
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	61 / 593 (10.29%) 105	0 / 622 (0.00%) 0	0 / 312 (0.00%) 0
Eye - other subjects affected / exposed occurrences (all)	97 / 593 (16.36%) 175	50 / 622 (8.04%) 74	19 / 312 (6.09%) 30
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	127 / 593 (21.42%) 203	89 / 622 (14.31%) 161	60 / 312 (19.23%) 95
Constipation subjects affected / exposed occurrences (all)	212 / 593 (35.75%) 436	125 / 622 (20.10%) 268	46 / 312 (14.74%) 81
Diarrhoea subjects affected / exposed occurrences (all)	233 / 593 (39.29%) 451	134 / 622 (21.54%) 274	85 / 312 (27.24%) 143
Dyspepsia subjects affected / exposed occurrences (all)	125 / 593 (21.08%) 208	97 / 622 (15.59%) 221	67 / 312 (21.47%) 110
Flatulence subjects affected / exposed occurrences (all)	78 / 593 (13.15%) 132	105 / 622 (16.88%) 252	48 / 312 (15.38%) 89
Haemorrhage subjects affected / exposed occurrences (all)	46 / 593 (7.76%) 74	48 / 622 (7.72%) 81	15 / 312 (4.81%) 28
Nausea subjects affected / exposed occurrences (all)	152 / 593 (25.63%) 265	80 / 622 (12.86%) 126	43 / 312 (13.78%) 57
Vomiting subjects affected / exposed occurrences (all)	65 / 593 (10.96%) 88	41 / 622 (6.59%) 52	23 / 312 (7.37%) 25
Stomatitis			

subjects affected / exposed	149 / 593 (25.13%)	22 / 622 (3.54%)	15 / 312 (4.81%)
occurrences (all)	216	32	17
Gastrointestinal - other			
subjects affected / exposed	143 / 593 (24.11%)	97 / 622 (15.59%)	52 / 312 (16.67%)
occurrences (all)	268	168	74
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	44 / 593 (7.42%)	27 / 622 (4.34%)	27 / 312 (8.65%)
occurrences (all)	78	49	52
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	194 / 593 (32.72%)	35 / 622 (5.63%)	16 / 312 (5.13%)
occurrences (all)	406	53	21
Rash			
subjects affected / exposed	70 / 593 (11.80%)	70 / 622 (11.25%)	48 / 312 (15.38%)
occurrences (all)	116	126	77
Alopecia			
subjects affected / exposed	69 / 593 (11.64%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences (all)	118	0	0
Skin - other			
subjects affected / exposed	216 / 593 (36.42%)	112 / 622 (18.01%)	37 / 312 (11.86%)
occurrences (all)	400	176	67
Renal and urinary disorders			
Urinary frequency			
subjects affected / exposed	279 / 593 (47.05%)	310 / 622 (49.84%)	146 / 312 (46.79%)
occurrences (all)	934	1130	514
Acute kidney injury			
subjects affected / exposed	75 / 593 (12.65%)	51 / 622 (8.20%)	25 / 312 (8.01%)
occurrences (all)	201	101	47
Haematuria			
subjects affected / exposed	35 / 593 (5.90%)	40 / 622 (6.43%)	21 / 312 (6.73%)
occurrences (all)	44	60	30
Chronic kidney disease			
subjects affected / exposed	75 / 593 (12.65%)	51 / 622 (8.20%)	25 / 312 (8.01%)
occurrences (all)	201	101	47
Renal - other			

subjects affected / exposed	94 / 593 (15.85%)	102 / 622 (16.40%)	55 / 312 (17.63%)
occurrences (all)	150	157	90
Urinary urgency			
subjects affected / exposed	0 / 593 (0.00%)	0 / 622 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	64 / 593 (10.79%)	87 / 622 (13.99%)	28 / 312 (8.97%)
occurrences (all)	97	154	45
Myalgia			
subjects affected / exposed	141 / 593 (23.78%)	101 / 622 (16.24%)	34 / 312 (10.90%)
occurrences (all)	265	158	60
Arthralgia			
subjects affected / exposed	214 / 593 (36.09%)	182 / 622 (29.26%)	87 / 312 (27.88%)
occurrences (all)	525	495	220
Bone pain			
subjects affected / exposed	232 / 593 (39.12%)	249 / 622 (40.03%)	114 / 312 (36.54%)
occurrences (all)	517	564	240
Musculoskeletal - other			
subjects affected / exposed	275 / 593 (46.37%)	254 / 622 (40.84%)	102 / 312 (32.69%)
occurrences (all)	617	559	183
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	83 / 593 (14.00%)	52 / 622 (8.36%)	27 / 312 (8.65%)
occurrences (all)	104	64	30
Sinusitis			
subjects affected / exposed	20 / 593 (3.37%)	27 / 622 (4.34%)	12 / 312 (3.85%)
occurrences (all)	28	52	23
Upper respiratory tract infection			
subjects affected / exposed	97 / 593 (16.36%)	61 / 622 (9.81%)	30 / 312 (9.62%)
occurrences (all)	128	79	36
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	57 / 593 (9.61%)	26 / 622 (4.18%)	16 / 312 (5.13%)
occurrences (all)	91	42	23
Anorexia nervosa			

subjects affected / exposed	74 / 593 (12.48%)	56 / 622 (9.00%)	32 / 312 (10.26%)
occurrences (all)	118	79	40
Glucose tolerance decreased			
subjects affected / exposed	30 / 593 (5.06%)	20 / 622 (3.22%)	13 / 312 (4.17%)
occurrences (all)	67	32	34
Metabolism - other			
subjects affected / exposed	56 / 593 (9.44%)	45 / 622 (7.23%)	24 / 312 (7.69%)
occurrences (all)	73	73	42
Hypokalaemia			
subjects affected / exposed	20 / 593 (3.37%)	5 / 622 (0.80%)	3 / 312 (0.96%)
occurrences (all)	28	6	4

<b>Non-serious adverse events</b>	Celecoxib + ZA	SOC (Arm A, G comparison)	Abiraterone (Arm G)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	297 / 311 (95.50%)	946 / 957 (98.85%)	953 / 960 (99.27%)
Vascular disorders			
Hypertension			
subjects affected / exposed	27 / 311 (8.68%)	180 / 957 (18.81%)	368 / 960 (38.33%)
occurrences (all)	43	349	955
Hot flush			
subjects affected / exposed	222 / 311 (71.38%)	819 / 957 (85.58%)	851 / 960 (88.65%)
occurrences (all)	1268	5295	6524
General disorders and administration site conditions			
Fever			
subjects affected / exposed	17 / 311 (5.47%)	35 / 957 (3.66%)	50 / 960 (5.21%)
occurrences (all)	17	39	55
Fatigue			
subjects affected / exposed	165 / 311 (53.05%)	612 / 957 (63.95%)	706 / 960 (73.54%)
occurrences (all)	536	2441	3557
Oedema			
subjects affected / exposed	51 / 311 (16.40%)	172 / 957 (17.97%)	235 / 960 (24.48%)
occurrences (all)	85	414	657
Influenza like illness			
subjects affected / exposed	74 / 311 (23.79%)	57 / 957 (5.96%)	106 / 960 (11.04%)
occurrences (all)	136	66	133
Pain			

subjects affected / exposed occurrences (all)	94 / 311 (30.23%) 180	285 / 957 (29.78%) 575	325 / 960 (33.85%) 585
General - other subjects affected / exposed occurrences (all)	14 / 311 (4.50%) 17	81 / 957 (8.46%) 109	123 / 960 (12.81%) 189
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 311 (0.00%) 0	35 / 957 (3.66%) 47	41 / 960 (4.27%) 52
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	135 / 311 (43.41%) 820	518 / 957 (54.13%) 3040	555 / 960 (57.81%) 3929
Gynaecomastia subjects affected / exposed occurrences (all)	17 / 311 (5.47%) 32	170 / 957 (17.76%) 390	170 / 960 (17.71%) 472
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	29 / 311 (9.32%) 36	155 / 957 (16.20%) 315	289 / 960 (30.10%) 638
Dyspnoea subjects affected / exposed occurrences (all)	38 / 311 (12.22%) 72	212 / 957 (22.15%) 546	306 / 960 (31.88%) 920
Rhinitis subjects affected / exposed occurrences (all)	21 / 311 (6.75%) 39	40 / 957 (4.18%) 65	73 / 960 (7.60%) 112
Respiratory - other subjects affected / exposed occurrences (all)	32 / 311 (10.29%) 39	66 / 957 (6.90%) 112	143 / 960 (14.90%) 229
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	78 / 311 (25.08%) 197	266 / 957 (27.80%) 780	336 / 960 (35.00%) 1105
Anxiety subjects affected / exposed occurrences (all)	0 / 311 (0.00%) 0	60 / 957 (6.27%) 98	103 / 960 (10.73%) 172

Depression			
subjects affected / exposed	0 / 311 (0.00%)	54 / 957 (5.64%)	92 / 960 (9.58%)
occurrences (all)	0	94	166
Libido decreased			
subjects affected / exposed	0 / 311 (0.00%)	38 / 957 (3.97%)	67 / 960 (6.98%)
occurrences (all)	0	43	103
Psychiatric - other			
subjects affected / exposed	44 / 311 (14.15%)	180 / 957 (18.81%)	236 / 960 (24.58%)
occurrences (all)	94	402	636
Investigations			
Neutrophil count			
subjects affected / exposed	9 / 311 (2.89%)	48 / 957 (5.02%)	80 / 960 (8.33%)
occurrences (all)	12	81	129
Alkaline phosphatase increased			
subjects affected / exposed	0 / 311 (0.00%)	28 / 957 (2.93%)	47 / 960 (4.90%)
occurrences (all)	0	35	62
cholesterol high			
subjects affected / exposed	0 / 311 (0.00%)	28 / 957 (2.93%)	45 / 960 (4.69%)
occurrences (all)	0	37	79
Investigations - other			
subjects affected / exposed	90 / 311 (28.94%)	323 / 957 (33.75%)	432 / 960 (45.00%)
occurrences (all)	201	713	1311
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 311 (3.54%)	34 / 957 (3.55%)	81 / 960 (8.44%)
occurrences (all)	21	57	171
Alanine aminotransferase increased			
subjects affected / exposed	26 / 311 (8.36%)	145 / 957 (15.15%)	267 / 960 (27.81%)
occurrences (all)	52	281	605
Platelet count decreased			
subjects affected / exposed	11 / 311 (3.54%)	44 / 957 (4.60%)	55 / 960 (5.73%)
occurrences (all)	37	99	118
Weight increased			
subjects affected / exposed	0 / 311 (0.00%)	45 / 957 (4.70%)	60 / 960 (6.25%)
occurrences (all)	0	54	90
Cardiac disorders			

cardiac - other subjects affected / exposed occurrences (all)	16 / 311 (5.14%) 32	64 / 957 (6.69%) 97	96 / 960 (10.00%) 163
Arrhythmia subjects affected / exposed occurrences (all)	15 / 311 (4.82%) 26	41 / 957 (4.28%) 61	68 / 960 (7.08%) 132
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	37 / 311 (11.90%) 65	137 / 957 (14.32%) 215	190 / 960 (19.79%) 389
Headache subjects affected / exposed occurrences (all)	38 / 311 (12.22%) 80	120 / 957 (12.54%) 264	186 / 960 (19.38%) 383
Nervous system - other subjects affected / exposed occurrences (all)	52 / 311 (16.72%) 81	104 / 957 (10.87%) 180	158 / 960 (16.46%) 307
Cognitive disorder subjects affected / exposed occurrences (all)	4 / 311 (1.29%) 8	52 / 957 (5.43%) 95	73 / 960 (7.60%) 142
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	108 / 311 (34.73%) 370	385 / 957 (40.23%) 1300	489 / 960 (50.94%) 1966
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 311 (0.00%) 0	45 / 957 (4.70%) 79	67 / 960 (6.98%) 112
Eye - other subjects affected / exposed occurrences (all)	25 / 311 (8.04%) 39	53 / 957 (5.54%) 83	98 / 960 (10.21%) 166
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	54 / 311 (17.36%) 106	142 / 957 (14.84%) 283	208 / 960 (21.67%) 414
Constipation subjects affected / exposed occurrences (all)	70 / 311 (22.51%) 147	259 / 957 (27.06%) 605	333 / 960 (34.69%) 895



Diarrhoea			
subjects affected / exposed	77 / 311 (24.76%)	286 / 957 (29.89%)	337 / 960 (35.10%)
occurrences (all)	133	637	726
Dyspepsia			
subjects affected / exposed	57 / 311 (18.33%)	120 / 957 (12.54%)	181 / 960 (18.85%)
occurrences (all)	102	223	374
Flatulence			
subjects affected / exposed	43 / 311 (13.83%)	149 / 957 (15.57%)	163 / 960 (16.98%)
occurrences (all)	105	377	357
Haemorrhage			
subjects affected / exposed	20 / 311 (6.43%)	79 / 957 (8.25%)	84 / 960 (8.75%)
occurrences (all)	35	154	139
Nausea			
subjects affected / exposed	37 / 311 (11.90%)	112 / 957 (11.70%)	180 / 960 (18.75%)
occurrences (all)	59	201	353
Vomiting			
subjects affected / exposed	24 / 311 (7.72%)	47 / 957 (4.91%)	94 / 960 (9.79%)
occurrences (all)	35	63	130
Stomatitis			
subjects affected / exposed	18 / 311 (5.79%)	22 / 957 (2.30%)	35 / 960 (3.65%)
occurrences (all)	26	30	59
Gastrointestinal - other			
subjects affected / exposed	40 / 311 (12.86%)	164 / 957 (17.14%)	230 / 960 (23.96%)
occurrences (all)	64	290	384
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	27 / 311 (8.68%)	53 / 957 (5.54%)	116 / 960 (12.08%)
occurrences (all)	44	77	195
Skin and subcutaneous tissue disorders			
Nail discolouration			
subjects affected / exposed	23 / 311 (7.40%)	53 / 957 (5.54%)	64 / 960 (6.67%)
occurrences (all)	47	98	103
Rash			
subjects affected / exposed	41 / 311 (13.18%)	92 / 957 (9.61%)	158 / 960 (16.46%)
occurrences (all)	67	167	262
Alopecia			

subjects affected / exposed occurrences (all)	0 / 311 (0.00%) 0	8 / 957 (0.84%) 12	6 / 960 (0.63%) 16
Skin - other subjects affected / exposed occurrences (all)	51 / 311 (16.40%) 69	171 / 957 (17.87%) 297	259 / 960 (26.98%) 489
Renal and urinary disorders			
Urinary frequency subjects affected / exposed occurrences (all)	138 / 311 (44.37%) 438	637 / 957 (66.56%) 2706	666 / 960 (69.38%) 3221
Acute kidney injury subjects affected / exposed occurrences (all)	57 / 311 (18.33%) 171	27 / 957 (2.82%) 35	37 / 960 (3.85%) 48
Haematuria subjects affected / exposed occurrences (all)	14 / 311 (4.50%) 16	78 / 957 (8.15%) 110	96 / 960 (10.00%) 129
Chronic kidney disease subjects affected / exposed occurrences (all)	57 / 311 (18.33%) 171	102 / 957 (10.66%) 233	114 / 960 (11.88%) 339
Renal - other subjects affected / exposed occurrences (all)	39 / 311 (12.54%) 60	219 / 957 (22.88%) 387	196 / 960 (20.42%) 362
Urinary urgency subjects affected / exposed occurrences (all)	0 / 311 (0.00%) 0	111 / 957 (11.60%) 164	118 / 960 (12.29%) 204
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	35 / 311 (11.25%) 71	89 / 957 (9.30%) 125	137 / 960 (14.27%) 215
Myalgia subjects affected / exposed occurrences (all)	53 / 311 (17.04%) 99	170 / 957 (17.76%) 340	208 / 960 (21.67%) 378
Arthralgia subjects affected / exposed occurrences (all)	94 / 311 (30.23%) 270	263 / 957 (27.48%) 614	330 / 960 (34.38%) 842
Bone pain			

subjects affected / exposed occurrences (all)	119 / 311 (38.26%) 300	350 / 957 (36.57%) 683	346 / 960 (36.04%) 721
Musculoskeletal - other subjects affected / exposed occurrences (all)	117 / 311 (37.62%) 228	355 / 957 (37.10%) 742	416 / 960 (43.33%) 1025
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	34 / 311 (10.93%) 39	90 / 957 (9.40%) 130	97 / 960 (10.10%) 147
Sinusitis subjects affected / exposed occurrences (all)	12 / 311 (3.86%) 34	24 / 957 (2.51%) 39	36 / 960 (3.75%) 59
Upper respiratory tract infection subjects affected / exposed occurrences (all)	36 / 311 (11.58%) 44	94 / 957 (9.82%) 125	159 / 960 (16.56%) 237
Metabolism and nutrition disorders			
Hypocalcaemia subjects affected / exposed occurrences (all)	25 / 311 (8.04%) 34	35 / 957 (3.66%) 42	69 / 960 (7.19%) 96
Anorexia nervosa subjects affected / exposed occurrences (all)	35 / 311 (11.25%) 47	79 / 957 (8.25%) 122	110 / 960 (11.46%) 189
Glucose tolerance decreased subjects affected / exposed occurrences (all)	10 / 311 (3.22%) 15	59 / 957 (6.17%) 138	110 / 960 (11.46%) 310
Metabolism - other subjects affected / exposed occurrences (all)	13 / 311 (4.18%) 16	117 / 957 (12.23%) 179	124 / 960 (12.92%) 236
Hypokalaemia subjects affected / exposed occurrences (all)	6 / 311 (1.93%) 11	30 / 957 (3.13%) 32	129 / 960 (13.44%) 234
<b>Non-serious adverse events</b>	SOC (Arm A, J comparison)	Enzalutamide + Abiraterone (Arm J)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	974 / 987 (98.68%)	975 / 989 (98.58%)	
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	190 / 987 (19.25%) 443	554 / 989 (56.02%) 1864	
Hot flush subjects affected / exposed occurrences (all)	863 / 987 (87.44%) 5792	899 / 989 (90.90%) 7236	
General disorders and administration site conditions			
Fever subjects affected / exposed occurrences (all)	48 / 987 (4.86%) 60	66 / 989 (6.67%) 79	
Fatigue subjects affected / exposed occurrences (all)	720 / 987 (72.95%) 3132	870 / 989 (87.97%) 5374	
Oedema subjects affected / exposed occurrences (all)	237 / 987 (24.01%) 569	245 / 989 (24.77%) 584	
Influenza like illness subjects affected / exposed occurrences (all)	46 / 987 (4.66%) 53	79 / 989 (7.99%) 85	
Pain subjects affected / exposed occurrences (all)	232 / 987 (23.51%) 379	215 / 989 (21.74%) 368	
General - other subjects affected / exposed occurrences (all)	66 / 987 (6.69%) 98	120 / 989 (12.13%) 159	
Immune system disorders			
Hypersensitivity subjects affected / exposed occurrences (all)	28 / 987 (2.84%) 30	38 / 989 (3.84%) 46	
Reproductive system and breast disorders			
Erectile dysfunction subjects affected / exposed occurrences (all)	524 / 987 (53.09%) 3227	591 / 989 (59.76%) 4160	
Gynaecomastia subjects affected / exposed occurrences (all)	264 / 987 (26.75%) 758	296 / 989 (29.93%) 1021	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	226 / 987 (22.90%)	218 / 989 (22.04%)	
occurrences (all)	456	443	
Dyspnoea			
subjects affected / exposed	262 / 987 (26.55%)	320 / 989 (32.36%)	
occurrences (all)	703	945	
Rhinitis			
subjects affected / exposed	44 / 987 (4.46%)	67 / 989 (6.77%)	
occurrences (all)	61	105	
Respiratory - other			
subjects affected / exposed	62 / 987 (6.28%)	99 / 989 (10.01%)	
occurrences (all)	83	135	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	329 / 987 (33.33%)	385 / 989 (38.93%)	
occurrences (all)	1051	1336	
Anxiety			
subjects affected / exposed	152 / 987 (15.40%)	209 / 989 (21.13%)	
occurrences (all)	340	533	
Depression			
subjects affected / exposed	143 / 987 (14.49%)	214 / 989 (21.64%)	
occurrences (all)	286	533	
Libido decreased			
subjects affected / exposed	104 / 987 (10.54%)	137 / 989 (13.85%)	
occurrences (all)	198	263	
Psychiatric - other			
subjects affected / exposed	147 / 987 (14.89%)	204 / 989 (20.63%)	
occurrences (all)	298	369	
Investigations			
Neutrophil count			
subjects affected / exposed	77 / 987 (7.80%)	99 / 989 (10.01%)	
occurrences (all)	119	193	
Alkaline phosphatase increased			
subjects affected / exposed	100 / 987 (10.13%)	96 / 989 (9.71%)	
occurrences (all)	156	197	

cholesterol high			
subjects affected / exposed	45 / 987 (4.56%)	60 / 989 (6.07%)	
occurrences (all)	79	112	
Investigations - other			
subjects affected / exposed	305 / 987 (30.90%)	363 / 989 (36.70%)	
occurrences (all)	626	866	
Aspartate aminotransferase increased			
subjects affected / exposed	38 / 987 (3.85%)	139 / 989 (14.05%)	
occurrences (all)	59	243	
Alanine aminotransferase increased			
subjects affected / exposed	170 / 987 (17.22%)	389 / 989 (39.33%)	
occurrences (all)	334	902	
Platelet count decreased			
subjects affected / exposed	58 / 987 (5.88%)	62 / 989 (6.27%)	
occurrences (all)	113	121	
Weight increased			
subjects affected / exposed	170 / 987 (17.22%)	159 / 989 (16.08%)	
occurrences (all)	269	254	
Cardiac disorders			
cardiac - other			
subjects affected / exposed	35 / 987 (3.55%)	63 / 989 (6.37%)	
occurrences (all)	46	115	
Arrhythmia			
subjects affected / exposed	32 / 987 (3.24%)	63 / 989 (6.37%)	
occurrences (all)	47	108	
Nervous system disorders			
Dizziness			
subjects affected / exposed	151 / 987 (15.30%)	253 / 989 (25.58%)	
occurrences (all)	312	476	
Headache			
subjects affected / exposed	139 / 987 (14.08%)	261 / 989 (26.39%)	
occurrences (all)	269	584	
Nervous system - other			
subjects affected / exposed	146 / 987 (14.79%)	211 / 989 (21.33%)	
occurrences (all)	235	412	
Cognitive disorder			

subjects affected / exposed occurrences (all)	55 / 987 (5.57%) 84	187 / 989 (18.91%) 377	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	456 / 987 (46.20%) 1559	502 / 989 (50.76%) 1978	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)  Eye - other subjects affected / exposed occurrences (all)	56 / 987 (5.67%) 81  50 / 987 (5.07%) 83	82 / 989 (8.29%) 146  98 / 989 (9.91%) 178	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)  Constipation subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Dyspepsia subjects affected / exposed occurrences (all)  Flatulence subjects affected / exposed occurrences (all)  Haemorrhage subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Vomiting	163 / 987 (16.51%) 305  317 / 987 (32.12%) 801  349 / 987 (35.36%) 823  141 / 987 (14.29%) 283  205 / 987 (20.77%) 413  77 / 987 (7.80%) 132  154 / 987 (15.60%) 252	196 / 989 (19.82%) 382  394 / 989 (39.84%) 987  419 / 989 (42.37%) 954  187 / 989 (18.91%) 350  248 / 989 (25.08%) 588  103 / 989 (10.41%) 159  267 / 989 (27.00%) 558	

subjects affected / exposed occurrences (all)	71 / 987 (7.19%) 98	113 / 989 (11.43%) 154	
Stomatitis subjects affected / exposed occurrences (all)	33 / 987 (3.34%) 41	35 / 989 (3.54%) 39	
Gastrointestinal - other subjects affected / exposed occurrences (all)	179 / 987 (18.14%) 299	236 / 989 (23.86%) 424	
Hepatobiliary disorders Hepatic failure subjects affected / exposed occurrences (all)	41 / 987 (4.15%) 60	59 / 989 (5.97%) 78	
Skin and subcutaneous tissue disorders Nail discolouration subjects affected / exposed occurrences (all)	66 / 987 (6.69%) 148	88 / 989 (8.90%) 168	
Rash subjects affected / exposed occurrences (all)	110 / 987 (11.14%) 166	124 / 989 (12.54%) 213	
Alopecia subjects affected / exposed occurrences (all)	22 / 987 (2.23%) 30	32 / 989 (3.24%) 50	
Skin - other subjects affected / exposed occurrences (all)	146 / 987 (14.79%) 262	238 / 989 (24.06%) 444	
Renal and urinary disorders Urinary frequency subjects affected / exposed occurrences (all)	731 / 987 (74.06%) 3435	733 / 989 (74.12%) 3869	
Acute kidney injury subjects affected / exposed occurrences (all)	48 / 987 (4.86%) 75	49 / 989 (4.95%) 76	
Haematuria subjects affected / exposed occurrences (all)	83 / 987 (8.41%) 122	78 / 989 (7.89%) 117	
Chronic kidney disease			



subjects affected / exposed	84 / 987 (8.51%)	96 / 989 (9.71%)	
occurrences (all)	187	245	
Renal - other			
subjects affected / exposed	240 / 987 (24.32%)	235 / 989 (23.76%)	
occurrences (all)	472	435	
Urinary urgency			
subjects affected / exposed	281 / 987 (28.47%)	324 / 989 (32.76%)	
occurrences (all)	605	774	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	230 / 987 (23.30%)	267 / 989 (27.00%)	
occurrences (all)	467	561	
Myalgia			
subjects affected / exposed	206 / 987 (20.87%)	300 / 989 (30.33%)	
occurrences (all)	414	598	
Arthralgia			
subjects affected / exposed	334 / 987 (33.84%)	401 / 989 (40.55%)	
occurrences (all)	813	957	
Bone pain			
subjects affected / exposed	354 / 987 (35.87%)	358 / 989 (36.20%)	
occurrences (all)	674	811	
Musculoskeletal - other			
subjects affected / exposed	292 / 987 (29.58%)	343 / 989 (34.68%)	
occurrences (all)	568	741	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	90 / 987 (9.12%)	98 / 989 (9.91%)	
occurrences (all)	114	162	
Sinusitis			
subjects affected / exposed	21 / 987 (2.13%)	41 / 989 (4.15%)	
occurrences (all)	27	58	
Upper respiratory tract infection			
subjects affected / exposed	102 / 987 (10.33%)	141 / 989 (14.26%)	
occurrences (all)	140	191	
Metabolism and nutrition disorders			

Hypocalcaemia			
subjects affected / exposed	37 / 987 (3.75%)	54 / 989 (5.46%)	
occurrences (all)	39	61	
Anorexia nervosa			
subjects affected / exposed	114 / 987 (11.55%)	182 / 989 (18.40%)	
occurrences (all)	186	354	
Glucose tolerance decreased			
subjects affected / exposed	79 / 987 (8.00%)	88 / 989 (8.90%)	
occurrences (all)	185	258	
Metabolism - other			
subjects affected / exposed	82 / 987 (8.31%)	115 / 989 (11.63%)	
occurrences (all)	145	186	
Hypokalaemia			
subjects affected / exposed	40 / 987 (4.05%)	142 / 989 (14.36%)	
occurrences (all)	64	247	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported