Clinical trial results:
Randomized, Open Label, Multi-Center Study comparing Cabazitaxel at 25 mg/m^2 and at 20 mg/m^2 in Combination with Prednisone Every 3 Weeks to Docetaxel in Combination with Prednisone in Patients with Metastatic Castration Resistant Prostate Cancer not Pretreated with Chemotherapy

Summary

EudraCT number	2010-022064-12
Trial protocol	SE CZ ES FI DK PT IT DE RO PL
Global end of trial date	

Results information

Result version number	v1
This version publication date	09 June 2017
First version publication date	09 June 2017

Trial information

Trial identification

Sponsor protocol code	EFC11784

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01308567
WHO universal trial number (UTN)	U1111-1117-8356

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, ChillyMazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, , Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	28 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the superiority of cabazitaxel plus prednisone at 25 mg/m^2 (Arm A) or 20 mg/m^2 (Arm B) versus docetaxel plus prednisone (Arm C) in terms of overall survival (OS) in subjects with metastatic castration resistant prostate cancer (MCRPC) not previously treated with chemotherapy.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2011
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	Australia: 103
Country: Number of subjects enrolled	Belarus: 21
Country: Number of subjects enrolled	Brazil: 37
Country: Number of subjects enrolled	Canada: 59
Country: Number of subjects enrolled	China: 10
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Japan: 18
Country: Number of subjects enrolled	Mexico: 36
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	Russian Federation: 85
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	Ukraine: 67
Country: Number of subjects enrolled	United States: 85
Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Portugal: 34
Country: Number of subjects enrolled	Romania: 32
Country: Number of subjects enrolled	Spain: 80

Country: Number of subjects enrolled	Sweden: 48
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	Denmark: 84
Country: Number of subjects enrolled	Finland: 35
Country: Number of subjects enrolled	France: 141
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Italy: 46
Worldwide total number of subjects	1168
EEA total number of subjects	606

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)	376
From 65 to 84 years	784
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 159 centers in 25 countries. A total of 1510 subjects were screened between 17 May 2011 and 09 September 2015 of whom 1168 subjects were randomized and 342 were considered as screen failures.

Pre-assignment

Screening details:

A total of 1168 subjects were randomized in this study. Of those, 21 subjects were randomized but were not treated. These subjects were included in intent-to-treat (ITT) population and not in safety population.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Docetaxel 75 mg/m^2

Arm description:

Docetaxel (TXT) 75 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until disease progression (DP), unacceptable toxicity or subject’s refusal.

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	XRP6976
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m^2 in 250 mL dextrose 5% or NaCl 0.9% IV over 1 hour on day 1 of each 21--day cycle.

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

Dosage and administration details:

Prednisone 10 mg, once daily in each 21-day cycle.

Arm title	Cabazitaxel 20 mg/m^2

Arm description:

Cabazitaxel 20 mg/m^2 IV infusion on Day 1 of each 21–day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject’s refusal.

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	Jevtana®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Cabazitaxel 20 mg/m^2 in dextrose 5% or NaCl 0.9% IV over 1 hour on Day 1 of each 21-day cycle.	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Prednisone 10 mg, once daily in each 21-day cycle.	
Arm title	Cabazitaxel 25 mg/m^2
Arm description: Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.	
Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	Jevtana®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Cabazitaxel 25 mg/m^2 in dextrose 5% or NaCl 0.9% IV over 1 hour on Day 1 of each 21-day cycle.	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Prednisone 10 mg, once daily in each 21-day cycle.	

Number of subjects in period 1	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2
Started	391	389	388
Treated	388 [1]	382 [2]	377 [3]
Ongoing Treatment at Data Cut-off	4 [4]	6 [5]	3 [6]
Completed	389	385	384
Not completed	2	4	4
Lost to follow-up	2	4	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: EudraCT Results Validation Rules warning intended to state: "It is expected the number of subjects will >=number that started minus those that left." Completed group = subjects with survival follow-up until death/end of study (randomized- lost to follow-up). Completed subjects included those who withdrew treatment consent but agreed to be followed for survival. Number of treated subjects was grouped by randomized assignment. For 1 subject, actual treatment received was Cabazitaxel 25 mg/m^2.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: EudraCT Results Validation Rules warning intended to state: "It is expected the number of subjects will >=number that started minus those that left." Completed group = subjects with survival follow-up until death/end of study (randomized- lost to follow-up). Completed subjects included those who withdrew treatment consent but agreed to be followed for survival. Number of treated subjects was grouped by randomized assignment. For 15 subjects, actual treatment received was Cabazitaxel 25 mg/m^2.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: EudraCT Results Validation Rules warning intended to state: "It is expected the number of subjects will be >=number that started minus those that left." Completed group = subjects with survival follow-up until death/end of study (randomized- lost to follow-up). Completed subjects included those who withdrew treatment consent but agreed to be followed for survival. Number of treated subjects was grouped by randomized assignment. For 2 subjects, actual treatment received was Cabazitaxel 20 mg/m^2.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The milestone is created for reporting the number of subjects who are still ongoing in the study.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The milestone is created for reporting the number of subjects who are still ongoing in the study.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The milestone is created for reporting the number of subjects who are still ongoing in the study.

Baseline characteristics

Reporting groups	
Reporting group title	Docetaxel 75 mg/m^2
Reporting group description:	
Docetaxel (TXT) 75 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until disease progression (DP), unacceptable toxicity or subject's refusal.	
Reporting group title	Cabazitaxel 20 mg/m^2
Reporting group description:	
Cabazitaxel 20 mg/m^2 IV infusion on Day 1 of each 21–day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.	
Reporting group title	Cabazitaxel 25 mg/m^2
Reporting group description:	
Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.	

Reporting group values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2
Number of subjects	391	389	388
Age categorical Units: Subjects			
<65 years	123	128	125
65-74 years	181	187	182
≥75 years	87	74	81
Gender categorical Units: Subjects			
Female	0	0	0
Male	391	389	388

Reporting group values	Total		
Number of subjects	1168		
Age categorical Units: Subjects			
<65 years	376		
65-74 years	550		
≥75 years	242		
Gender categorical Units: Subjects			
Female	0		
Male	1168		

End points

End points reporting groups

Reporting group title	Docetaxel 75 mg/m^2
Reporting group description:	
Docetaxel (TXT) 75 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until disease progression (DP), unacceptable toxicity or subject's refusal.	
Reporting group title	Cabazitaxel 20 mg/m^2
Reporting group description:	
Cabazitaxel 20 mg/m^2 IV infusion on Day 1 of each 21–day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.	
Reporting group title	Cabazitaxel 25 mg/m^2
Reporting group description:	
Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time interval from the date of randomization to the date of death due to any cause. In the absence of confirmation of death, survival time was censored at the last date subject was known to be alive, or at the cut-off date if the subject's last contact was after the cut-off date. The study cut-off date for the final analysis of OS was the date when the 774th death had been observed. Analysis was performed by Kaplan-Meier method. ITT population that included all the randomized subjects.	
End point type	Primary
End point timeframe:	
Baseline up to death or study cut-off date, whichever was earlier (maximum duration: 51 months)	

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	24.3 (22.18 to 27.6)	24.5 (21.75 to 27.2)	25.2 (22.9 to 26.97)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2
Statistical analysis description:	
Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by Eastern Cooperative Oncology Group performance status (ECOG PS) score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.	
Comparison groups	Cabazitaxel 25 mg/m^2 v Docetaxel 75 mg/m^2

Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7574 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.819
upper limit	1.16

Notes:

[1] - P-value from two-sided stratified log-rank test, stratified for ECOG PS score at baseline, measurable disease at baseline and region with commercial availability of cabazitaxel at time of randomization. Threshold for statistical significance = 0.0479

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9967 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.197

Notes:

[2] - P-value from two-sided stratified log-rank test, stratified for ECOG PS score at baseline, measurable disease at baseline and region with commercial availability of cabazitaxel at time of randomization. Threshold for statistical significance = 0.0479

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS: time interval between date of randomization to date of first occurrence of any of following events: tumor progression according to Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1; Prostate Specific Antigen (PSA) progression; pain progression or death due to any cause. Analysis was performed by Kaplan-Meier method. ITT population included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression, PSA progression, pain progression or death (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	5.3 (4.86 to 5.78)	4.4 (3.91 to 5.09)	5.1 (4.6 to 5.72)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2
Statistical analysis description:	
Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.	
Comparison groups	Cabazitaxel 25 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.989
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.849
upper limit	1.152

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2
Statistical analysis description:	
Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.	
Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.063
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.913
upper limit	1.236

Secondary: Time to Tumor Progression Free Survival

End point title	Time to Tumor Progression Free Survival

End point description:

Time to tumor progression free survival was defined as the time interval between randomization and the date of first occurrence of tumor progression (assessed using RECIST version 1.1) or death, whichever was earlier. Analysis was performed by Kaplan-Meier method. ITT population included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression or death due to any cause or study cut-off date, whichever was earlier (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	12.1 (11.3 to 13.77)	13.4 (11.37 to 14.75)	13.1 (11.66 to 14.32)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Docetaxel 75 mg/m^2 v Cabazitaxel 25 mg/m^2
Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.958
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.785
upper limit	1.17

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2

Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.916
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.118

Secondary: Percentage of Subjects With Overall Objective Tumor Response

End point title	Percentage of Subjects With Overall Objective Tumor Response

End point description:

Overall objective tumor response was defined as having a partial response (PR) or complete response (CR) according to the RECIST version 1.1. CR was defined as disappearance of all target and non-target lesions and normalization of tumor marker level. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Analysis was performed on ITT population. Number of subjects analysed=subjects with measurable disease at baseline and at least one valid post-baseline value analysed for specified endpoint.

End point type	Secondary

End point timeframe:

Baseline up to DP or death due to any cause or study cut-off date, whichever was earlier (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	175	188	173	
Units: percentage of subjects				
number (confidence interval 95%)	30.9 (24 to 37.7)	32.4 (25.8 to 39.1)	41.6 (34.3 to 49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Prostate Serum Antigen-Progression Free Survival (PSA-PFS)

End point title	Time to Prostate Serum Antigen-Progression Free Survival (PSA-PFS)

End point description:

Time to PSA-PFS: time interval between date of randomization & first occurrence of PSA progression/ death, whichever was earlier. PSA progression:1) In PSA responders(>=50% decline from baseline PSA of ≥10 ng/mL):increase of ≥25%(at least 2 ng/mL)over nadir value, confirmed by second PSA value at least 3 weeks later;2)In PSA non-responders(not achieved ≥50% decline from baseline PSA ≥10 ng/mL):increase of ≥25% (at least 2 ng/mL) over baseline value, confirmed by second PSA value at least 3 weeks later;3)In subjects not eligible for PSA response(baseline PSA <10 ng/mL):(a)in subjects

with baseline PSA>0 ng/mL&<10 ng/mL: increase in PSA by 25% (at least 2 ng/mL) above baseline level, confirmed by second PSA value at least 3weeks apart;(b)in subjects with baseline value=0ng/mL: a post baseline PSA value ≥2ng/mL.Early rise in PSA only indicated progression if it was associated with another sign of DP or if it continued beyond 12 weeks. It was done by Kaplan-Meier method on ITT population.

End point type	Secondary

End point timeframe:

Baseline up to PSA progression or death due to any cause or study cut-off date, whichever was earlier (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	8.3 (7.66 to 9.2)	8.2 (7.43 to 8.9)	9.2 (8.44 to 9.92)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 25 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.948
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.123

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a COX Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2

Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.886
upper limit	1.238

Secondary: Percentage of Subjects With PSA Response

End point title	Percentage of Subjects With PSA Response

End point description:

PSA response was defined as ≥50% decrease from baseline in serum PSA levels, confirmed by a second PSA value at least 3 weeks later in subjects with baseline PSA value ≥10 ng/mL. Analysis was performed on ITT population. Number of subjects analysed=subjects with PSA value ≥10 ng/mL at baseline and at least one valid post-baseline value for specified endpoint.

End point type	Secondary

End point timeframe:

Baseline up to PSA progression or death due to any cause or study cut-off date, whichever was earlier (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	354	346	342	
Units: percentage of subjects				
number (confidence interval 95%)	68.4 (63.5 to 73.2)	60.7 (55.5 to 65.8)	68.7 (63.8 to 73.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Pain Progression Free Survival (Pain PFS)

End point title	Time to Pain Progression Free Survival (Pain PFS)

End point description:

Time to pain PFS was defined as the time interval between date of randomization and the date of the first occurrence of pain progression or death, whichever was earlier. Pain progression was defined as an increase of ≥1 point in the median present pain intensity (PPI) score from the nadir confirmed by a second assessment at least 3 weeks later or ≥25 % increase in the mean analgesic score from baseline, due to cancer related pain confirmed by a second assessment at least 3 weeks later or requirement for local palliative radiotherapy. PPI was rated by subject in a diary using a scale of 0=no pain, 1=mild, 2=discomforting, 3=distressing, 4=horrible 5=excruciating. Analgesic use was recorded by the subject in a diary. Analgesic score was calculated from the analgesic use data based on a table of analgesic medications, with non-narcotic medications assigned a value of 1 point and narcotic medications assigned a value of 4 points. Analysis was done by Kaplan-Meier method on ITT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression, death or study cut-off date (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	10.1 (8.28 to 11.76)	8 (6.9 to 9.66)	7.3 (6.44 to 9.3)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 25 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.189
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.986
upper limit	1.434

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a Cox Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.189

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.985
upper limit	1.435

Secondary: Percentage of Subjects With Pain Response

End point title	Percentage of Subjects With Pain Response

End point description:

Pain response was defined as either a ≥2-point decrease from baseline median PPI score without increase in analgesic score, or a ≥50% decrease in analgesic use from baseline mean analgesic score (only in subjects with baseline mean analgesic score≥10) without increase in the pain. Either criterion was maintained for 2 consecutive evaluations at least 3 weeks apart. PPI was rated by subject in a diary using a scale of 0=no pain, 1=mild, 2=discomforting, 3=distressing, 4=horrible 5=excruciating. Analgesic use was recorded by the subject in a diary. Analgesic score was calculated from the analgesic use data based on a table of analgesic medications, with non-narcotic medications assigned a value of 1 point and narcotic medications assigned a value of 4 points. Analysis was done on ITT population. Number of subjects analysed=subjects with pain score with median PPI ≥2 and/or mean analgesic score≥10 points at baseline and at least one valid post-baseline value for specified endpoint.

End point type	Secondary

End point timeframe:

Baseline until pain progression, death or study cut-off date (maximum duration: 51 months).

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	99	104	
Units: percentage of subjects				
number (confidence interval 95%)	40.7 (30 to 51.4)	42.4 (32.7 to 52.2)	39.4 (30 to 48.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Skeletal Related Events (SRE) Free Survival

End point title	Skeletal Related Events (SRE) Free Survival

End point description:

SRE free survival was defined as the time interval between the date of randomization and the date of the occurrence of the first event defining a SRE or death due to any cause, whichever was earlier. SRE were assessed by clinical evaluation. Occurrence of SRE was defined as: pathological fracture(s) and/or spinal cord compression; need for bone irradiation, including radioisotopes or bone surgery; and change of antineoplastic therapy (including introduction of bisphosphonates or denosumab in the setting of increased pain) to treat bone pain. Analysis was performed by Kaplan-Meier method on ITT population which included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline until occurrence of first SRE or death (maximum duration: 51 months)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	389	388	
Units: months				
median (confidence interval 95%)	19 (15.24 to 22.44)	19.2 (15.21 to 24.61)	17.1 (14.59 to 20.5)	

Statistical analyses

Statistical analysis title	Cabazitaxel 25 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a COX Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 25 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	779
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.121
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.886
upper limit	1.417

Statistical analysis title	Cabazitaxel 20 mg/m^2 vs Docetaxel 75 mg/m^2

Statistical analysis description:

Hazard ratio was estimated using a COX Proportional Hazards regression model. The Cox proportional hazard model was adjusted by ECOG PS score at baseline, measurable disease at baseline, and region with commercial availability of cabazitaxel at the time of randomization.

Comparison groups	Cabazitaxel 20 mg/m^2 v Docetaxel 75 mg/m^2
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.798
upper limit	1.288

Secondary: Change From Baseline in Functional Assessment of Cancer Therapy-Prostate (FACT-P) Total Score as a Measure of Health Related Quality of Life (HRQoL)

End point title	Change From Baseline in Functional Assessment of Cancer Therapy-Prostate (FACT-P) Total Score as a Measure of Health Related Quality of Life (HRQoL)

End point description:

FACT-P was a 39-item subject rated questionnaire that measures the concerns of subjects with prostate cancer. It consisted of 5 sub-scales assessing physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items), and prostate-specific concerns (12 items). FACT-P total score was the sum of all 5 subscale scores. It ranged from 0 to 156 with higher score indicated better quality of life with fewer symptoms. Analysis was performed on FACT-P population that included all subjects with evaluable individual FACT-P subscale score at baseline and post-baseline on at least 1 of the subscale domains.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 (each cycle 21-day); post-treatment follow up 1, 2, 3, 4, 5, 6 (each up to 12 weeks)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	370	361	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Change at Cycle 1 (n=333, 323, 321)	4.17 (1.3 to 7.05)	7.66 (4.79 to 10.53)	6.93 (3.97 to 9.88)	
Change at Cycle 2 (n=339, 339, 323)	5.33 (2.46 to 8.2)	7.15 (4.28 to 10.01)	5.28 (2.32 to 8.24)	
Change at Cycle 3 (n=330, 332, 316)	4.94 (2.06 to 7.82)	6.79 (3.93 to 9.66)	4.61 (1.64 to 7.58)	
Change at Cycle 4 (n=316, 323, 302)	4.07 (1.17 to 6.96)	5.22 (2.35 to 8.09)	4.01 (1.03 to 6.99)	
Change at Cycle 5 (n=293, 290, 283)	4.36 (1.44 to 7.27)	5.16 (2.26 to 8.06)	4.09 (1.09 to 7.08)	
Change at Cycle 6 (n=272, 267, 262)	3.46 (0.53 to 6.39)	3.8 (0.88 to 6.73)	3.37 (0.35 to 6.39)	
Change at Cycle 7 (n=244, 246, 241)	3.16 (0.2 to 6.12)	3.66 (0.71 to 6.61)	3.42 (0.38 to 6.45)	
Change at Cycle 8 (n=228, 222, 225)	2.61 (-0.37 to 5.59)	2.71 (-0.27 to 5.68)	1.67 (-1.39 to 4.73)	
Change at Cycle 9 (n=174, 196, 190)	2.2 (-0.87 to 5.27)	2.67 (-0.35 to 5.68)	1.89 (-1.22 to 5.01)	
Change at Cycle 10 (n=149, 164, 166)	2.08 (-1.05 to 5.21)	2.09 (-0.99 to 5.18)	1.84 (-1.32 to 5)	
Change at Cycle 11 (n=101, 115, 111)	0.15 (-3.18 to 3.47)	3.35 (0.1 to 6.6)	2.68 (-0.67 to 6.02)	
Change at Cycle 12 (n=83, 98, 98)	0.52 (-2.94 to 3.97)	3.95 (0.61 to 7.29)	0.63 (-2.78 to 4.05)	
Change at Cycle 13 (n=58, 85, 80)	1.79 (-1.94 to 5.53)	2.48 (-0.95 to 5.91)	0.55 (-3 to 4.09)	

Change at Cycle 14 (n=55, 78, 71)	-1.78 (-5.56 to 2)	2.2 (-1.29 to 5.69)	-0.42 (-4.06 to 3.21)	
Change at Cycle 15 (n=44, 71, 63)	-3.49 (-7.5 to 0.51)	1.74 (-1.82 to 5.3)	1.22 (-2.51 to 4.95)	
Change at Cycle 16 (n=42, 58, 58)	-3.83 (-7.89 to 0.23)	1.62 (-2.11 to 5.35)	0.5 (-3.3 to 4.3)	
Change at Follow-up 1 (n=176, 185, 175)	-1.08 (-4.15 to 1.99)	-1.45 (-4.48 to 1.59)	-1.82 (-4.97 to 1.32)	
Change at Follow-up 2 (n=145, 129, 133)	-0.02 (-3.16 to 3.13)	-1.98 (-5.17 to 1.21)	-1.78 (-5.04 to 1.47)	
Change at Follow-up 3 (n=110, 103, 101)	-0.55 (-3.83 to 2.74)	-2.16 (-5.47 to 1.14)	-2.68 (-6.08 to 0.72)	
Change at Follow-up 4 (n=87, 73, 81)	-1.19 (-4.61 to 2.23)	-3.64 (-7.18 to -0.1)	-1.7 (-5.25 to 1.84)	
Change at Follow-up 5 (n=72, 63, 76)	-2.05 (-5.61 to 1.51)	-6.73 (-10.39 to -3.06)	-0.6 (-4.18 to 2.99)	
Change at Follow-up 6 (n=58, 46, 57)	-1.17 (-4.92 to 2.58)	-5.36 (-9.32 to -1.4)	-4.05 (-7.87 to -0.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Cancer Therapy-Prostate (FACT-P):Trial Outcome Index as a Measure of HRQoL

End point title	Change From Baseline in Functional Assessment of Cancer Therapy-Prostate (FACT-P):Trial Outcome Index as a Measure of HRQoL

End point description:

FACT-P was a 39-item subject rated questionnaire that measures the concerns of subjects with prostate cancer. It consisted of 5 sub-scales assessing physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items), and prostate-specific concerns (12 items). Physical well being, functional well being, and prostate-specific concerns sub-scales of the FACT-P questionnaire were combined to calculate TOI. Total TOI score ranges from 0 to 104, with higher scores representing a better quality of life with fewer symptoms. Analysis was performed on FACT-P population that included all subjects with evaluable individual FACT-P subscale score at baseline and post-baseline on at least 1 of the subscale domains.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 (each cycle 21-day); post-treatment follow up 1, 2, 3, 4, 5, 6 (each up to 12 weeks)

End point values	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	371	361	
Units: units on a scale				
least squares mean (confidence interval 95%)				
Change at Cycle 1 (n=331, 324, 318)	3.31 (1.05 to 5.58)	6.09 (3.83 to 8.35)	5.76 (3.43 to 8.09)	
Change at Cycle 2 (n=334, 337, 318)	4.37 (2.1 to 6.64)	5.96 (3.7 to 8.21)	4.26 (1.92 to 6.59)	

Change at Cycle 3 (n=325, 332, 314)	4.31 (2.04 to 6.58)	5.28 (3.02 to 7.53)	3.65 (1.31 to 5.99)	
Change at Cycle 4 (n=313, 321, 301)	3.39 (1.11 to 5.67)	4.1 (1.83 to 6.36)	3.2 (0.85 to 5.55)	
Change at Cycle 5 (n=289, 285, 282)	3.41 (1.11 to 5.7)	4.05 (1.76 to 6.34)	3.1 (0.74 to 5.46)	
Change at Cycle 6 (n=270, 264, 260)	2.76 (0.45 to 5.07)	3.15 (0.85 to 5.46)	2.88 (0.5 to 5.26)	
Change at Cycle 7 (n=239, 241, 240)	2.29 (-0.05 to 4.62)	3.14 (0.81 to 5.47)	2.94 (0.54 to 5.34)	
Change at Cycle 8 (n=223, 220, 222)	1.67 (-0.69 to 4.02)	2.26 (-0.09 to 4.61)	1.49 (-0.92 to 3.91)	
Change at Cycle 9 (n=174, 192, 189)	1.75 (-0.67 to 4.18)	2.15 (-0.24 to 4.53)	1.73 (-0.73 to 4.19)	
Change at Cycle 10 (n=148, 163, 163)	1.52 (-0.96 to 4)	1.56 (-0.88 to 3.99)	1.62 (-0.89 to 4.12)	
Change at Cycle 11 (n=99, 115, 110)	0.35 (-2.29 to 3)	2.72 (0.15 to 5.3)	2.19 (-0.46 to 4.84)	
Change at Cycle 12 (n=82, 97, 98)	1.04 (-1.7 to 3.79)	3.08 (0.43 to 5.73)	0.75 (-1.95 to 3.46)	
Change at Cycle 13 (n=57, 85, 81)	2.13 (-0.85 to 5.11)	1.78 (-0.94 to 4.5)	0.82 (-1.98 to 3.62)	
Change at Cycle 14 (n=54, 78, 71)	-0.13 (-3.15 to 2.89)	1.59 (-1.18 to 4.36)	-0.07 (-2.95 to 2.81)	
Change at Cycle 15 (n=44, 71, 63)	-2.1 (-5.29 to 1.09)	1.29 (-1.53 to 4.11)	1.49 (-1.47 to 4.45)	
Change at Cycle 16 (n=42, 58, 57)	-2.26 (-5.49 to 0.97)	1.23 (-1.73 to 4.19)	1.44 (-1.59 to 4.47)	
Change at Follow-up 1 (n=173, 183, 171)	-0.96 (-3.38 to 1.47)	-1.26 (-3.66 to 1.14)	-1.62 (-4.11 to 0.86)	
Change at Follow-up 2 (n=143, 127, 132)	-0.07 (-2.56 to 2.42)	-1.12 (-3.65 to 1.41)	-1.05 (-3.62 to 1.53)	
Change at Follow-up 3 (n=109, 101, 99)	-0.32 (-2.92 to 2.28)	-1.67 (-4.29 to 0.96)	-1.98 (-4.68 to 0.72)	
Change at Follow-up 4 (n=87, 71, 81)	-0.91 (-3.62 to 1.8)	-2.54 (-5.36 to 0.29)	-1.03 (-3.84 to 1.78)	
Change at Follow-up 5 (n=70, 62, 76)	-2.15 (-4.99 to 0.69)	-5.36 (-8.27 to -2.44)	-0.82 (-3.67 to 2.02)	
Change at Follow-up 6 (n=58, 45, 55)	-1.77 (-4.75 to 1.2)	-5.32 (-8.49 to -2.16)	-2.76 (-5.82 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (up to 51 months) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (time from first dose of study drug until 30 days after the last administration of study drug). Analysis was done on safety population (randomized subjects receiving study drug and analysed as per the treatment actually received).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Docetaxel 75 mg/m^2

Reporting group description:

Docetaxel (TXT) 75 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.

Reporting group title	Cabazitaxel 20 mg/m^2

Reporting group description:

Cabazitaxel 20 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.

Reporting group title	Cabazitaxel 25 mg/m^2

Reporting group description:

Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle in combination with Prednisone 10 mg orally, once daily until DP, unacceptable toxicity or subject's refusal.

Serious adverse events	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	126 / 387 (32.56%)	127 / 369 (34.42%)	187 / 391 (47.83%)
number of deaths (all causes)	259	254	249
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma Of Colon			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon Cancer			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Colorectal Cancer Metastatic			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Malignant Neoplasm Of Ampulla Of Vater			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Metastases To Central Nervous System			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases To Meninges			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Metastatic Pain			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Small Cell Lung Cancer			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Prostate Cancer Metastatic			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cancer			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Sebaceous Carcinoma			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional Cell Carcinoma			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour Pain			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Neoplasm			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Dissection			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Deep Vein Thrombosis			
subjects affected / exposed	5 / 387 (1.29%)	2 / 369 (0.54%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	2 / 5	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Hypertension			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Hypovolaemic Shock			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic Venous Thrombosis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Peripheral Ischaemia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Shock			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Death			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Device Issue			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Disease Progression			
subjects affected / exposed	1 / 387 (0.26%)	4 / 369 (1.08%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 2
Fatigue			
subjects affected / exposed	2 / 387 (0.52%)	2 / 369 (0.54%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			

subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion Site Extravasation			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Multi-Organ Failure			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oedema			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Oedema Peripheral			
subjects affected / exposed	2 / 387 (0.52%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 387 (0.52%)	1 / 369 (0.27%)	4 / 391 (1.02%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Death			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 2
Immune system disorders			
Anaphylactic Reaction			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine Release Syndrome			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Hypersensitivity			
subjects affected / exposed	2 / 387 (0.52%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic Pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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			
Aspiration			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Bronchospasm			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choking			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			

subjects affected / exposed	2 / 387 (0.52%)	0 / 369 (0.00%)	0 / 391 (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
Cough			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Epistaxis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Interstitial Lung Disease			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Pleural Effusion			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Aspiration			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Pulmonary Congestion			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Pulmonary Embolism			
subjects affected / exposed	3 / 387 (0.78%)	8 / 369 (2.17%)	8 / 391 (2.05%)
occurrences causally related to treatment / all	3 / 3	4 / 8	1 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary Oedema			
subjects affected / exposed	2 / 387 (0.52%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	2 / 391 (0.51%)
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			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Creatinine Increased			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creatinine Renal Clearance Decreased			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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

Hepatic Enzyme Increased			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International Normalised Ratio Increased			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil Count Decreased			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	1 / 1	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral Injury			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Cystitis Radiation			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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

Hand Fracture			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Recall Phenomenon			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Toxicity To Various Agents			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Traumatic Fracture			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Limb Fracture			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrong Drug Administered			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute Coronary Syndrome			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Pectoris			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Angina Unstable			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Atrial Fibrillation			
subjects affected / exposed	1 / 387 (0.26%)	2 / 369 (0.54%)	4 / 391 (1.02%)
occurrences causally related to treatment / all	1 / 1	1 / 3	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Flutter			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Bundle Branch Block Left			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Arrest			
subjects affected / exposed	2 / 387 (0.52%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac Failure			

subjects affected / exposed	1 / 387 (0.26%)	2 / 369 (0.54%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			
subjects affected / exposed	3 / 387 (0.78%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebellar Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral Haematoma			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Infarction			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral Ischaemia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Cerebrovascular Accident			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coma			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Haemorrhagic Stroke			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic Stroke			
subjects affected / exposed	0 / 387 (0.00%)	3 / 369 (0.81%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukoencephalopathy			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Movement Disorder			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Peripheral Motor Neuropathy			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Presyncope			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Cord Compression			
subjects affected / exposed	1 / 387 (0.26%)	4 / 369 (1.08%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 387 (0.26%)	2 / 369 (0.54%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 387 (0.00%)	3 / 369 (0.81%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 387 (0.52%)	8 / 369 (2.17%)	5 / 391 (1.28%)
occurrences causally related to treatment / all	2 / 2	5 / 9	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	27 / 387 (6.98%)	7 / 369 (1.90%)	40 / 391 (10.23%)
occurrences causally related to treatment / all	30 / 30	7 / 7	44 / 44
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Leukopenia			
subjects affected / exposed	2 / 387 (0.52%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	3 / 3	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	4 / 387 (1.03%)	4 / 369 (1.08%)	10 / 391 (2.56%)
occurrences causally related to treatment / all	4 / 4	4 / 4	10 / 10
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract Subcapsular			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Macular Fibrosis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal Pain			
subjects affected / exposed	1 / 387 (0.26%)	3 / 369 (0.81%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Barrett's Oesophagus			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	4 / 391 (1.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis Ischaemic			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis Ulcerative			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Constipation			
subjects affected / exposed	1 / 387 (0.26%)	2 / 369 (0.54%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	4 / 387 (1.03%)	2 / 369 (0.54%)	10 / 391 (2.56%)
occurrences causally related to treatment / all	3 / 4	2 / 2	12 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular Perforation			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer			

subjects affected / exposed	2 / 387 (0.52%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Enterovesical Fistula			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Faecal Incontinence			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Gastric Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	0 / 391 (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
Gastric Perforation			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer			
subjects affected / exposed	1 / 387 (0.26%)	2 / 369 (0.54%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Gastritis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Angiodysplasia Haemorrhagic			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Ulcer Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic Erosive Gastritis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable Bowel Syndrome			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Large Intestinal Obstruction			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Large Intestine Perforation			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Large Intestine Polyp			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Mechanical Ileus			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	3 / 387 (0.78%)	1 / 369 (0.27%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	2 / 3	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising Colitis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Oesophageal Ulcer Haemorrhage			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Pancreatitis Acute			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Vomiting			
subjects affected / exposed	3 / 387 (0.78%)	2 / 369 (0.54%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	2 / 3	2 / 2	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Acute			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Hepatic Function Abnormal			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic Foot			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	3 / 387 (0.78%)	3 / 369 (0.81%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	1 / 3	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bladder Obstruction			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Bladder Perforation			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Calculus Bladder			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Calculus Urinary			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis Glandularis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis Noninfective			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 387 (0.52%)	10 / 369 (2.71%)	13 / 391 (3.32%)
occurrences causally related to treatment / all	0 / 2	1 / 10	4 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 387 (0.26%)	5 / 369 (1.36%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive Uropathy			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	0 / 391 (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
Renal Colic			

subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Renal Failure			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Renal Impairment			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric Obstruction			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Ureteric Stenosis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral Stenosis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Urethritis Noninfective			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Urinary Bladder Haemorrhage			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Urinary Bladder Rupture			

subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Retention			
subjects affected / exposed	0 / 387 (0.00%)	3 / 369 (0.81%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Obstruction			
subjects affected / exposed	1 / 387 (0.26%)	4 / 369 (1.08%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 4	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Pain			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Back Pain			
subjects affected / exposed	2 / 387 (0.52%)	3 / 369 (0.81%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Pain			
subjects affected / exposed	2 / 387 (0.52%)	3 / 369 (0.81%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank Pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	4 / 391 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Intervertebral Disc Protrusion			
subjects affected / exposed	2 / 387 (0.52%)	0 / 369 (0.00%)	0 / 391 (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
Joint Effusion			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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 Pain			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Neck Pain			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Pathological Fracture			
subjects affected / exposed	1 / 387 (0.26%)	3 / 369 (0.81%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Osteoarthritis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Infections and infestations			
Abscess Intestinal			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Abscess Jaw			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Abscess Oral			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Anal Abscess			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Appendicitis Perforated			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Bacteraemia			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (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
Bronchopneumonia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Cholecystitis Infective			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Erysipelas			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Gastroenteritis			

subjects affected / exposed	0 / 387 (0.00%)	2 / 369 (0.54%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Abscess			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	5 / 387 (1.29%)	1 / 369 (0.27%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	4 / 5	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Neutropenic Infection			
subjects affected / exposed	12 / 387 (3.10%)	3 / 369 (0.81%)	21 / 391 (5.37%)
occurrences causally related to treatment / all	11 / 12	3 / 3	20 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Neutropenic Sepsis			

subjects affected / exposed	3 / 387 (0.78%)	1 / 369 (0.27%)	4 / 391 (1.02%)
occurrences causally related to treatment / all	3 / 3	1 / 1	4 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	2 / 2
Peritonitis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	8 / 387 (2.07%)	3 / 369 (0.81%)	11 / 391 (2.81%)
occurrences causally related to treatment / all	4 / 8	0 / 3	6 / 11
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Post Procedural Cellulitis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Abscess			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	1 / 387 (0.26%)	1 / 369 (0.27%)	0 / 391 (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
Sepsis			
subjects affected / exposed	1 / 387 (0.26%)	3 / 369 (0.81%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	1 / 1	2 / 3	2 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Septic Shock			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	3 / 391 (0.77%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Skin Infection			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Staphylococcal Osteomyelitis			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Staphylococcal Sepsis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	0 / 391 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	2 / 387 (0.52%)	9 / 369 (2.44%)	8 / 391 (2.05%)
occurrences causally related to treatment / all	1 / 2	6 / 13	5 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 387 (0.00%)	1 / 369 (0.27%)	2 / 391 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection			

subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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 disorders			
Dehydration			
subjects affected / exposed	0 / 387 (0.00%)	3 / 369 (0.81%)	5 / 391 (1.28%)
occurrences causally related to treatment / all	0 / 0	2 / 3	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure To Thrive			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hyperglycaemia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	1 / 387 (0.26%)	0 / 369 (0.00%)	0 / 391 (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
Hypoglycaemia			
subjects affected / exposed	2 / 387 (0.52%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic Acidosis			

subjects affected / exposed	0 / 387 (0.00%)	0 / 369 (0.00%)	1 / 391 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

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

Non-serious adverse events	Docetaxel 75 mg/m^2	Cabazitaxel 20 mg/m^2	Cabazitaxel 25 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	353 / 387 (91.21%)	323 / 369 (87.53%)	353 / 391 (90.28%)
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 387 (4.13%)	20 / 369 (5.42%)	12 / 391 (3.07%)
occurrences (all)	16	27	13
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	94 / 387 (24.29%)	84 / 369 (22.76%)	90 / 391 (23.02%)
occurrences (all)	186	139	149
Fatigue			
subjects affected / exposed	110 / 387 (28.42%)	105 / 369 (28.46%)	125 / 391 (31.97%)
occurrences (all)	154	141	173
Oedema Peripheral			
subjects affected / exposed	78 / 387 (20.16%)	36 / 369 (9.76%)	30 / 391 (7.67%)
occurrences (all)	97	43	35
Pyrexia			
subjects affected / exposed	36 / 387 (9.30%)	22 / 369 (5.96%)	28 / 391 (7.16%)
occurrences (all)	43	24	38
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	38 / 387 (9.82%)	26 / 369 (7.05%)	33 / 391 (8.44%)
occurrences (all)	43	29	37
Dyspnoea			
subjects affected / exposed	36 / 387 (9.30%)	36 / 369 (9.76%)	32 / 391 (8.18%)
occurrences (all)	38	41	34
Epistaxis			

subjects affected / exposed	22 / 387 (5.68%)	10 / 369 (2.71%)	17 / 391 (4.35%)
occurrences (all)	29	12	17
Psychiatric disorders			
Insomnia			
subjects affected / exposed	28 / 387 (7.24%)	24 / 369 (6.50%)	20 / 391 (5.12%)
occurrences (all)	33	26	21
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	14 / 387 (3.62%)	27 / 369 (7.32%)	16 / 391 (4.09%)
occurrences (all)	14	29	17
Weight Decreased			
subjects affected / exposed	19 / 387 (4.91%)	17 / 369 (4.61%)	40 / 391 (10.23%)
occurrences (all)	20	17	44
Injury, poisoning and procedural complications			
Incorrect Dose Administered			
subjects affected / exposed	0 / 387 (0.00%)	6 / 369 (1.63%)	30 / 391 (7.67%)
occurrences (all)	0	7	30
Nervous system disorders			
Dizziness			
subjects affected / exposed	25 / 387 (6.46%)	27 / 369 (7.32%)	34 / 391 (8.70%)
occurrences (all)	35	28	40
Dysgeusia			
subjects affected / exposed	70 / 387 (18.09%)	41 / 369 (11.11%)	59 / 391 (15.09%)
occurrences (all)	106	41	62
Headache			
subjects affected / exposed	31 / 387 (8.01%)	21 / 369 (5.69%)	27 / 391 (6.91%)
occurrences (all)	40	28	32
Paraesthesia			
subjects affected / exposed	24 / 387 (6.20%)	25 / 369 (6.78%)	14 / 391 (3.58%)
occurrences (all)	26	30	19
Peripheral Sensory Neuropathy			
subjects affected / exposed	97 / 387 (25.06%)	43 / 369 (11.65%)	48 / 391 (12.28%)
occurrences (all)	105	48	53
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	8 / 387 (2.07%)	11 / 369 (2.98%)	25 / 391 (6.39%)
occurrences (all)	9	12	25
Eye disorders			
Lacrimation Increased			
subjects affected / exposed	37 / 387 (9.56%)	8 / 369 (2.17%)	3 / 391 (0.77%)
occurrences (all)	38	8	3
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	14 / 387 (3.62%)	34 / 369 (9.21%)	32 / 391 (8.18%)
occurrences (all)	20	43	42
Constipation			
subjects affected / exposed	69 / 387 (17.83%)	90 / 369 (24.39%)	78 / 391 (19.95%)
occurrences (all)	94	128	110
Diarrhoea			
subjects affected / exposed	140 / 387 (36.18%)	120 / 369 (32.52%)	190 / 391 (48.59%)
occurrences (all)	269	225	341
Dyspepsia			
subjects affected / exposed	13 / 387 (3.36%)	20 / 369 (5.42%)	15 / 391 (3.84%)
occurrences (all)	13	24	16
Nausea			
subjects affected / exposed	86 / 387 (22.22%)	92 / 369 (24.93%)	125 / 391 (31.97%)
occurrences (all)	130	133	210
Stomatitis			
subjects affected / exposed	53 / 387 (13.70%)	18 / 369 (4.88%)	26 / 391 (6.65%)
occurrences (all)	83	21	35
Vomiting			
subjects affected / exposed	44 / 387 (11.37%)	44 / 369 (11.92%)	75 / 391 (19.18%)
occurrences (all)	64	53	97
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	151 / 387 (39.02%)	33 / 369 (8.94%)	51 / 391 (13.04%)
occurrences (all)	156	35	53
Nail Disorder			
subjects affected / exposed	35 / 387 (9.04%)	1 / 369 (0.27%)	3 / 391 (0.77%)
occurrences (all)	35	1	4
Rash			

subjects affected / exposed	23 / 387 (5.94%)	3 / 369 (0.81%)	5 / 391 (1.28%)
occurrences (all)	26	3	6
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	9 / 387 (2.33%)	23 / 369 (6.23%)	21 / 391 (5.37%)
occurrences (all)	10	28	36
Haematuria			
subjects affected / exposed	13 / 387 (3.36%)	69 / 369 (18.70%)	91 / 391 (23.27%)
occurrences (all)	17	102	131
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	31 / 387 (8.01%)	34 / 369 (9.21%)	43 / 391 (11.00%)
occurrences (all)	42	45	55
Back Pain			
subjects affected / exposed	52 / 387 (13.44%)	65 / 369 (17.62%)	55 / 391 (14.07%)
occurrences (all)	63	79	67
Bone Pain			
subjects affected / exposed	24 / 387 (6.20%)	30 / 369 (8.13%)	29 / 391 (7.42%)
occurrences (all)	31	35	31
Muscle Spasms			
subjects affected / exposed	15 / 387 (3.88%)	28 / 369 (7.59%)	13 / 391 (3.32%)
occurrences (all)	17	33	14
Myalgia			
subjects affected / exposed	28 / 387 (7.24%)	22 / 369 (5.96%)	22 / 391 (5.63%)
occurrences (all)	42	30	24
Pain In Extremity			
subjects affected / exposed	38 / 387 (9.82%)	26 / 369 (7.05%)	19 / 391 (4.86%)
occurrences (all)	54	36	25
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	25 / 387 (6.46%)	19 / 369 (5.15%)	14 / 391 (3.58%)
occurrences (all)	31	23	15
Urinary Tract Infection			
subjects affected / exposed	7 / 387 (1.81%)	35 / 369 (9.49%)	33 / 391 (8.44%)
occurrences (all)	7	45	47
Metabolism and nutrition disorders			

Decreased Appetite subjects affected / exposed occurrences (all)	66 / 387 (17.05%) 109	50 / 369 (13.55%) 81	74 / 391 (18.93%) 105

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2011	Amendment 1: It included the following change: Body Surface Area (BSA) capping at 2.1 m^2 for the calculation of the dose was removed, following the Food & Drug Administration (FDA) request.
04 May 2011	Amendment 2: It included the following changes: Implemented the recommendations made by the renal expert board. Addition of pharmacogenomics for subjects with pharmacokinetics in selected sites. An exploratory objective was included to evaluate circulating free plasma Deoxyribonucleic acid (total and tumor specific) for biomarker studies in selected sites.
23 January 2012	Amendment 3: It included the following changes: Premedication with oral anti-histamines was allowed in countries where no IV formulation was available. Updated information on preparation and administration of Cabazitaxel, and storage of the premix and infusion solution according to Investigational Brochure edition 13 was incorporated.
29 March 2012	Amendment 4: It included the following changes: In order to avoid any confusion on the circumstances in which the text was applicable, relocated within protocol, the text that had been added in amendment#3, regarding situations in which, an investigator might wish to continue study treatment because a subject had a strong benefit from the treatment despite a criterion of treatment discontinuation being met. It was clearly specified that biomarker samples had to be done before cycle administration.
22 November 2013	Amendment 5: It included the following change: Although the first interim analysis suggested that the study was unlikely to achieve the primary endpoint of demonstrating superiority of Cabazitaxel to Docetaxel in first line mCRPC based on OS, as the study was fully enrolled and no subject group was disadvantaged based on the early data, and after consultation with the US FDA and DMC, Sanofi had elected to continue the study and allowed subjects currently on treatment to continue protocol therapy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported