



Clinical trial results:

Randomized, Open Label, Multi-Center Study comparing Cabazitaxel at 25 mg/m² and at 20 mg/m² 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/m² (Arm A) or 20 mg/m² (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/m² 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/m² 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/m² 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/m².

[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 \geq 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/m².

[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 \geq 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/m².

[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)

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|---|--|
| 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($\geq 50\%$ decline from baseline PSA of ≥ 10 ng/mL):increase of $\geq 25\%$ (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 $\geq 50\%$ decline from baseline PSA ≥ 10 ng/mL):increase of $\geq 25\%$ (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 3 weeks apart; (b) in subjects with baseline value = 0 ng/mL: a post baseline PSA value ≥ 2 ng/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 $\geq 50\%$ 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 $\geq 25\%$ 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 $\geq 50\%$ 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/m² 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/m² 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/m² 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/m² | Cabazitaxel 20 mg/m² | Cabazitaxel 25 mg/m² |
|---|--------------------------------------|--|--|
| 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 occurrences (all) | 22 / 387 (5.68%) 29 | 10 / 369 (2.71%) 12 | 17 / 391 (4.35%) 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 occurrences (all) | 8 / 387 (2.07%) 9 | 11 / 369 (2.98%) 12 | 25 / 391 (6.39%) 25 |
| Eye disorders Lacrimation Increased subjects affected / exposed occurrences (all) | 37 / 387 (9.56%) 38 | 8 / 369 (2.17%) 8 | 3 / 391 (0.77%) 3 |
| Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) | 14 / 387 (3.62%) 20 | 34 / 369 (9.21%) 43 | 32 / 391 (8.18%) 42 |
| Constipation subjects affected / exposed occurrences (all) | 69 / 387 (17.83%) 94 | 90 / 369 (24.39%) 128 | 78 / 391 (19.95%) 110 |
| Diarrhoea subjects affected / exposed occurrences (all) | 140 / 387 (36.18%) 269 | 120 / 369 (32.52%) 225 | 190 / 391 (48.59%) 341 |
| Dyspepsia subjects affected / exposed occurrences (all) | 13 / 387 (3.36%) 13 | 20 / 369 (5.42%) 24 | 15 / 391 (3.84%) 16 |
| Nausea subjects affected / exposed occurrences (all) | 86 / 387 (22.22%) 130 | 92 / 369 (24.93%) 133 | 125 / 391 (31.97%) 210 |
| Stomatitis subjects affected / exposed occurrences (all) | 53 / 387 (13.70%) 83 | 18 / 369 (4.88%) 21 | 26 / 391 (6.65%) 35 |
| Vomiting subjects affected / exposed occurrences (all) | 44 / 387 (11.37%) 64 | 44 / 369 (11.92%) 53 | 75 / 391 (19.18%) 97 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 151 / 387 (39.02%) 156 | 33 / 369 (8.94%) 35 | 51 / 391 (13.04%) 53 |
| Nail Disorder subjects affected / exposed occurrences (all) | 35 / 387 (9.04%) 35 | 1 / 369 (0.27%) 1 | 3 / 391 (0.77%) 4 |
| Rash | | | |

| | | | |
|--|------------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 23 / 387 (5.94%) 26 | 3 / 369 (0.81%) 3 | 5 / 391 (1.28%) 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