



Clinical trial results:

A Phase 3, Multicenter, Open-label, Randomized Study of nab-Paclitaxel Plus Gemcitabine

Versus Gemcitabine Alone as Adjuvant Therapy in Subjects With Surgically Resected

Pancreatic Adenocarcinoma

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2013-003398-91 |
| Trial protocol | CZ AT HU ES IT PT BE FI IE DK GB NL |
| Global end of trial date | 30 June 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 29 June 2023 |
| First version publication date | 29 June 2023 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | ABI-007-PANC-003 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01964430 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 23 August 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 June 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare disease-free survival (DFS) between subjects randomized to nabpaclitaxel in combination with gemcitabine and subjects randomized to gemcitabine alone

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 28 March 2014 |
| 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 | Canada: 31 |
| Country: Number of subjects enrolled | United States: 269 |
| Country: Number of subjects enrolled | Austria: 27 |
| Country: Number of subjects enrolled | Belgium: 13 |
| Country: Number of subjects enrolled | Czechia: 6 |
| Country: Number of subjects enrolled | Denmark: 10 |
| Country: Number of subjects enrolled | Finland: 19 |
| Country: Number of subjects enrolled | France: 37 |
| Country: Number of subjects enrolled | Germany: 85 |
| Country: Number of subjects enrolled | Hungary: 19 |
| Country: Number of subjects enrolled | Ireland: 4 |
| Country: Number of subjects enrolled | Italy: 106 |
| Country: Number of subjects enrolled | Netherlands: 6 |
| Country: Number of subjects enrolled | Portugal: 12 |
| Country: Number of subjects enrolled | Spain: 54 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Australia: 50 |
| Country: Number of subjects enrolled | Hong Kong: 4 |
| Country: Number of subjects enrolled | Korea, Republic of: 51 |

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Singapore: 6 |
| Country: Number of subjects enrolled | Taiwan: 47 |
| Worldwide total number of subjects | 866 |
| EEA total number of subjects | 398 |

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) | 446 |
| From 65 to 84 years | 419 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

The study randomized participants at 160 sites in 21 countries: Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Hong Kong, Hungary, Ireland, Italy, Netherlands, Portugal, Singapore, Republic of Korea, Spain, Taiwan, United Kingdom and the US.

Pre-assignment

Screening details:

Participants were randomized using a stratified randomization with a 1:1 ratio to either nab-paclitaxel followed by gemcitabine, or gemcitabine alone. Stratification factors were tumor resection status (R0 versus R1), nodal status lymph node positive versus lymph node negative, and region [North America, Europe, and Australia versus Asia Pacific]).

Period 1

| | |
|------------------------------|--------------------------------------|
| Period 1 title | Pre-Treatment (Randomization) Period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | nab-Paclitaxel and Gemcitabine |

Arm description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1000 mg/m² as a 30- to 40-minute infusion

| | |
|--|-----------------------|
| Investigational medicinal product name | nab-Paclitaxel |
| Investigational medicinal product code | |
| Other name | ABRAXANE |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

125 mg/m² as a 30- to 40-minute infusion

| | |
|------------------|-------------|
| Arm title | Gemcitabine |
|------------------|-------------|

Arm description:

Participants received gemcitabine 1000 mg/m² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1000 mg/m² as a 30- to 40-minute infusion

| Number of subjects in period 1 | nab-Paclitaxel and Gemcitabine | Gemcitabine |
|--------------------------------|--------------------------------|-------------|
| Started | 432 | 434 |
| Completed | 429 | 423 |
| Not completed | 3 | 11 |
| Consent withdrawn by subject | 2 | 9 |
| Adverse event, non-fatal | 1 | - |
| Protocol Deviation | - | 2 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | nab-Paclitaxel and Gemcitabine |

Arm description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1000 mg/m² as a 30- to 40-minute infusion

| | |
|--|-----------------------|
| Investigational medicinal product name | nab-Paclitaxel |
| Investigational medicinal product code | |
| Other name | ABRAXANE |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
125 mg/m² as a 30- to 40-minute infusion

| | |
|---|-----------------------|
| Arm title | Gemcitabine |
| Arm description: Participants received gemcitabine 1000 mg/m ² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death. | |
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
1000 mg/m² as a 30- to 40-minute infusion

| Number of subjects in period 2 | nab-Paclitaxel and Gemcitabine | Gemcitabine |
|---------------------------------------|--------------------------------|-------------|
| Started | 429 | 423 |
| Completed | 287 | 310 |
| Not completed | 142 | 113 |
| Adverse event, serious fatal | 1 | 3 |
| Consent withdrawn by subject | 36 | 27 |
| Physician decision | 5 | 4 |
| Disease Relapse | 28 | 38 |
| Adverse event, non-fatal | 71 | 37 |
| Protocol Deviation | - | 1 |
| Other reasons | 1 | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | nab-Paclitaxel and Gemcitabine |
|-----------------------|--------------------------------|

Reporting group description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|-----------------------|-------------|
| Reporting group title | Gemcitabine |
|-----------------------|-------------|

Reporting group description:

Participants received gemcitabine 1000 mg/m² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| Reporting group values | nab-Paclitaxel and Gemcitabine | Gemcitabine | Total |
|--|--------------------------------|-------------|-------|
| Number of subjects | 432 | 434 | 866 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 221 | 225 | 446 |
| From 65-84 years | 211 | 208 | 419 |
| 85 years and over | 0 | 1 | 1 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 63.4 | 62.9 | - |
| standard deviation | ± 9.58 | ± 8.84 | - |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 204 | 181 | 385 |
| Male | 228 | 253 | 481 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 11 | 15 | 26 |
| Not Hispanic or Latino | 400 | 393 | 793 |
| Unknown or Not Reported | 21 | 26 | 47 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | 1 |
| Asian | 60 | 56 | 116 |
| Black or African American | 4 | 8 | 12 |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | 2 |
| White | 333 | 339 | 672 |

| | | | |
|--|-----|-----|-----|
| Other | 11 | 6 | 17 |
| Not Collected or Reported | 24 | 22 | 46 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| North America | 144 | 156 | 300 |
| Europe | 203 | 205 | 408 |
| Australia | 30 | 20 | 50 |
| Asia Pacific | 55 | 53 | 108 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| ECOG performance status is used to describe a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). The scale ranges from 0 to 5: 0 = Fully active, no restrictions; 1 = Restricted activity but ambulatory, able to carry out work of a light nature; 2 = Ambulatory and capable of all self-care but unable to carry out work activities; 3 = Limited self-care, confined to bed or chair more than 50% of waking hours; 4 = Completely disabled, no self-care, confined to bed or chair; 5 = Dead | | | |
| Units: Subjects | | | |
| 0 = Fully Active | 252 | 268 | 520 |
| 1 = Restricted but Ambulatory | 180 | 166 | 346 |
| 2 = Ambulatory but Unable to Work | 0 | 0 | 0 |
| 3 = Limited Self-care | 0 | 0 | 0 |
| 4 = Completely Disabled | 0 | 0 | 0 |
| Physician Assessment of Peripheral Neuropathy | | | |
| Physician assessment for grading of peripheral neuropathy in participants receiving chemotherapy according to National Cancer Institute Common Toxicity Criteria (NCICTC): - Grade 1 = Asymptomatic: loss of deep tendon reflexes or paresthesia; - Grade 2 = Moderate symptoms: limiting instrumental Activities of Daily Living (ADLs); - Grade 3 = Severe symptoms: limiting self-care ADL; assistance device indicated; - Grade 4 = Life-threatening consequences: urgent intervention indicated. | | | |
| Units: Subjects | | | |
| Grade 0 | 404 | 408 | 812 |
| Grade 1 | 26 | 21 | 47 |
| Grade 2 | 0 | 1 | 1 |
| Grade 3 | 0 | 0 | 0 |
| Grade 4 | 0 | 0 | 0 |
| Missing | 2 | 4 | 6 |
| TNM Classification | | | |
| The TNM system is the most widely used cancer staging system. Most hospitals and medical centers use the TNM system as their main method for cancer reporting. In the TNM system: The T refers to the size and extent of the main tumor. The main tumor is usually called the primary tumor and the "T" followed by a number shows the size of the tumor. The N refers to the number of nearby lymph nodes that have cancer. The M refers to whether the cancer has metastasized. This means that the cancer has spread from the primary tumor to other parts of the body. | | | |
| Units: Subjects | | | |
| T1 = Tumor is 2 cm or smaller | 16 | 13 | 29 |
| T2 = Tumor is > 2 cm, but not larger than 5 cm | 38 | 37 | 75 |
| T3 = Tumor is larger than 5 cm | 377 | 384 | 761 |
| T4 = Tumor is any size, but has spread | 1 | 0 | 1 |
| Nodal Status | | | |
| The nodal status refers to the N and includes the number of nearby lymph nodes that are positive or negative for cancer. | | | |
| Units: Subjects | | | |
| Lymph Node Positive (LN+) | 311 | 312 | 623 |
| Lymph Node Negative (LN-) | 121 | 122 | 243 |
| Resection Status | | | |

| Resection status was based on investigational site data (pathology reports were collected, but central pathology review and/or standardization was not conducted). | | | |
|--|--------------|--------------|-----|
| Units: Subjects | | | |
| R0 (tumor-negative resection margin) | 327 | 334 | 661 |
| R1 (tumor- positive resection margin) | 105 | 100 | 205 |
| Time from Surgery to Randomization | | | |
| Units: Days | | | |
| median | 57.0 | 56.0 | |
| full range (min-max) | 23.0 to 90.0 | 17.0 to 88.0 | - |
| Body Surface Area (BSA) | | | |
| Units: m ² | | | |
| arithmetic mean | 1.77 | 1.78 | |
| standard deviation | ± 0.226 | ± 0.221 | - |

End points

End points reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | nab-Paclitaxel and Gemcitabine |
|-----------------------|--------------------------------|

Reporting group description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|-----------------------|-------------|
| Reporting group title | Gemcitabine |
|-----------------------|-------------|

Reporting group description:

Participants received gemcitabine 1000 mg/m² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|-----------------------|--------------------------------|
| Reporting group title | nab-Paclitaxel and Gemcitabine |
|-----------------------|--------------------------------|

Reporting group description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|-----------------------|-------------|
| Reporting group title | Gemcitabine |
|-----------------------|-------------|

Reporting group description:

Participants received gemcitabine 1000 mg/m² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

Primary: Kaplan Meier Estimate for Disease Free Survival (DFS) According to the Independent Radiological Review Committee

| | |
|-----------------|---|
| End point title | Kaplan Meier Estimate for Disease Free Survival (DFS) According to the Independent Radiological Review Committee |
|-----------------|---|

End point description:

Disease free survival was defined as the time from the date of randomization to the date of disease recurrence or death, whichever occurred earlier. Disease recurrence was determined by the independent radiological review of computed tomography (CT) or magnetic resonance imaging (MRI) scans. Participants who did not have disease recurrence or did not die were censored at the last tumor assessment date with disease-free status or the randomization date if the last tumor assessment with disease-free status was missing. Disease-free status referred to a status that was neither being disease recurrent nor indeterminate or not evaluable. Participants who received new anti-cancer therapy or cancer-related surgery prior to disease recurrence or death were censored at the date of last tumor assessment with disease-free status prior to the start of new anti-cancer therapy or cancer-related surgery or the randomization date.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Date of randomization up to data cut off date of 31 December 2018; median DFS follow-up time for censored participants was 22.242 months for nab-Paclitaxel and gemcitabine and 13.832 months for gemcitabine alone

| | | | | |
|----------------------------------|--------------------------------|-----------------------|--|--|
| End point values | nab-Paclitaxel and Gemcitabine | Gemcitabine | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 432 | 434 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 19.4 (16.62 to 21.91) | 18.8 (13.83 to 20.30) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Disease Free Survival (DFS) |
| Comparison groups | nab-Paclitaxel and Gemcitabine v Gemcitabine |
| Number of subjects included in analysis | 866 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1824 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.729 |
| upper limit | 1.063 |

Secondary: Kaplan Meier Estimate of Overall Survival (OS)

| | |
|------------------------|--|
| End point title | Kaplan Meier Estimate of Overall Survival (OS) |
| End point description: | Overall survival was defined as the time from the date of randomization to the date of death. Participants who were alive at the end of study or clinical data cut were censored on the last-known-to-be-alive date or the clinical cutoff date, whichever was earlier. 99999 = N/A - insufficient number of participants with events. |
| End point type | Secondary |
| End point timeframe: | From randomization to date of death; median OS follow-up time for censored participants was 77.832 months for nab-Paclitaxel and gemcitabine and 77.799 months for gemcitabine alone |

| | | | | |
|----------------------------------|--------------------------------|-----------------------|--|--|
| End point values | nab-Paclitaxel and Gemcitabine | Gemcitabine | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 432 | 434 | | |
| Units: months | | | | |
| median (confidence interval 95%) | | | | |
| 25th Quartile | 20.7 (19.38 to 22.83) | 17.7 (14.78 to 19.91) | | |

| | | | | |
|---------------|-----------------------|-----------------------|--|--|
| 50th Quartile | 41.8 (35.55 to 47.28) | 37.7 (31.11 to 40.51) | | |
| 75th Quartile | 90.2 (83.55 to 99999) | 83.0 (61.93 to 99999) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Overall Survival (OS) |
| Comparison groups | nab-Paclitaxel and Gemcitabine v Gemcitabine |
| Number of subjects included in analysis | 866 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0128 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.691 |
| upper limit | 0.957 |

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAE's)

| | |
|-----------------|--|
| End point title | Number of Participants with Treatment Emergent Adverse Events (TEAE's) |
|-----------------|--|

End point description:

TEAEs are defined as any adverse event (AE) that begin or worsen on or after the start of study drug or procedure of the study period through the maximum duration of the period plus 28 days. The severity of AEs was graded based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0 and the scale: Grade 1 = Mild Grade 2 = Moderate Grade 3 = Severe Grade 4 = Life threatening Grade 5 = Death. Relation to study drug was determined by the investigator. A treatment-related TEAE is defined as TEAE which was considered to be related to one or both of the study drugs and reported as 'Suspected' on the case report form. AEs with a missing relationship were treated as 'treatment-related' in data summaries. IP (investigational product) refers to nab-Paclitaxel and/or Gemcitabine. "Related" TEAE refers to relation to study drug (IP).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From day 1 of study drug up to 28 days after the last dose of study drug; up to the data cut off date of 31 December 2018 (up to approximately 37 weeks).

| | | | | |
|-----------------------------|--------------------------------|-----------------|--|--|
| End point values | nab-Paclitaxel and Gemcitabine | Gemcitabine | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 429 | 423 | | |
| Units: Participants | | | | |
| ≥1 TEAE | 429 | 417 | | |

| | | | | |
|--|-----|-----|--|--|
| ≥1 Related TEAE | 423 | 399 | | |
| ≥1 TEAE of Severity Grade 3 or Higher | 371 | 286 | | |
| ≥ 1 Related TEAE of Severity Grade 3 or Higher | 332 | 239 | | |
| ≥1 Serious TEAE | 176 | 96 | | |
| ≥1 Serious Related TEAE | 102 | 55 | | |
| ≥1 TEAE Leading to Withdrawal of IP | 117 | 43 | | |
| ≥1 Related TEAE Leading to Withdrawal of IP | 98 | 35 | | |
| ≥1 TEAE Lead Dose Reduction: nab-Paclitaxel or Gem | 276 | 210 | | |
| ≥1 Related TEAE Dose Reduct: nab-Paclitaxel or Gem | 270 | 205 | | |
| TEAE Lead Dose Interruption nab-Paclitaxel or Gem | 266 | 158 | | |
| ≥1 Related TEAE Dose Interruption to IP | 221 | 125 | | |
| TEAE Leading to Death | 2 | 2 | | |
| >=1 Related TEAE Leading to Death | 2 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Clinical Chemistry Laboratory-Detected Abnormalities (Grade 3-4)

| | | | | |
|------------------------|---|--|--|--|
| End point title | The Number of Participants with Clinical Chemistry Laboratory-Detected Abnormalities (Grade 3-4) | | | |
| End point description: | The number of participants with grade 3-4 laboratory abnormalities in selected clinically significant parameters. Grades for chemistry parameters were coded using National Cancer Institute Common Terminology Criteria for Adverse Events (Grade 3= severe, Grade 4= life-threatening). | | | |
| End point type | Secondary | | | |
| End point timeframe: | From day 1 of study drug up to 28 days after the last dose of study drug, or the treatment discontinuation date, whichever was later (up to approximately 37 weeks). | | | |

| End point values | nab-Paclitaxel and Gemcitabine | Gemcitabine | | |
|-----------------------------|--------------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 421 | 416 | | |
| Units: Participants | | | | |
| Alkaline phosphatase | 7 | 3 | | |
| Alanine aminotransferase | 9 | 3 | | |
| Aspartate aminotransferase | 9 | 2 | | |
| Bilirubin | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and NSAEs were assessed from first dose to 100 days following last dose (up to approximately 46 weeks)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Gemcitabine |
|-----------------------|-------------|

Reporting group description:

Participants received gemcitabine 1000 mg/m² administered as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| | |
|-----------------------|--------------------------------|
| Reporting group title | nab-Paclitaxel and Gemcitabine |
|-----------------------|--------------------------------|

Reporting group description:

Participants received nab-Paclitaxel 125 mg/m² administered as an intravenous (IV) infusion over 30 to 40 minutes, followed by gemcitabine 1000 mg/m² as an IV infusion over 30 to 40 minutes on Days 1, 8 and 15 of each 28-day treatment cycle for 6 cycles, unless there was evidence of radiologic disease recurrence, unacceptable toxicity, subject or physician decision, withdrawal of consent, or death.

| Serious adverse events | Gemcitabine | nab-Paclitaxel and Gemcitabine | |
|---|-------------------|--------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 96 / 423 (22.70%) | 181 / 429 (42.19%) | |
| number of deaths (all causes) | 294 | 284 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour inflammation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 5 / 429 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Capillary leak syndrome | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jugular vein thrombosis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chills | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 7 / 429 (1.63%) | |
| occurrences causally related to treatment / all | 0 / 0 | 7 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 423 (0.71%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 5 / 429 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 5 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyserositis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 24 / 423 (5.67%) | 29 / 429 (6.76%) | |
| occurrences causally related to treatment / all | 0 / 32 | 16 / 41 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alveolitis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 423 (1.18%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 5 | 4 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiogenic pulmonary oedema | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 5 / 423 (1.18%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 2 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 5 / 429 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram ST segment elevation | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram T wave inversion | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram repolarisation abnormality | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Liver function test increased subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases increased subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Post procedural inflammation subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical vertebral fracture subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripancreatic fluid collection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural fistula | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transfusion-related circulatory overload | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic fracture | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound secretion | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Hypertrophic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial thrombosis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 423 (0.95%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Left ventricular failure | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 6 / 423 (1.42%) | 12 / 429 (2.80%) | |
| occurrences causally related to treatment / all | 0 / 6 | 9 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 5 / 429 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic uraemic syndrome | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Microangiopathic haemolytic anaemia | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 16 / 429 (3.73%) | |
| occurrences causally related to treatment / all | 0 / 3 | 15 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 5 / 429 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic microangiopathy | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic thrombocytopenic purpura | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Intra-abdominal fluid collection | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal hernia | | | |

| | | |
|---|-----------------|------------------|
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Abdominal pain | | |
| subjects affected / exposed | 4 / 423 (0.95%) | 7 / 429 (1.63%) |
| occurrences causally related to treatment / all | 0 / 4 | 3 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Anal incontinence | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Anastomotic ulcer perforation | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Ascites | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Colitis | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 4 / 429 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Diarrhoea | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 12 / 429 (2.80%) |
| occurrences causally related to treatment / all | 0 / 0 | 9 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Enteritis | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Internal hernia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jejunal perforation | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Obstruction gastric | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 0 / 429 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Oesophageal haemorrhage | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pancreatic pseudocyst | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 2 / 429 (0.47%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pancreatitis | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 3 / 429 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Proctitis | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 2 / 429 (0.47%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Stomatitis | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 8 / 429 (1.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct obstruction | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct stenosis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 3 / 423 (0.71%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 3 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic failure | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertransaminaemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myositis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|-----------------|-----------------|--|
| Appendicitis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis clostridial | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 5 / 423 (1.18%) | 8 / 429 (1.86%) | |
| occurrences causally related to treatment / all | 0 / 5 | 6 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholera | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colonic abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corona virus infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 4 / 429 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis infectious | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 9 / 429 (2.10%) | |
| occurrences causally related to treatment / all | 0 / 1 | 9 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious colitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella bacteraemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella sepsis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 423 (1.42%) | 9 / 429 (2.10%) | |
| occurrences causally related to treatment / all | 0 / 6 | 5 / 10 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth infection | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 0 / 429 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 7 / 429 (1.63%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 5 / 423 (1.18%) | 12 / 429 (2.80%) | |
| occurrences causally related to treatment / all | 0 / 5 | 9 / 13 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 1 | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 8 / 429 (1.86%) | |
| occurrences causally related to treatment / all | 0 / 2 | 4 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid retention | | | |
| subjects affected / exposed | 1 / 423 (0.24%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 423 (0.24%) | 3 / 429 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 423 (0.47%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 2 / 429 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 423 (0.00%) | 1 / 429 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Gemcitabine | nab-Paclitaxel and Gemcitabine | |
|--|--------------------|--------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 407 / 423 (96.22%) | 426 / 429 (99.30%) | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 22 / 423 (5.20%) | 52 / 429 (12.12%) | |
| occurrences (all) | 22 | 60 | |
| Neutrophil count decreased | | | |

| | | | |
|--|-------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 32 / 423 (7.57%) 69 | 23 / 429 (5.36%) 51 | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 17 / 423 (4.02%) 24 | 23 / 429 (5.36%) 34 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 21 / 423 (4.96%) 31 | 31 / 429 (7.23%) 46 | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 33 / 423 (7.80%) 51 | 42 / 429 (9.79%) 54 | |
| Vascular disorders | | | |
| Hypotension subjects affected / exposed occurrences (all) | 12 / 423 (2.84%) 14 | 30 / 429 (6.99%) 37 | |
| Hypertension subjects affected / exposed occurrences (all) | 49 / 423 (11.58%) 70 | 35 / 429 (8.16%) 51 | |
| Nervous system disorders | | | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 26 / 423 (6.15%) 30 | 112 / 429 (26.11%) 128 | |
| Headache subjects affected / exposed occurrences (all) | 66 / 423 (15.60%) 90 | 65 / 429 (15.15%) 91 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 36 / 423 (8.51%) 39 | 86 / 429 (20.05%) 95 | |
| Dizziness subjects affected / exposed occurrences (all) | 34 / 423 (8.04%) 39 | 64 / 429 (14.92%) 77 | |
| Paraesthesia subjects affected / exposed occurrences (all) | 9 / 423 (2.13%) 9 | 39 / 429 (9.09%) 50 | |
| Polyneuropathy | | | |

| | | | |
|---|---------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 6 / 423 (1.42%) 8 | 23 / 429 (5.36%) 27 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 16 / 423 (3.78%) 20 | 144 / 429 (33.57%) 177 | |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 203 / 423 (47.99%) 315 | 233 / 429 (54.31%) 350 | |
| Asthenia subjects affected / exposed occurrences (all) | 49 / 423 (11.58%) 116 | 95 / 429 (22.14%) 192 | |
| Chills subjects affected / exposed occurrences (all) | 23 / 423 (5.44%) 27 | 38 / 429 (8.86%) 63 | |
| Pyrexia subjects affected / exposed occurrences (all) | 115 / 423 (27.19%) 194 | 171 / 429 (39.86%) 369 | |
| Peripheral swelling subjects affected / exposed occurrences (all) | 16 / 423 (3.78%) 21 | 22 / 429 (5.13%) 24 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 108 / 423 (25.53%) 130 | 162 / 429 (37.76%) 207 | |
| Influenza like illness subjects affected / exposed occurrences (all) | 25 / 423 (5.91%) 53 | 27 / 429 (6.29%) 41 | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 85 / 423 (20.09%) 174 | 94 / 429 (21.91%) 212 | |
| Neutropenia subjects affected / exposed occurrences (all) | 230 / 423 (54.37%) 568 | 263 / 429 (61.31%) 638 | |
| Leukopenia | | | |

| | | | |
|--|---------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 72 / 423 (17.02%) 151 | 84 / 429 (19.58%) 201 | |
| Anaemia subjects affected / exposed occurrences (all) | 142 / 423 (33.57%) 214 | 179 / 429 (41.72%) 267 | |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 192 / 423 (45.39%) 321 | 231 / 429 (53.85%) 431 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 24 / 423 (5.67%) 25 | 21 / 429 (4.90%) 21 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 125 / 423 (29.55%) 183 | 242 / 429 (56.41%) 458 | |
| Constipation subjects affected / exposed occurrences (all) | 89 / 423 (21.04%) 112 | 114 / 429 (26.57%) 150 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 40 / 423 (9.46%) 47 | 35 / 429 (8.16%) 38 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 87 / 423 (20.57%) 100 | 119 / 429 (27.74%) 158 | |
| Stomatitis subjects affected / exposed occurrences (all) | 24 / 423 (5.67%) 35 | 81 / 429 (18.88%) 102 | |
| Vomiting subjects affected / exposed occurrences (all) | 77 / 423 (18.20%) 140 | 122 / 429 (28.44%) 208 | |
| Flatulence subjects affected / exposed occurrences (all) | 27 / 423 (6.38%) 31 | 23 / 429 (5.36%) 25 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-------------------------|---------------------------|--|
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 18 / 423 (4.26%) 18 | 28 / 429 (6.53%) 34 | |
| Epistaxis subjects affected / exposed occurrences (all) | 13 / 423 (3.07%) 14 | 76 / 429 (17.72%) 101 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 50 / 423 (11.82%) 57 | 65 / 429 (15.15%) 71 | |
| Cough subjects affected / exposed occurrences (all) | 51 / 423 (12.06%) 55 | 61 / 429 (14.22%) 73 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 20 / 423 (4.73%) 27 | 35 / 429 (8.16%) 46 | |
| Rash subjects affected / exposed occurrences (all) | 20 / 423 (4.73%) 23 | 49 / 429 (11.42%) 62 | |
| Pruritus subjects affected / exposed occurrences (all) | 20 / 423 (4.73%) 22 | 37 / 429 (8.62%) 40 | |
| Alopecia subjects affected / exposed occurrences (all) | 52 / 423 (12.29%) 55 | 252 / 429 (58.74%) 264 | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 34 / 423 (8.04%) 35 | 64 / 429 (14.92%) 72 | |
| Anxiety subjects affected / exposed occurrences (all) | 38 / 423 (8.98%) 38 | 34 / 429 (7.93%) 35 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 33 / 423 (7.80%) 36 | 45 / 429 (10.49%) 56 | |

| | | | |
|------------------------------------|-------------------|--------------------|--|
| Myalgia | | | |
| subjects affected / exposed | 29 / 423 (6.86%) | 57 / 429 (13.29%) | |
| occurrences (all) | 42 | 72 | |
| Muscular weakness | | | |
| subjects affected / exposed | 6 / 423 (1.42%) | 25 / 429 (5.83%) | |
| occurrences (all) | 7 | 33 | |
| Bone pain | | | |
| subjects affected / exposed | 15 / 423 (3.55%) | 23 / 429 (5.36%) | |
| occurrences (all) | 16 | 27 | |
| Back pain | | | |
| subjects affected / exposed | 44 / 423 (10.40%) | 41 / 429 (9.56%) | |
| occurrences (all) | 49 | 55 | |
| Arthralgia | | | |
| subjects affected / exposed | 31 / 423 (7.33%) | 68 / 429 (15.85%) | |
| occurrences (all) | 37 | 89 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 20 / 423 (4.73%) | 29 / 429 (6.76%) | |
| occurrences (all) | 27 | 32 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 84 / 423 (19.86%) | 143 / 429 (33.33%) | |
| occurrences (all) | 97 | 167 | |
| Dehydration | | | |
| subjects affected / exposed | 8 / 423 (1.89%) | 28 / 429 (6.53%) | |
| occurrences (all) | 10 | 39 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 23 / 423 (5.44%) | 55 / 429 (12.82%) | |
| occurrences (all) | 34 | 77 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 28 / 423 (6.62%) | 34 / 429 (7.93%) | |
| occurrences (all) | 39 | 55 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 23 June 2014 | Significant changes included: Regional stratification, sample size calculating, assessment of disease recurrence, and eligibility. |
| 03 December 2015 | Clarification on how to define a subject that has completed 6 cycles of study treatment versus discontinued early from study treatment, what is considered to be new/subsequent anticancer therapy, and dose modifications. Updated treatment administration and schedule section to include flushing requirement. |
| 21 December 2016 | Removal of the second interim analysis of efficacy and modification of stratification by Region. |
| 12 September 2018 | Revised the final disease-free survival (DFS) analysis to be earlier than was originally planned (489 events). |
| 03 September 2019 | Revise the protocol procedures to be performed after achieving the primary endpoint. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported