



Clinical trial results:

An open-label, randomised, multicentre, phase III study of irinotecan liposome injection, oxaliplatin, 5-fluorouracil/leucovorin versus nab-paclitaxel plus gemcitabine in subjects who have not previously received chemotherapy for metastatic adenocarcinoma of the pancreas

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2018-003585-14 |
| Trial protocol | DE ES GB HU BE CZ AT FR PT GR IT |
| Global end of trial date | |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 06 April 2024 |
| First version publication date | 06 April 2024 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | D-US-60010-001 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04083235 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Ipsen Bioscience |
| Sponsor organisation address | One Main Street, Cambridge, MA, United States, 02142 |
| Public contact | Medical Director, Ipsen Bioscience, clinical.trials@ipsen.com |
| Scientific contact | Medical Director, Ipsen Bioscience, clinical.trials@ipsen.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 | 23 July 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 July 2022 |
| Global end of trial reached? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of the regimen of irinotecan liposome injection + oxaliplatin + 5-fluorouracil (5-FU)/leucovorin (LV) [NALIRIFOX] versus nab-paclitaxel + gemcitabine in improving overall survival (OS) in participants who have not previously received chemotherapy for metastatic adenocarcinoma of the pancreas.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, in accordance with the International Council for Harmonization Good Clinical Practice and in compliance with independent ethics committees/institutional review boards and informed consent regulations. This study adhered to the United States of America Food and Drug Administration regulations and all applicable local regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 February 2020 |
| 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 | Portugal: 10 |
| Country: Number of subjects enrolled | Spain: 143 |
| Country: Number of subjects enrolled | United Kingdom: 13 |
| Country: Number of subjects enrolled | Austria: 17 |
| Country: Number of subjects enrolled | Belgium: 19 |
| Country: Number of subjects enrolled | Czechia: 38 |
| Country: Number of subjects enrolled | France: 50 |
| Country: Number of subjects enrolled | Germany: 44 |
| Country: Number of subjects enrolled | Greece: 4 |
| Country: Number of subjects enrolled | Hungary: 18 |
| Country: Number of subjects enrolled | Italy: 55 |
| Country: Number of subjects enrolled | Korea, Republic of: 22 |
| Country: Number of subjects enrolled | United States: 230 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Australia: 25 |
| Country: Number of subjects enrolled | Brazil: 40 |
| Country: Number of subjects enrolled | Israel: 5 |
| Country: Number of subjects enrolled | Russian Federation: 25 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 770 |
| 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) | 384 |
| From 65 to 84 years | 385 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This Phase 3, open-label study was conducted in participants with metastatic adenocarcinoma of the pancreas at 187 investigational sites in 18 countries. First participant was recruited on 11 February 2020 and data cut-off (DCO) date 23 July 2022.

Pre-assignment

Screening details:

The study had screening period (up to 28 days), treatment period: 28-day cycles until radiologically determined disease progression per RECIST Version 1.1, unacceptable treatment related toxicity/withdrawal; survival follow-up (until death/study closure). Participants were randomized in 1:1 ratio using an interactive web response system (IWRS).

Period 1

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

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | NALIRIFOX |

Arm description:

Participants were treated with irinotecan liposome injection 50 milligram per square meter (mg/m²) followed by oxaliplatin 60 mg/m², followed by LV 400 mg/m² and then 5-FU 2400 mg/m² intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Irinotecan liposome injection |
| Investigational medicinal product code | IPN60010 |
| Other name | Onivyde® |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Irinotecan liposome injection was administered as IV infusion over 90 minutes (±10 minutes).

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin® |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Oxaliplatin was administered as IV infusion over 120 minutes (±10 minutes).

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

Dosage and administration details:

LV was administered as IV infusion over 30 minutes (±5 minutes).

| | |
|--|----------------|
| Investigational medicinal product name | 5-Fluorouracil |
| Investigational medicinal product code | |
| Other name | 5-FU, Adrucil® |

| | |
|--------------------------|-----------------------|
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

5-FU was administered as IV infusion over 46-hours (± 120 minutes).

| | |
|------------------|----------------------------|
| Arm title | Nab-paclitaxel+Gemcitabine |
|------------------|----------------------------|

Arm description:

Participants were treated with nab-paclitaxel 125 mg/m² followed by gemcitabine 1000 mg/m² IV on Days 1, 8 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent.

| | |
|--|----------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | Abraxane® |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Nab-paclitaxel was administered as IV infusion over 35 minutes (± 5 minutes).

| | |
|--|----------------------------------|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | Gemzar® |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine was administered as IV infusion over 30 minutes (± 5 minutes).

| Number of subjects in period 1 | NALIRIFOX | Nab-paclitaxel+Gemcitabine |
|--------------------------------|-----------|----------------------------|
| | | |
| Started | 383 | 387 |
| Received Treatment | 370 | 379 |
| Completed | 59 | 77 |
| Not completed | 324 | 310 |
| Consent withdrawn by subject | 13 | 17 |
| Death | 252 | 277 |
| Ongoing at the time of DCO | 44 | 7 |
| Lost to follow-up | 1 | 1 |
| Did not receive treatment | 13 | 8 |
| Does not meet entry criteria | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|----------------------------|
| Reporting group title | NALIRIFOX |
| Reporting group description: Participants were treated with irinotecan liposome injection 50 milligram per square meter (mg/m ²) followed by oxaliplatin 60 mg/m ² , followed by LV 400 mg/m ² and then 5-FU 2400 mg/m ² intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent. | |
| Reporting group title | Nab-paclitaxel+Gemcitabine |
| Reporting group description: Participants were treated with nab-paclitaxel 125 mg/m ² followed by gemcitabine 1000 mg/m ² IV on Days 1, 8 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent. | |

| Reporting group values | NALIRIFOX | Nab-paclitaxel+Gemcitabine | Total |
|---|----------------|----------------------------|-------|
| Number of subjects | 383 | 387 | 770 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 62.8 ± 9.71 | 64.0 ± 8.34 | - |
| Gender categorical Units: Subjects | | | |
| Female | 179 | 157 | 336 |
| Male | 204 | 230 | 434 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 49 | 30 | 79 |
| Not Hispanic or Latino | 305 | 328 | 633 |
| Not Reported | 29 | 29 | 58 |
| Race Units: Subjects | | | |
| White | 315 | 324 | 639 |
| Not Reported | 26 | 29 | 55 |
| Asian | 20 | 18 | 38 |
| Black or African American | 12 | 7 | 19 |
| Other | 7 | 6 | 13 |
| Multiple | 3 | 0 | 3 |
| American Indian or Alaska Native | 0 | 2 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |

End points

End points reporting groups

| | |
|--|----------------------------|
| Reporting group title | NALIRIFOX |
| Reporting group description: Participants were treated with irinotecan liposome injection 50 milligram per square meter (mg/m ²) followed by oxaliplatin 60 mg/m ² , followed by LV 400 mg/m ² and then 5-FU 2400 mg/m ² intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent. | |
| Reporting group title | Nab-paclitaxel+Gemcitabine |
| Reporting group description: Participants were treated with nab-paclitaxel 125 mg/m ² followed by gemcitabine 1000 mg/m ² IV on Days 1, 8 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent. | |

Primary: OS

| | |
|--|---------|
| End point title | OS |
| End point description: The OS was defined as time from the date of randomization to the date of death due to any cause. Participants who did not have a date of death recorded at the time of the final analysis were censored at the last known time that the participant was alive. The median OS was measured using Kaplan-Meier technique. The Intent-to-Treat (ITT) population consisted of all randomized participants to whom study treatment was assigned by randomization. | |
| End point type | Primary |
| End point timeframe: Assessments performed at baseline (within 28 days before start of study treatment), every 8 weeks after first dose, end of treatment (EoT) visit, then every 2 months thereafter up to DCO date of 23 July 2022 (maximum of 893 days) | |

| End point values | NALIRIFOX | Nab-paclitaxel+Gemcitabine | | |
|----------------------------------|---------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 383 | 387 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 11.1 (10.0 to 12.1) | 9.2 (8.3 to 10.6) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Treatment difference in OS |
| Comparison groups | NALIRIFOX v Nab-paclitaxel+Gemcitabine |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 770 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.04 |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.99 |

Notes:

[1] - The HR and 95% confidence interval (CI) was based on a stratified Cox proportional hazards regression model, stratified by baseline Eastern Cooperative Oncology Group (ECOG) performance status, region and liver metastases as per IWRS.

Secondary: Progression Free Survival (PFS)

| | |
|--|---------------------------------|
| End point title | Progression Free Survival (PFS) |
| End point description: | |
| PFS was defined as the time from the date of randomization to the first documented disease progression using response evaluation criteria in solid tumors (RECIST Version 1.1) as per Investigator assessment or death due to any cause. The median PFS was measured using Kaplan-Meier technique. The ITT population consisted of all randomized participants to whom study treatment was assigned by randomization. Only participants with PFS event are reported. | |
| End point type | Secondary |
| End point timeframe: | |
| Assessments performed at baseline (within 28 days before start of study treatment), every 8 weeks after first dose until EoT visit (maximum of 893 days) | |

| End point values | NALIRIFOX | Nab-paclitaxel+Gemcitabine | | |
|----------------------------------|------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 259 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 7.4 (6.0 to 7.7) | 5.6 (5.3 to 5.8) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Treatment difference in PFS |
| Comparison groups | NALIRIFOX v Nab-paclitaxel+Gemcitabine |
| Number of subjects included in analysis | 508 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| P-value | < 0.0001 |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.69 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.83 |

Notes:

[2] - The HR and 95% CI was based on a stratified Cox proportional hazards regression model, stratified by baseline ECOG performance status, region and liver metastases as per IWRS.

Secondary: Overall Response Rate (ORR)

| | |
|-----------------|-----------------------------|
| End point title | Overall Response Rate (ORR) |
|-----------------|-----------------------------|

End point description:

The ORR was defined as the percentage of participants with a best overall response (BOR) characterized as either a complete response or partial response per RECIST Version 1.1. BOR was defined as the best response as recorded from randomization until documented objective disease progression using RECIST Version 1.1. The ORR was calculated using Clopper-Pearson method. The ITT population consisted of all randomized participants to whom study treatment was assigned by randomization.

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

End point timeframe:

Assessments performed at baseline (within 28 days before start of study treatment), every 8 weeks after first dose until EoT visit (maximum of 893 days)

| End point values | NALIRIFOX | Nab-paclitaxel+Gemcitabine | | |
|-----------------------------------|---------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 383 | 387 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 41.8 (36.8 to 46.9) | 36.2 (31.4 to 41.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Comparison of odds ratio (OR) |
| Comparison groups | NALIRIFOX v Nab-paclitaxel+Gemcitabine |
| Number of subjects included in analysis | 770 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| P-value | = 0.1131 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.69 |

Notes:

[3] - OR, 95% CI and p-value were obtained from the Cochran-Mantel-Haenszel test adjusting by baseline ECOG performance status, region and liver metastases as per IWRS.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are reported from the time of first study treatment administration (Day 1) up to DCO date of 23 July 2022 (maximum of 893 days)

Adverse event reporting additional description:

The Safety population was a subset of the ITT population that received at least 1 dose (including a partial dose) of any component of the study medication in the combination.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | NALIRIFOX |
|-----------------------|-----------|

Reporting group description:

Participants were treated with irinotecan liposome injection 50 mg/m² followed by oxaliplatin 60 mg/m², followed by LV 400 mg/m² and then 5-FU 2400 mg/m² IV infusion on Days 1 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent.

| | |
|-----------------------|----------------------------|
| Reporting group title | Nab-paclitaxel+Gemcitabine |
|-----------------------|----------------------------|

Reporting group description:

Participants were treated with nab-paclitaxel 125 mg/m² followed by gemcitabine 1000 mg/m² IV on Days 1, 8 and 15 of each 28-day cycle until disease progression, death, unacceptable study treatment-related toxicity or withdrawal of consent.

| Serious adverse events | NALIRIFOX | Nab-paclitaxel+Gemcitabine | |
|---|--------------------|----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 201 / 370 (54.32%) | 195 / 379 (51.45%) | |
| number of deaths (all causes) | 252 | 277 | |
| number of deaths resulting from adverse events | 22 | 23 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Peritumoural oedema | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Tumour pain | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 4 / 370 (1.08%) | 8 / 379 (2.11%) | |
| occurrences causally related to treatment / all | 1 / 4 | 2 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Embolism arterial | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iliac vein occlusion | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral embolism | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | | | |
| Asthenia | | | |
| subjects affected / exposed | 7 / 370 (1.89%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 3 / 7 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Condition aggravated | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Fatigue | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 7 / 370 (1.89%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 6 / 379 (1.58%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 6 | |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inadequate analgesia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammation | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Performance status decreased | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 8 / 370 (2.16%) | 12 / 379 (3.17%) | |
| occurrences causally related to treatment / all | 1 / 9 | 4 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden cardiac death | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Penile vein thrombosis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Priapism | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspiration | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 5 / 379 (1.32%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrothorax | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 370 (0.54%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pneumonitis aspiration | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | 10 / 370 (2.70%) | 7 / 379 (1.85%) | |
| occurrences causally related to treatment / all | 3 / 10 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Thrombosis in device | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood bilirubin increased | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 5 / 370 (1.35%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood glucose abnormal | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical condition abnormal | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell count decreased | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Exposure to SARS-CoV-2 | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac flutter | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 4 / 370 (1.08%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Embolic stroke | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 4 / 370 (1.08%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pineal gland cyst | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 370 (1.35%) | 8 / 379 (2.11%) | |
| occurrences causally related to treatment / all | 4 / 6 | 7 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 7 / 370 (1.89%) | 6 / 379 (1.58%) | |
| occurrences causally related to treatment / all | 7 / 9 | 6 / 6 | |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | |
| Neutropenia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 370 (0.54%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 370 (2.43%) | 8 / 379 (2.11%) | |
| occurrences causally related to treatment / all | 2 / 10 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|-----------------|--|
| Ascites | | | |
| subjects affected / exposed | 6 / 370 (1.62%) | 5 / 379 (1.32%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 7 / 370 (1.89%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 6 / 7 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 6 / 379 (1.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 23 / 370 (6.22%) | 9 / 379 (2.37%) | |
| occurrences causally related to treatment / all | 22 / 28 | 6 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal obstruction | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal stenosis | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer perforation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Food poisoning | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric fistula | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorder | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal pseudo-obstruction | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesenteric vein thrombosis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 18 / 370 (4.86%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 15 / 24 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic colitis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstruction gastric | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal haemorrhage | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Terminal ileitis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 22 / 370 (5.95%) | 6 / 379 (1.58%) | |
| occurrences causally related to treatment / all | 15 / 26 | 4 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary obstruction | | | |
| subjects affected / exposed | 6 / 370 (1.62%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 4 / 370 (1.08%) | 6 / 379 (1.58%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cholecystitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholestasis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 2 / 370 (0.54%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | | | |
| Decubitus ulcer | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 9 / 379 (2.37%) | |
| occurrences causally related to treatment / all | 2 / 3 | 5 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Renal impairment | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest wall haematoma | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |

| | | | |
|---|-----------------|-----------------|--|
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asymptomatic COVID-19 | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary sepsis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary tract infection | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 370 (0.54%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 18 / 370 (4.86%) | 14 / 379 (3.69%) | |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter colitis | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site infection | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis infective | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related bacteraemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterococcal infection | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| 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 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder abscess | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 370 (0.81%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic infection | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis E | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Implant site cellulitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective spondylitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine infection | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis bacterial | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 370 (1.89%) | 13 / 379 (3.43%) | |
| occurrences causally related to treatment / all | 0 / 7 | 3 / 13 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 3 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Post procedural cellulitis | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 6 / 370 (1.62%) | 16 / 379 (4.22%) | |
| occurrences causally related to treatment / all | 4 / 6 | 9 / 18 | |
| deaths causally related to treatment / all | 1 / 2 | 5 / 8 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal infection | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suspected COVID-19 | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 370 (0.81%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Adult failure to thrive | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 5 / 370 (1.35%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 10 / 370 (2.70%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 8 / 11 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic metabolic decompensation | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 370 (0.00%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 370 (0.00%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 4 / 379 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 6 / 370 (1.62%) | 3 / 379 (0.79%) | |
| occurrences causally related to treatment / all | 4 / 7 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 2 / 379 (0.53%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 1 / 379 (0.26%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 370 (0.27%) | 0 / 379 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | NALIRIFOX | Nab- paclitaxel+Gemcitabine | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 364 / 370 (98.38%) | 371 / 379 (97.89%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 45 / 370 (12.16%) | 48 / 379 (12.66%) | |
| occurrences (all) | 64 | 64 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 40 / 370 (10.81%) | 40 / 379 (10.55%) | |
| occurrences (all) | 58 | 55 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 39 / 370 (10.54%) | 31 / 379 (8.18%) | |
| occurrences (all) | 42 | 33 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 21 / 370 (5.68%) | 22 / 379 (5.80%) | |
| occurrences (all) | 23 | 23 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 44 / 370 (11.89%) | 34 / 379 (8.97%) | |
| occurrences (all) | 54 | 35 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 73 / 370 (19.73%) | 69 / 379 (18.21%) | |
| occurrences (all) | 208 | 112 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 39 / 370 (10.54%) | 67 / 379 (17.68%) | |
| occurrences (all) | 71 | 109 | |
| Weight decreased | | | |
| subjects affected / exposed | 82 / 370 (22.16%) | 33 / 379 (8.71%) | |
| occurrences (all) | 92 | 34 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 16 / 370 (4.32%) | 32 / 379 (8.44%) | |
| occurrences (all) | 24 | 54 | |
| Vascular disorders | | | |

| | | | |
|---|--------------------------|---------------------------|--|
| Hypertension subjects affected / exposed occurrences (all) | 21 / 370 (5.68%) 24 | 15 / 379 (3.96%) 19 | |
| Hypotension subjects affected / exposed occurrences (all) | 21 / 370 (5.68%) 27 | 25 / 379 (6.60%) 26 | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 24 / 370 (6.49%) 25 | 40 / 379 (10.55%) 44 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 63 / 370 (17.03%) 74 | 58 / 379 (15.30%) 67 | |
| Headache subjects affected / exposed occurrences (all) | 23 / 370 (6.22%) 37 | 19 / 379 (5.01%) 24 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 66 / 370 (17.84%) 89 | 66 / 379 (17.41%) 92 | |
| Neurotoxicity subjects affected / exposed occurrences (all) | 21 / 370 (5.68%) 35 | 13 / 379 (3.43%) 22 | |
| Paraesthesia subjects affected / exposed occurrences (all) | 44 / 370 (11.89%) 53 | 33 / 379 (8.71%) 41 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 56 / 370 (15.14%) 79 | 51 / 379 (13.46%) 60 | |
| Polyneuropathy subjects affected / exposed occurrences (all) | 16 / 370 (4.32%) 19 | 19 / 379 (5.01%) 20 | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 94 / 370 (25.41%) 134 | 151 / 379 (39.84%) 196 | |
| Leukopenia | | | |

| | | | |
|--|---------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 18 / 370 (4.86%) 24 | 40 / 379 (10.55%) 43 | |
| Neutropenia subjects affected / exposed occurrences (all) | 108 / 370 (29.19%) 264 | 121 / 379 (31.93%) 278 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 50 / 370 (13.51%) 84 | 93 / 379 (24.54%) 173 | |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 110 / 370 (29.73%) 164 | 101 / 379 (26.65%) 166 | |
| Chills subjects affected / exposed occurrences (all) | 6 / 370 (1.62%) 6 | 19 / 379 (5.01%) 20 | |
| Fatigue subjects affected / exposed occurrences (all) | 120 / 370 (32.43%) 173 | 143 / 379 (37.73%) 183 | |
| Mucosal inflammation subjects affected / exposed occurrences (all) | 50 / 370 (13.51%) 60 | 16 / 379 (4.22%) 20 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 52 / 370 (14.05%) 60 | 107 / 379 (28.23%) 134 | |
| Pyrexia subjects affected / exposed occurrences (all) | 33 / 370 (8.92%) 43 | 84 / 379 (22.16%) 129 | |
| Gastrointestinal disorders | | | |
| Abdominal distension subjects affected / exposed occurrences (all) | 22 / 370 (5.95%) 26 | 13 / 379 (3.43%) 15 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 92 / 370 (24.86%) 110 | 75 / 379 (19.79%) 80 | |
| Abdominal pain upper | | | |

| | | | |
|---|--------------------|--------------------|--|
| subjects affected / exposed | 27 / 370 (7.30%) | 21 / 379 (5.54%) | |
| occurrences (all) | 34 | 29 | |
| Constipation | | | |
| subjects affected / exposed | 93 / 370 (25.14%) | 113 / 379 (29.82%) | |
| occurrences (all) | 115 | 141 | |
| Diarrhoea | | | |
| subjects affected / exposed | 258 / 370 (69.73%) | 135 / 379 (35.62%) | |
| occurrences (all) | 566 | 221 | |
| Dry mouth | | | |
| subjects affected / exposed | 28 / 370 (7.57%) | 14 / 379 (3.69%) | |
| occurrences (all) | 29 | 16 | |
| Dyspepsia | | | |
| subjects affected / exposed | 23 / 370 (6.22%) | 18 / 379 (4.75%) | |
| occurrences (all) | 32 | 20 | |
| Flatulence | | | |
| subjects affected / exposed | 30 / 370 (8.11%) | 18 / 379 (4.75%) | |
| occurrences (all) | 33 | 21 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 19 / 370 (5.14%) | 12 / 379 (3.17%) | |
| occurrences (all) | 22 | 13 | |
| Nausea | | | |
| subjects affected / exposed | 215 / 370 (58.11%) | 162 / 379 (42.74%) | |
| occurrences (all) | 406 | 216 | |
| Stomatitis | | | |
| subjects affected / exposed | 50 / 370 (13.51%) | 45 / 379 (11.87%) | |
| occurrences (all) | 81 | 54 | |
| Vomiting | | | |
| subjects affected / exposed | 139 / 370 (37.57%) | 96 / 379 (25.33%) | |
| occurrences (all) | 222 | 168 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 14 / 370 (3.78%) | 30 / 379 (7.92%) | |
| occurrences (all) | 18 | 31 | |
| Dyspnoea | | | |

| | | | |
|---|-------------------------|---------------------------|--|
| subjects affected / exposed occurrences (all) | 24 / 370 (6.49%) 28 | 45 / 379 (11.87%) 48 | |
| Epistaxis subjects affected / exposed occurrences (all) | 14 / 370 (3.78%) 15 | 43 / 379 (11.35%) 49 | |
| Pulmonary embolism subjects affected / exposed occurrences (all) | 20 / 370 (5.41%) 20 | 24 / 379 (6.33%) 24 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 52 / 370 (14.05%) 53 | 119 / 379 (31.40%) 120 | |
| Pruritus subjects affected / exposed occurrences (all) | 12 / 370 (3.24%) 14 | 22 / 379 (5.80%) 26 | |
| Rash subjects affected / exposed occurrences (all) | 11 / 370 (2.97%) 12 | 34 / 379 (8.97%) 37 | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 3 / 370 (0.81%) 3 | 25 / 379 (6.60%) 30 | |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 10 / 370 (2.70%) 10 | 24 / 379 (6.33%) 25 | |
| Insomnia subjects affected / exposed occurrences (all) | 28 / 370 (7.57%) 28 | 32 / 379 (8.44%) 32 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 13 / 370 (3.51%) 16 | 30 / 379 (7.92%) 41 | |
| Back pain subjects affected / exposed occurrences (all) | 28 / 370 (7.57%) 37 | 33 / 379 (8.71%) 36 | |
| Muscular weakness | | | |

| | | | |
|--|---------------------------|--------------------------|--|
| subjects affected / exposed occurrences (all) | 17 / 370 (4.59%) 22 | 21 / 379 (5.54%) 24 | |
| Myalgia subjects affected / exposed occurrences (all) | 13 / 370 (3.51%) 15 | 31 / 379 (8.18%) 43 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 7 / 370 (1.89%) 8 | 30 / 379 (7.92%) 35 | |
| Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) | 27 / 370 (7.30%) 29 | 23 / 379 (6.07%) 29 | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 132 / 370 (35.68%) 157 | 68 / 379 (17.94%) 136 | |
| Dehydration subjects affected / exposed occurrences (all) | 35 / 370 (9.46%) 40 | 29 / 379 (7.65%) 31 | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 26 / 370 (7.03%) 33 | 30 / 379 (7.92%) 31 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 116 / 370 (31.35%) 190 | 49 / 379 (12.93%) 70 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 34 / 370 (9.19%) 44 | 16 / 379 (4.22%) 22 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 18 / 370 (4.86%) 21 | 20 / 379 (5.28%) 21 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 28 November 2019 | The study name was updated with the branding logo. Study duration was clarified. Adverse event causality assessment clarified by the investigator. Adverse events of special interest were defined as thromboembolic disease. Collection of electronic serious adverse events (SAE) were clarified. Clarification that disease progression was not classified as an SAE. The use of contraceptive were aligned with all packaging information in all localities of the study. Minor editorial changes to provide additional details. |
| 03 June 2020 | The electrocardiogram assessment timepoint were clarified. |
| 19 August 2021 | Eligibility criterion and protocol procedures were clarified. Details specific to conduct of the study during the COVID-19 pandemic were added. Secondary endpoint analysis was updated to refine the interim analysis of OS. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported