# Clinical trial results:
# A randomized, double-blind, phase III study, comparing NIS793 in combination with gemcitabine and nab-paclitaxel versus (vs.) placebo combined with gemcitabine and nab-paclitaxel for first line treatment of metastatic pancreatic ductal adenocarcinoma (mPDAC) - daNIS-2

## Summary

| | |
|---|---|
| EudraCT number | 2021-000591-10 |
| Trial protocol | HU DE BE ES SK FR SE FI IT NO NL |
| Global end of trial date | 13 August 2024 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 17 June 2026 |
| First version publication date | 27 August 2025 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CNIS793B12301 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04935359 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Lichtstrasse 35, Basel, Switzerland, 4056 |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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 | 13 August 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 13 August 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of NIS793 in combination with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel and placebo in first-line metastatic pancreatic ductal adenocarcinoma (mPDAC). This study aimed to explore whether blockade of Transforming Growth Factor β (TGFβ) in combination with gemcitabine/nab-paclitaxel could reduce fibrosis in PDAC, restore chemo-sensitivity and ultimately lead to improvements in overall survival (OS) and other clinically relevant outcomes.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 30 September 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 9 |
| Country: Number of subjects enrolled | Belgium: 18 |
| Country: Number of subjects enrolled | Brazil: 14 |
| Country: Number of subjects enrolled | Canada: 10 |
| Country: Number of subjects enrolled | China: 78 |
| Country: Number of subjects enrolled | Czechia: 18 |
| Country: Number of subjects enrolled | Finland: 3 |
| Country: Number of subjects enrolled | France: 24 |
| Country: Number of subjects enrolled | Germany: 35 |
| Country: Number of subjects enrolled | United Kingdom: 27 |
| Country: Number of subjects enrolled | Greece: 5 |
| Country: Number of subjects enrolled | Hungary: 15 |
| Country: Number of subjects enrolled | Israel: 10 |
| Country: Number of subjects enrolled | Italy: 15 |
| Country: Number of subjects enrolled | Japan: 53 |
| Country: Number of subjects enrolled | Korea, Republic of: 19 |
| Country: Number of subjects enrolled | Netherlands: 2 |

| | |
|---|---|
| Country: Number of subjects enrolled | Norway: 4 |
| Country: Number of subjects enrolled | Russian Federation: 3 |
| Country: Number of subjects enrolled | Singapore: 2 |
| Country: Number of subjects enrolled | Slovakia: 7 |
| Country: Number of subjects enrolled | Spain: 23 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Switzerland: 9 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | Türkiye: 23 |
| Country: Number of subjects enrolled | United States: 68 |
| Worldwide total number of subjects | 511 |
| EEA total number of subjects | 172 |

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) | 268 |
| From 65 to 84 years | 243 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study was conducted globally across 27 countries.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo |

Arm description:

Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | NIS793 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

2100 mg (Days 1 and 15)

| | |
|---|---|
| Investigational medicinal product name | Nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

125 mg/m² (Days 1, 8 and 15)

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

Dosage and administration details:

1000 mg/m² (Days 1, 8 and 15)

| | |
|---|---|
| **Arm title** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel |

Arm description:

Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)

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

| | |
|---|---|
| Investigational medicinal product name | NIS793 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

2100 mg (Days 1 and 15) assuming this was the confirmed RP3D in the safety run-in part or NIS793 at 2100 mg on Day 1 if dose level -1 was the confirmed RP3D in the safety run-in

| | |
|---|---|
| Investigational medicinal product name | Nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

125 mg/m² (Days 1, 8 and 15)

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

Dosage and administration details:

1000 mg/m² (Days 1, 8 and 15)

| | |
|---|---|
| **Arm title** | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel |

Arm description:

Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)

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

Dosage and administration details:

1000 mg/m² (Days 1, 8 and 15)

| | |
|---|---|
| Investigational medicinal product name | Nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

125 mg/m² (Days 1, 8 and 15)

| | |
|---|---|
| Investigational medicinal product name | Placebo for NIS793 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dextrose 5% in water (D5W) Days 1 and 15

| **Number of subjects in period 1** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel |
|---|---|---|---|
| Started | 21 | 245 | 245 |
| Entered post treatment follow-up | 18 | 192 | 200 |
| Completed | 0 | 0 | 0 |
| Not completed | 21 | 245 | 245 |
| Adverse event, serious fatal | - | 16 | 8 |
| Physician decision | 2 | 20 | 24 |
| Participant decision | - | 25 | 24 |
| Adverse event, non-fatal | 1 | 25 | 24 |
| Participants not treated due to Protocol deviation | - | 1 | - |
| Progressive disease | 17 | 148 | 149 |
| Lost to follow-up | 1 | - | - |
| Sponsor decision | - | 9 | 16 |
| Guardian decision | - | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo |
| Reporting group description: | |
| Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |
| Reporting group title | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel |
| Reporting group description: | |
| Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |
| Reporting group title | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel |
| Reporting group description: | |
| Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |

| Reporting group values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel |
|---|---|---|---|
| Number of subjects | 21 | 245 | 245 |
| Age Categorical<br>Units: Participants | | | |
| <= 65 years | 13 | 130 | 125 |
| Between 65 and 75 years | 7 | 97 | 91 |
| >= 75 years | 1 | 18 | 29 |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 6 | 109 | 99 |
| Male | 15 | 136 | 146 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 3 | 0 |
| Asian | 2 | 87 | 87 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 0 |
| Black or African American | 0 | 9 | 6 |
| White | 19 | 137 | 143 |
| More than one race | 0 | 1 | 0 |
| Unknown or Not Reported | 0 | 7 | 9 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 511 | | |
| Age Categorical<br>Units: Participants | | | |
| <= 65 years | 268 | | |
| Between 65 and 75 years | 195 | | |
| >= 75 years | 48 | | |

| | | | |
|---|---|---|---|
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 214 | | |
| Male | 297 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 3 | | |
| Asian | 176 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |
| Black or African American | 15 | | |
| White | 299 | | |
| More than one race | 1 | | |
| Unknown or Not Reported | 16 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo |
| Reporting group description: | |
| Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |
| Reporting group title | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel |
| Reporting group description: | |
| Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |
| Reporting group title | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel |
| Reporting group description: | |
| Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15) | |

### Primary: Safety run-in part: Percentage of participants with dose limiting toxicities (DLTs) during the first cycle (4 weeks) of treatment.

| | |
|---|---|
| End point title | Safety run-in part: Percentage of participants with dose limiting toxicities (DLTs) during the first cycle (4 weeks) of treatment.[1][2] |
| End point description: | |
| A dose-limiting toxicity (DLT) was defined as an adverse event or abnormal laboratory value assessed as unrelated to disease, disease progression, inter-current illness, or concomitant medications that occurred within the first cycle (i.e., 28 days or 4 weeks) of the treatment with NIS793 in combination with gemcitabine/nab-paclitaxel. The National Cancer Institute Common Terminology Criteria for Adverse events (NCI CTCAE) version 5 was used for all grading. | |
| End point type | Primary |
| End point timeframe: | |
| Up to 4 weeks | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Endpoint only applicable to Safety run-in arm

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Safety run-in arm

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: Participants | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Randomized part: Overall Survival (OS)

| End point title | Randomized part: Overall Survival (OS)[3][4] |
|---|---|

End point description:

Overall Survival (OS) was defined as the time from date of randomization/start of treatment to date of death due to any cause. If a patient was not known to have died, survival was censored at the date of last known date patient alive.

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

End point timeframe:

From randomization up to death, assessed up to approximately 34 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Endpoint only applicable to Randomized part Arms A and B

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part Arms A and B

| End point values | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 245 | 245 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 9.2 (8.1 to 10.5) | 11.2 (9.6 to 12.1) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with Adverse Events (AEs)

| End point title | Percentage of participants with Adverse Events (AEs) |
|---|---|

End point description:

An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of a medicinal (investigational) product.

Treatment emergent Adverse Event (TEAEs) in this study are events that started after the first dose of study treatment and until 30 days after last dose of SOC chemotherapies and up to 90 days after NIS793, whichever is later.

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

End point timeframe:

Up to approximately 32 months

| End point values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 239 | 241 | |
| Units: Participants | | | | |
| Adverse Events (AEs) | 21 | 239 | 239 | |
| Serious Adverse Events (SAEs) | 13 | 144 | 110 | |
| Fatal SAEs | 0 | 12 | 8 | |
| AEs leading to discontinuation | 2 | 46 | 50 | |
| AEs leading to dose adjustment/interruption | 16 | 205 | 208 | |
| AEs requiring additional therapy | 21 | 231 | 227 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with dose interruptions and dose reductions of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Percentage of participants with dose interruptions and dose reductions of NIS793 in combination with gemcitabine and nab-paclitaxel |
|---|---|

End point description:

No dose reductions were allowed for NIS793 in the Randomized part and beyond the first 28 days period of the Safety Run-in part. Increasing the dosing interval from every 2 weeks (Q2W) to every 2 weeks (Q4W) was allowed.
Dose interruption for NIS793 was permitted if adverse drug reaction was suspected to be related to NIS793. If NIS793 was interrupted or delayed for > 8 weeks due to toxicity that was suspected to be related to treatment, study treatment was permanently discontinued.

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

End point timeframe:

Up to approximately 32 months

| End point values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 239 | 241 | |
| Units: Participants | | | | |
| With no dose interruption | 5 | 92 | 82 | |
| With at least one dose interruption | 16 | 147 | 159 | |
| With no dose reduction | 21 | 237 | 241 | |
| With at least one dose reduction | 0 | 2 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Dose intensity of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Dose intensity of NIS793 in combination with gemcitabine and nab-paclitaxel |
|---|---|

End point description:

Dose intensity was computed as the ratio of actual cumulative dose received and actual duration of exposure.

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

End point timeframe:

Up to approximately 32 months

| End point values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 239 | 241 | |
| Units: mg/cycle | | | | |
| arithmetic mean (standard deviation) | 3669.2 (± 528.07) | 3134.1 (± 573.15) | 3183.4 (± 593.92) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS)

| End point title | Progression-Free Survival (PFS) |
|---|---|

End point description:

Progression-Free Survival (PFS) was defined as the time from the enrollment (run-in part) or randomization (randomized part) to the date of the first documented disease progression based on local investigator assessment as per RECIST 1.1 or date of death due to any cause, whichever occurs first. PFS was censored if no PFS event was observed before the analysis cut-off date. The censoring date was the date of the last adequate tumor assessment prior to the analysis cut-off.

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

End point timeframe:

From enrollment (run-in part) or randomization (randomized part) up to disease progression or death, assessed up to approximately 34 months

| End point values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 245 | 245 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.4 (3.6 to 7.3) | 4.6 (3.7 to 5.4) | 5.4 (5.3 to 6.6) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Response Rate (ORR)

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

End point description:

Overall Response Rate (ORR) was defined as the proportion of participants with a Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR) as per local review. ORR was evaluated according to RECIST 1.1. The BOR was determined from response assessments undertaken while on treatment.

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

End point timeframe:

Up to approximately 34 months

| End point values | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 245 | 245 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 19.0 (5.4 to 41.9) | 21.6 (16.6 to 27.3) | 25.3 (20.0 to 31.2) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR)

| End point title | Duration of Response (DOR) |
|---|---|

End point description:

Duration of Response (DOR) was defined as the duration of time between the date of first documented response (CR or PR) and the date of first documented progression or death due to any cause.

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

End point timeframe:

Up to approximately 34 months

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 53 | 62 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 8.6 (3.5 to 999) | 6.2 (4.7 to 7.4) | 5.6 (5.0 to 7.2) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Disease Control Rate (DCR)**

| End point title | Disease Control Rate (DCR) |
|---|---|

End point description:

Disease Control Rate (DCR) was defined as the proportion of participants with Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR), or Stable Disease (SD) or Non-CR/Non-progressive disease as per local review. DCR was evaluated according to RECIST 1.1.

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

End point timeframe:

Up to approximately 34 months

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 245 | 245 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 76.2 (52.8 to 91.8) | 66.9 (60.7 to 72.8) | 72.2 (66.2 to 77.8) | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Safety run-in part: Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Safety run-in part: Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel[5] |
|---|---|

End point description:

Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Ctrough was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3 Day 15 (0 hour (pre-dose)), Cycles 2, 4, 6 and 12 Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Safety run-in arm

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 15 | 230000 (± 250000) | | | |
| Cycle 2 Day 1 | 207000 (± 82400) | | | |
| Cycle 3 Day 1 | 300000 (± 123000) | | | |
| Cycle 3 Day 15 | 309000 (± 130000) | | | |
| Cycle 4 Day 1 | 370000 (± 148000) | | | |
| Cycle 6 Day 1 | 425000 (± 86800) | | | |
| Cycle 12 Day 1 | 553000 (± 999) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Response (TTR)

| End point title | Time to Response (TTR) |
|---|---|

End point description:

Time to Response (TTR) was defined as the duration of time between the date of enrollment (run-in part) or randomization (randomized part) and the date of first documented response of either CR or PR as per local review, which was subsequently confirmed. TTR was evaluated according to RECIST 1.1. Participants without a confirmed CR or PR were censored at the time of PFS event (i.e., disease progression or death due to any cause) for participants with a PFS event (i.e., disease progression or death due to any cause), or at the date of the last adequate tumor assessment for participants without a

PFS event.

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

End point timeframe:

From enrollment (run-in part) or randomization (randomized part) up to first documented response, assessed up to approximately 34 months

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | Randomized part (Arm B): Placebo + Gem/Nab-paclitaxel | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 245 | 245 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999 (999 to 999) | 999 (999 to 999) | 999 (999 to 999) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety run-in part: Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Safety run-in part: Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[6] |
|---|---|

End point description:

Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Cmax was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Safety run-in arm

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 549000 (± 193000) | | | |
| Cycle 3 Day 1 | 837000 (± 394000) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Safety run-in part: Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Safety run-in part: Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[7] |
|---|---|

End point description:

Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Tmax was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Safety run-in arm

| **End point values** | Safety run-in: NIS793 + Gem/Nab-paclitaxel combo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 17 | | | |
| Units: Hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 | 1.12 (0.583 to 5.00) | | | |
| Cycle 3 Day 1 | 0.883 (0.5 to 4.17) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (Chinese participants with intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (Chinese participants with intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel[8] |
|---|---|

End point description:

In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory

manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Ctrough was summarized using descriptive statistics.

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

End point timeframe:

Cycle 1 Day 15, Cycle 3 Day 1, Cycle 3 Day 15, Cycle 4 Day 1 and Cycle 6 Day 1: 0 hour (pre-dose). 1 cycle = 28 days.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Chinese participants with intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 15: 0 hour (pre-dose) | 149000 (± 36400) | | | |
| Cycle 3 Day 1: 0 hour (pre-dose) | 366000 (± 114000) | | | |
| Cycle 3 Day 15: 0 hour (pre-dose) | 380000 (± 187000) | | | |
| Cycle 4 Day 1: 0 hour (pre-dose) | 371000 (± 131000) | | | |
| Cycle 6 Day 1: 0 hour (pre-dose) | 493000 (± 221000) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (Chinese participants with intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (Chinese participants with intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[9] |
|---|---|

End point description:

In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Cmax was summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Chinese participants with intensive PK sampling)

| End point values | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 691000 (± 113000) | | | |
| Cycle 3 Day 1 | 978000 (± 131000) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (Chinese participants with intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (Chinese participants with intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[10] |
|---|---|

End point description:

In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Tmax was summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Chinese participants with intensive PK sampling)

| End point values | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 | | | |
| Units: Hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 | 1.52 (0.583 to 7.00) | | | |
| Cycle 3 Day 1 | 3.98 (0.567 to 7.75) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (Chinese participants with intensive PK sampling): Area under the curve calculated to the end of a dosing interval (tau) at steady-state (AUCtau) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (Chinese participants with intensive PK sampling): Area under the curve calculated to the end of a dosing interval (tau) at steady-state (AUCtau) of NIS793 in combination with gemcitabine and nab-paclitaxel[11] |
|---|---|

End point description:

In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected and AUCtau was summarized using descriptive statistics.

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

End point timeframe:

Cycles 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Chinese participants with intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 159000000 (± 25.5) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (participants without intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (participants without intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel[12] |
|---|---|

End point description:

For participants without intensive PK sampling, venous whole blood samples were collected for activity-based pharmacokinetics characterization. Ctrough was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 2, 3, 4, 6 and 12 Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (participants without intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 129 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 Day 1: 0 hour (pre-dose) | 249000 (± 105000) | | | |
| Cycle 3 Day 1: 0 hour (pre-dose) | 331000 (± 133000) | | | |
| Cycle 4 Day 1: 0 hour (pre-dose) | 335000 (± 138000) | | | |
| Cycle 6 Day 1: 0 hour (pre-dose) | 334000 (± 136000) | | | |
| Cycle 12 Day 1: 0 hour (pre-dose) | 302000 (± 63600) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (Chinese participants with intensive PK sampling): Area under the curve from time zero to the last measurable concentration sampling time (AUClast) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (Chinese participants with intensive PK sampling): Area under the curve from time zero to the last measurable concentration sampling time (AUClast) of NIS793 in combination with gemcitabine and nab-paclitaxel[13] |
|---|---|

End point description:

In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and AUClast was summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Chinese participants with intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 | | | |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 48900000 (± 104.3) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (participants without intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (participants without intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[14] |
|---|---|

End point description:

For Chinese participants without intensive PK sampling schedule and global participants in the randomized part, for which only sparse PK samples were collected for activity-based pharmacokinetics characterization, Cmax was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3: Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (participants without intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 152 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1: 0 hour (pre-dose) | 625000 (± 185000) | | | |
| Cycle 3 Day 1: 0 hour (pre-dose) | 807000 (± 228000) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part (participants without intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel

| End point title | Randomized part (participants without intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel[15] |
|---|---|

End point description:

For Chinese participants without intensive PK sampling schedule and global participants in the randomized part, for which only sparse PK samples were collected for activity-based pharmacokinetics characterization, Tmax was listed and summarized using descriptive statistics.

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

End point timeframe:

Cycles 1 and 3: Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (participants without intensive PK sampling)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 152 | | | |
| Units: Hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1: 0 hour (pre-dose) | 1.08 (0.5 to 5.17) | | | |
| Cycle 3 Day 1: 0 hour (pre-dose) | 0.833 (0.5 to 2.83) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part: Anti-drug antibodies (ADA) against NIS793 prevalence at baseline

| End point title | Randomized part: Anti-drug antibodies (ADA) against NIS793 prevalence at baseline[16] |
|---|---|

End point description:

Anti-drug antibodies (ADA) against NIS793 prevalence at baseline refers to the proportion of subjects

who have developed antibodies against the drug NIS793 before starting treatment. This is calculated by dividing the number of subjects with ADA-positive samples at baseline by the total number of subjects whose baseline samples were tested for ADA.

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

End point timeframe:

Baseline

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Arm A)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 196 | | | |
| Units: Participants | | | | |
| ADA-negative sample at baseline | 196 | | | |
| ADA-positive sample at baseline | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Randomized part: Anti-drug antibodies (ADA) against NIS793 incidence on treatment

| End point title | Randomized part: Anti-drug antibodies (ADA) against NIS793 incidence on treatment[17] |
|---|---|

End point description:

Anti-drug antibodies (ADA) against NIS793 incidence on treatment refers to the proportion of participants who developed antibodies against the drug NIS793 during the treatment period. This can be categorized into two types:
1) Treatment-induced ADA positive: Participants who were ADA-negative at baseline but became ADA-positive after starting the treatment.
2) Treatment-boosted ADA positive: Participants who were ADA-positive at baseline and showed a significant increase in ADA titer during the treatment.

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

End point timeframe:

From date of first study drug intake up to approximately 34 months

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Randomized part (Arm A)

| **End point values** | Randomized part (Arm A): NIS793 + Gem/Nab-paclitaxel | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 196 | | | |

| Units: Participants | | | | |
|---|---|---|---|---|
| Treatment-boosted ADA-positive | 0 | | | |
| Treatment-induced ADA-positive | 0 | | | |
| ADA-negative | 196 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from first dose of study medication until end of extended follow-up phase (end of study), assessed up to approximately 34 months.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 27.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | NIS793 2100mg Q2W + Gem/NabP @On-treatment period |

Reporting group description:

NIS793 2100 mg Q2W plus Gemcitabine and Nab-paclitaxel@On-treatment period

| | |
|---|---|
| Reporting group title | NIS793 2100mg Q2W + Gem/NabP @Post-treatment period |

Reporting group description:

NIS793 2100 mg Q2W plus Gemcitabine and Nab-paclitaxel@Post treatment period

| | |
|---|---|
| Reporting group title | NIS793 + Gem/NabP @On-treatment period |

Reporting group description:

NIS793 and (Gem + Nab)@On-treatment period

| | |
|---|---|
| Reporting group title | NIS793 + Gem/NabP @Post treatment period |

Reporting group description:

NIS793 and (Gem + Nab)@Post treatment period

| | |
|---|---|
| Reporting group title | Placebo + Gem/NabP @On-treatment period |

Reporting group description:

Placebo and (Gem + Nab)@On-treatment period

| | |
|---|---|
| Reporting group title | Placebo + Gem/NabP @Post treatment period |

Reporting group description:

Placebo and (Gem + Nab)@Post treatment period

| **Serious adverse events** | NIS793 2100mg Q2W + Gem/NabP @On-treatment period | NIS793 2100mg Q2W + Gem/NabP @Post-treatment period | NIS793 + Gem/NabP @On-treatment period |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 21 (61.90%) | 2 / 21 (9.52%) | 144 / 239 (60.25%) |
| number of deaths (all causes) | 0 | 19 | 24 |
| number of deaths resulting from adverse events | 0 | 0 | 3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Transitional cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Distributive shock | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 21 (4.76%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral vein thrombosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Condition aggravated | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malaise | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 6 / 239 (2.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 11 / 239 (4.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 5 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiogenic pulmonary oedema | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrothorax | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Stent malfunction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device dislocation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Anastomotic ulcer | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured sacrum | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic rupture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular pseudoaneurysm ruptured | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardiac arrest | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve disease | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Heart failure with preserved ejection fraction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysstasia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coma | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Motor dysfunction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurotoxicity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Putamen haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Atypical haemolytic uraemic syndrome | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood loss anaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 21 (4.76%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 13 / 239 (5.44%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 12 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombotic microangiopathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Retinal vasculitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal ischaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute abdomen | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric stenosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric perforation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal stenosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant ascites | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic enteritis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal hypertensive gastropathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstruction gastric | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant gastrointestinal obstruction | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal perforation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 8 / 239 (3.35%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 5 / 239 (2.09%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 3 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 7 / 239 (2.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder fistula | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sarcopenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporotic fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis infective | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 21 (4.76%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Giardiasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Focal peritonitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nail infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreas infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngitis fungal | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Penile infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 7 / 239 (2.93%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 2 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 5 / 239 (2.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 5 / 239 (2.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | NIS793 + Gem/NabP @Post treatment period | Placebo + Gem/NabP @On-treatment period | Placebo + Gem/NabP @Post treatment period |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 239 (8.79%) | 110 / 241 (45.64%) | 28 / 241 (11.62%) |
| number of deaths (all causes) | 135 | 16 | 132 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour associated fever | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic dissection | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Distributive shock | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 4 / 241 (1.66%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral vein thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Condition aggravated | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 239 (1.26%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 11 / 241 (4.56%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 15 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiogenic pulmonary oedema | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrothorax | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 239 (0.84%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Product issues | | | |
| Stent malfunction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Anastomotic ulcer | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured sacrum | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic rupture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular pseudoaneurysm ruptured | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorder | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve disease | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Heart failure with preserved ejection fraction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysstasia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coma | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Motor dysfunction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurotoxicity | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Putamen haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| **Blood and lymphatic system disorders** | | | |
| Atypical haemolytic uraemic syndrome | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood loss anaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombotic microangiopathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Retinal vasculitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal ischaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 8 / 241 (3.32%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 9 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute abdomen | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 6 / 241 (2.49%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 6 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric stenosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric perforation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal stenosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant ascites | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic enteritis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal hypertensive gastropathy | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstruction gastric | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malignant gastrointestinal obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Small intestinal perforation | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 5 / 241 (2.07%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 6 / 241 (2.49%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 7 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder fistula | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disease | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal vein thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sarcopenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 5 / 241 (2.07%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis infective | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Giardiasis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Focal peritonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nail infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreas infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngitis fungal | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Penile infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 7 / 241 (2.90%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 8 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 7 / 241 (2.90%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 8 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Septic shock | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 1 / 241 (0.41%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | NIS793 2100mg Q2W + Gem/NabP @On-treatment period | NIS793 2100mg Q2W + Gem/NabP @Post-treatment period | NIS793 + Gem/NabP @On-treatment period |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 21 (100.00%) | 6 / 21 (28.57%) | 228 / 239 (95.40%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 11 / 239 (4.60%) |
| occurrences (all) | 1 | 0 | 13 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 12 / 239 (5.02%) |
| occurrences (all) | 2 | 0 | 15 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 13 / 239 (5.44%) |
| occurrences (all) | 1 | 0 | 15 |
| Asthenia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 39 / 239 (16.32%) |
| occurrences (all) | 3 | 0 | 54 |
| Fatigue | | | |
| subjects affected / exposed | 12 / 21 (57.14%) | 0 / 21 (0.00%) | 76 / 239 (31.80%) |
| occurrences (all) | 14 | 0 | 100 |
| Malaise | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 21 / 239 (8.79%) |
| occurrences (all) | 1 | 0 | 27 |
| Mucosal inflammation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 11 / 239 (4.60%) |
| occurrences (all) | 0 | 0 | 15 |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 36 / 239 (15.06%) |
| occurrences (all) | 4 | 0 | 41 |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | 1 / 21 (4.76%) | 75 / 239 (31.38%) |
| occurrences (all) | 11 | 1 | 149 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 23 / 239 (9.62%) |
| occurrences (all) | 2 | 0 | 25 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 18 / 239 (7.53%) |
| occurrences (all) | 1 | 0 | 22 |
| Epistaxis | | | |
| subjects affected / exposed | 7 / 21 (33.33%) | 0 / 21 (0.00%) | 66 / 239 (27.62%) |
| occurrences (all) | 8 | 0 | 87 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 0 / 239 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 18 / 239 (7.53%) |
| occurrences (all) | 3 | 0 | 18 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 54 / 239 (22.59%) |
| occurrences (all) | 5 | 0 | 85 |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 9 / 239 (3.77%) |
| occurrences (all) | 5 | 0 | 14 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 59 / 239 (24.69%) |
| occurrences (all) | 8 | 0 | 96 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 20 / 239 (8.37%) |
| occurrences (all) | 5 | 0 | 24 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 19 / 239 (7.95%) |
| occurrences (all) | 0 | 0 | 20 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 6 / 239 (2.51%) |
| occurrences (all) | 9 | 0 | 11 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 27 / 239 (11.30%) |
| occurrences (all) | 3 | 0 | 32 |
| Lipase increased | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 15 / 239 (6.28%) |
| occurrences (all) | 5 | 0 | 22 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 17 / 239 (7.11%) |
| occurrences (all) | 3 | 0 | 52 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 63 / 239 (26.36%) |
| occurrences (all) | 16 | 0 | 166 |
| Platelet count decreased | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 52 / 239 (21.76%) |
| occurrences (all) | 21 | 0 | 127 |
| Weight decreased | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | 1 / 21 (4.76%) | 44 / 239 (18.41%) |
| occurrences (all) | 7 | 1 | 46 |
| White blood cell count increased | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 3 / 239 (1.26%) |
| occurrences (all) | 3 | 0 | 4 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 48 / 239 (20.08%) |
| occurrences (all) | 8 | 0 | 140 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Dizziness | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 15 / 239 (6.28%) |
| occurrences (all) | 2 | 0 | 17 |
| Dysgeusia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 20 / 239 (8.37%) |
| occurrences (all) | 2 | 0 | 22 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 22 / 239 (9.21%) |
| occurrences (all) | 0 | 0 | 26 |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 10 / 239 (4.18%) |
| occurrences (all) | 3 | 0 | 16 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 31 / 239 (12.97%) |
| occurrences (all) | 2 | 0 | 34 |
| Headache | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 17 / 239 (7.11%) |
| occurrences (all) | 5 | 0 | 19 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 36 / 239 (15.06%) |
| occurrences (all) | 5 | 0 | 84 |
| Neutropenia | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | 0 / 21 (0.00%) | 49 / 239 (20.50%) |
| occurrences (all) | 19 | 0 | 148 |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 15 / 239 (6.28%) |
| occurrences (all) | 3 | 0 | 44 |
| Anaemia | | | |
| subjects affected / exposed | 14 / 21 (66.67%) | 0 / 21 (0.00%) | 165 / 239 (69.04%) |
| occurrences (all) | 19 | 0 | 257 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 9 / 239 (3.77%) |
| occurrences (all) | 2 | 0 | 9 |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 21 (38.10%) | 1 / 21 (4.76%) | 25 / 239 (10.46%) |
| occurrences (all) | 10 | 1 | 34 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 13 / 239 (5.44%) |
| occurrences (all) | 1 | 0 | 15 |
| Constipation | | | |
| subjects affected / exposed | 7 / 21 (33.33%) | 0 / 21 (0.00%) | 47 / 239 (19.67%) |
| occurrences (all) | 11 | 0 | 57 |
| Nausea | | | |
| subjects affected / exposed | 12 / 21 (57.14%) | 0 / 21 (0.00%) | 89 / 239 (37.24%) |
| occurrences (all) | 12 | 0 | 130 |
| Mouth ulceration | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 5 / 239 (2.09%) |
| occurrences (all) | 2 | 0 | 5 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 14 / 239 (5.86%) |
| occurrences (all) | 1 | 0 | 15 |
| Gingival bleeding | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 9 / 239 (3.77%) |
| occurrences (all) | 3 | 0 | 11 |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 21 (42.86%) | 1 / 21 (4.76%) | 70 / 239 (29.29%) |
| occurrences (all) | 12 | 1 | 111 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 8 / 239 (3.35%) |
| occurrences (all) | 2 | 0 | 9 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 57 / 239 (23.85%) |
| occurrences (all) | 6 | 0 | 94 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 25 / 239 (10.46%) |
| occurrences (all) | 0 | 0 | 39 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 9 / 21 (42.86%) | 0 / 21 (0.00%) | 83 / 239 (34.73%) |
| occurrences (all) | 9 | 0 | 83 |

| | | | |
|---|---|---|---|
| Pruritus | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 1 / 21 (4.76%) | 28 / 239 (11.72%) |
| occurrences (all) | 2 | 0 | 39 |
| Rash papular | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences (all) | 4 | 0 | 1 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 13 / 239 (5.44%) |
| occurrences (all) | 1 | 0 | 15 |
| Rash | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | 0 / 21 (0.00%) | 67 / 239 (28.03%) |
| occurrences (all) | 8 | 0 | 89 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 4 / 239 (1.67%) |
| occurrences (all) | 2 | 0 | 8 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 14 / 239 (5.86%) |
| occurrences (all) | 2 | 0 | 17 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 16 / 239 (6.69%) |
| occurrences (all) | 0 | 0 | 20 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 18 / 239 (7.53%) |
| occurrences (all) | 1 | 0 | 19 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 17 / 239 (7.11%) |
| occurrences (all) | 0 | 0 | 21 |
| Joint swelling | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 1 / 239 (0.42%) |
| occurrences (all) | 4 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 3 / 21 (14.29%) | 18 / 239 (7.53%) |
| occurrences (all) | 5 | 2 | 24 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 28 / 239 (11.72%) |
| occurrences (all) | 3 | 0 | 36 |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 20 / 239 (8.37%) |
| occurrences (all) | 1 | 0 | 20 |
| Metabolism and nutrition disorders | | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 39 / 239 (16.32%) |
| occurrences (all) | 1 | 0 | 56 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 21 (0.00%) | 12 / 239 (5.02%) |
| occurrences (all) | 5 | 0 | 23 |
| Decreased appetite | | | |
| subjects affected / exposed | 8 / 21 (38.10%) | 0 / 21 (0.00%) | 66 / 239 (27.62%) |
| occurrences (all) | 9 | 0 | 83 |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 28 / 239 (11.72%) |
| occurrences (all) | 8 | 0 | 36 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 12 / 239 (5.02%) |
| occurrences (all) | 0 | 0 | 20 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 21 (0.00%) | 26 / 239 (10.88%) |
| occurrences (all) | 0 | 0 | 43 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 0 / 21 (0.00%) | 35 / 239 (14.64%) |
| occurrences (all) | 4 | 0 | 64 |
| Iron deficiency | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 0 / 21 (0.00%) | 5 / 239 (2.09%) |
| occurrences (all) | 4 | 0 | 5 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 21 (0.00%) | 30 / 239 (12.55%) |
| occurrences (all) | 2 | 0 | 57 |

| **Non-serious adverse events** | NIS793 + Gem/NabP @Post treatment period | Placebo + Gem/NabP @On-treatment period | Placebo + Gem/NabP @Post treatment period |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 29 / 239 (12.13%) | 236 / 241 (97.93%) | 36 / 241 (14.94%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 13 / 241 (5.39%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 17 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 12 / 241 (4.98%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 12 | 2 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 13 / 241 (5.39%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 14 | 1 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 45 / 241 (18.67%) | 4 / 241 (1.66%) |
| occurrences (all) | 0 | 60 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 78 / 241 (32.37%) | 5 / 241 (2.07%) |
| occurrences (all) | 0 | 96 | 4 |
| Malaise | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 15 / 241 (6.22%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 22 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 13 / 241 (5.39%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 15 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 66 / 241 (27.39%) | 3 / 241 (1.24%) |
| occurrences (all) | 0 | 79 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 63 / 241 (26.14%) | 3 / 241 (1.24%) |
| occurrences (all) | 2 | 112 | 4 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 26 / 241 (10.79%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 28 | 0 |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 18 / 241 (7.47%) | 1 / 241 (0.41%) |
| occurrences (all) | 1 | 18 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 20 / 241 (8.30%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 26 | 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 26 / 241 (10.79%) | 1 / 241 (0.41%) |
| occurrences (all) | 1 | 26 | 0 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 56 / 241 (23.24%) | 5 / 241 (2.07%) |
| occurrences (all) | 3 | 92 | 2 |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 7 / 241 (2.90%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 8 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 63 / 241 (26.14%) | 4 / 241 (1.66%) |
| occurrences (all) | 4 | 113 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 21 / 241 (8.71%) | 3 / 241 (1.24%) |
| occurrences (all) | 3 | 26 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 14 / 241 (5.81%) | 4 / 241 (1.66%) |
| occurrences (all) | 2 | 22 | 2 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 7 / 241 (2.90%) | 2 / 241 (0.83%) |
| occurrences (all) | 0 | 11 | 2 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 4 / 239 (1.67%) | 25 / 241 (10.37%) | 2 / 241 (0.83%) |
| occurrences (all) | 1 | 28 | 0 |
| Lipase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 239 (0.42%) | 11 / 241 (4.56%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 11 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 8 / 241 (3.32%) | 0 / 241 (0.00%) |
| occurrences (all) | 3 | 20 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 78 / 241 (32.37%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 278 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 70 / 241 (29.05%) | 2 / 241 (0.83%) |
| occurrences (all) | 3 | 222 | 2 |
| Weight decreased | | | |
| subjects affected / exposed | 4 / 239 (1.67%) | 34 / 241 (14.11%) | 3 / 241 (1.24%) |
| occurrences (all) | 3 | 41 | 3 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 63 / 241 (26.14%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 223 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 16 / 241 (6.64%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 19 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 21 / 241 (8.71%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 26 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 36 / 241 (14.94%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 43 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 10 / 241 (4.15%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 11 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 35 / 241 (14.52%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 39 | 0 |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 17 / 241 (7.05%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 24 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 32 / 241 (13.28%) | 2 / 241 (0.83%) |
| occurrences (all) | 1 | 84 | 3 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 66 / 241 (27.39%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 161 | 1 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 29 / 241 (12.03%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 73 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 16 / 239 (6.69%) | 143 / 241 (59.34%) | 10 / 241 (4.15%) |
| occurrences (all) | 2 | 206 | 4 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 7 / 241 (2.90%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 8 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 28 / 241 (11.62%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 37 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 12 / 241 (4.98%) | 1 / 241 (0.41%) |
| occurrences (all) | 2 | 14 | 0 |
| Constipation | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 57 / 241 (23.65%) | 1 / 241 (0.41%) |
| occurrences (all) | 2 | 63 | 1 |
| Nausea | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 86 / 241 (35.68%) | 5 / 241 (2.07%) |
| occurrences (all) | 0 | 123 | 4 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 80 / 241 (33.20%) | 2 / 241 (0.83%) |
| occurrences (all) | 2 | 115 | 3 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 3 / 241 (1.24%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 53 / 241 (21.99%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 78 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 8 / 241 (3.32%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 9 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 71 / 241 (29.46%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 71 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 18 / 241 (7.47%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 22 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 0 / 241 (0.00%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 8 / 241 (3.32%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 9 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 45 / 241 (18.67%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 53 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 239 (0.00%) | 5 / 241 (2.07%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 18 / 241 (7.47%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 23 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 15 / 241 (6.22%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 21 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 17 / 241 (7.05%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 20 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 2 / 241 (0.83%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 19 / 241 (7.88%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 21 | 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 17 / 241 (7.05%) | 2 / 241 (0.83%) |
| occurrences (all) | 1 | 23 | 2 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 23 / 241 (9.54%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 23 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 24 / 241 (9.96%) | 6 / 241 (2.49%) |
| occurrences (all) | 1 | 30 | 2 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 239 (0.42%) | 20 / 241 (8.30%) | 1 / 241 (0.41%) |
| occurrences (all) | 1 | 27 | 1 |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 239 (1.67%) | 63 / 241 (26.14%) | 4 / 241 (1.66%) |
| occurrences (all) | 2 | 77 | 2 |
| Hypokalaemia | | | |
| subjects affected / exposed | 5 / 239 (2.09%) | 24 / 241 (9.96%) | 2 / 241 (0.83%) |
| occurrences (all) | 5 | 36 | 3 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 9 / 241 (3.73%) | 1 / 241 (0.41%) |
| occurrences (all) | 0 | 13 | 1 |
| Hyponatraemia | | | |
| subjects affected / exposed | 6 / 239 (2.51%) | 14 / 241 (5.81%) | 0 / 241 (0.00%) |
| occurrences (all) | 5 | 21 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 2 / 239 (0.84%) | 6 / 241 (2.49%) | 0 / 241 (0.00%) |
| occurrences (all) | 2 | 10 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 239 (0.00%) | 4 / 241 (1.66%) | 0 / 241 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 3 / 239 (1.26%) | 13 / 241 (5.39%) | 0 / 241 (0.00%) |
| occurrences (all) | 1 | 21 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 November 2021 | Amendment 1:<br>• Clarification to exclusion criterion #11 to specify where history of HCV with a confirmation of a cure is acceptable for study entry.<br>• Update to allow global or local sourcing of Placebo (i.e., 5% dextrose in water) for NIS793 (randomized part) and update to dosage form of gemcitabine and nab-paclitaxel.<br>• Update to overview of NIS793 with most recent safety data from CNIS793X2101 and CNIS793B12201 studies |
| 13 April 2023 | Amendment 2:<br>• In light of the most recently released NIS793 IB Ed 8, this protocol amendment is to update the relevant sections to reflect the changes made in the IB including the schedule of cardiac assessments (echocardiogram/cardiac imaging; ECG and cardiac specific enzymes, Troponin- I and NTproBNP; providing clearer guidance to investigators for collection and reporting of all relevant data in case of a cardiac AE to help with better characterization of a potential cardiac risk) and the most recent updates from NIS793 studies.<br>• Introduction of an interim analysis (IA) for OS that allows the study to stop for lack of efficacy after approximately 50% of the targeted OS events for the final analysis have been documented. The initial study protocol did not foresee for an interim analysis for futility. This was justified by the assumption that data emerging from the ongoing phase 2 study (CNIS793B12201 - daNIS-1) would be available before the randomized part of the daNIS-2 study would be open to recruitment to further inform the study design. Unfortunately, recruitment in daNIS-1 was delayed and no efficacy data were available when enrolment to the randomized part of daNIS-2 was initiated. This newly introduced IA will provide an early opportunity to stop the study in case of insufficient benefit. |
| 18 August 2023 | Amendment 3: As of 07-Jul-2023, treatment with NIS793/placebo was stopped based upon the DMC's recommendation due to an unfavorable benefit-risk profile observed in the investigational treatment group (NIS793 + gemcitabine + nab-paclitaxel). This protocol amendment was implemented to reduce the assessment burden for ongoing participants, redefine the study completion date, incorporate updates to protocol per template language, and amend the planned data analysis milestones. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please go to

https://www.novctrd.com/#/ for complete trial results

Notes: