



Clinical trial results:

A Phase II, open label, randomized, parallel arm study of NIS793 (with and without spartalizumab) in combination with SOC chemotherapy gemcitabine/nab-paclitaxel, and gemcitabine/nab-paclitaxel alone in first-line metastatic pancreatic ductal adenocarcinoma (mPDAC)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2020-000349-14 |
| Trial protocol | FI FR GB AT BE DE IT |
| Global end of trial date | 02 May 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 20 March 2025 |
| First version publication date | 20 March 2025 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | CNIS793B12201 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04390763 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Novartis campus, Basel, Switzerland, CH-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 | 02 May 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 May 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were:

Safety run-in part:

- To assess the safety and tolerability of NIS793+spartalizumab in combination with gemcitabine/nab-paclitaxel

Randomized part:

- To evaluate the progression free survival (PFS) of NIS793 with spartalizumab in combination with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel
- To evaluate the PFS of NIS793 with gemcitabine/nab-paclitaxel versus gemcitabine /nab-paclitaxel

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 | 16 October 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 11 |
| Country: Number of subjects enrolled | Austria: 9 |
| Country: Number of subjects enrolled | Belgium: 6 |
| Country: Number of subjects enrolled | Czechia: 11 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | France: 12 |
| Country: Number of subjects enrolled | Germany: 11 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Singapore: 12 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | Switzerland: 7 |
| Country: Number of subjects enrolled | Taiwan: 23 |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | United States: 22 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 164 |
| EEA total number of subjects | 80 |

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) | 71 |
| From 65 to 84 years | 93 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in 31 investigative sites in 14 countries.

Pre-assignment

Screening details:

Screening evaluations had to be completed within 21 days prior to the first dose of study treatment (\leq 28 days for baseline radiological assessments). After screening, the treatment period started on Cycle 1 Day 1. The study consisted of two parts: Safety run-in part and Randomized part (Arm 1, 2 and 3).

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |

Arm description:

NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the safety run-in part

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

Dosage and administration details:

NIS793 was administered at a flat dose of 2100 mg every 2 weeks.

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

Dosage and administration details:

Gemcitabine (1000 mg/m² on Days 1, 8, and 15) and nab-paclitaxel (125 mg/m² on Days 1, 8, and 15) were given as per label. 1 cycle=28 days.

| | |
|--|-----------------------|
| Investigational medicinal product name | Spartalizumab |
| Investigational medicinal product code | PDR001 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Spartalizumab was administered at a flat dose of 400 mg every 4 weeks.

| | |
|------------------|--|
| Arm title | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
|------------------|--|

Arm description:

NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the randomized part

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

| | |
|---|--|
| Investigational medicinal product name | NIS793 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| NIS793 was administered at a flat dose of 2100 mg every 2 weeks. | |
| Investigational medicinal product name | Gemcitabine/nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Gemcitabine (1000 mg/m ² on Days 1, 8, and 15) and nab-paclitaxel (125 mg/m ² on Days 1, 8, and 15) were given as per label. 1 cycle=28 days. | |
| Investigational medicinal product name | Spartalizumab |
| Investigational medicinal product code | PDR001 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Spartalizumab was administered at a flat dose of 400 mg every 4 weeks. | |
| Arm title | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
| Arm description: | |
| NIS793 2100 mg every 2 weeks i.v. with standard of care chemotherapy in the randomized part | |
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine/nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Gemcitabine (1000 mg/m ² on Days 1, 8, and 15) and nab-paclitaxel (125 mg/m ² on Days 1, 8, and 15) were given as per label. 1 cycle=28 days. | |
| Investigational medicinal product name | NIS793 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| NIS793 was administered at a flat dose of 2100 mg every 2 weeks. | |
| Arm title | Arm 3: gemcitabine/nab-paclitaxel |
| Arm description: | |
| Standard of care chemotherapy in the randomized part | |
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine/nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Gemcitabine (1000 mg/m ² on Days 1, 8, and 15) and nab-paclitaxel (125 mg/m ² on Days 1, 8, and 15) | |

were given as per label. 1 cycle=28 days.

| Number of subjects in period 1 | Run-in: NIS793 + spartalizumab + gemcitabine/nab- paclitaxel | Arm 1: NIS793 + spartalizumab + gemcitabine/nab- paclitaxel | Arm 2: NIS793 + gemcitabine/nab- paclitaxel |
|---------------------------------------|---|--|---|
| Started | 11 | 50 | 51 |
| Full Analysis Set (FAS) | 0 | 50 | 51 |
| Completed | 0 | 0 | 0 |
| Not completed | 11 | 50 | 51 |
| Participant Decision | - | 5 | 7 |
| Physician decision | 1 | 2 | 2 |
| Death | - | 3 | 4 |
| Progressive Disease | 6 | 24 | 31 |
| Adverse event | 4 | 11 | 5 |
| Study terminated by sponsor | - | 1 | - |
| Not treated | - | 4 | 2 |

| Number of subjects in period 1 | Arm 3: gemcitabine/nab- paclitaxel |
|---------------------------------------|--|
| Started | 52 |
| Full Analysis Set (FAS) | 52 |
| Completed | 0 |
| Not completed | 52 |
| Participant Decision | 6 |
| Physician decision | 9 |
| Death | 2 |
| Progressive Disease | 23 |
| Adverse event | 5 |
| Study terminated by sponsor | - |
| Not treated | 7 |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the safety run-in part | |
| Reporting group title | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the randomized part | |
| Reporting group title | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with standard of care chemotherapy in the randomized part | |
| Reporting group title | Arm 3: gemcitabine/nab-paclitaxel |
| Reporting group description: Standard of care chemotherapy in the randomized part | |

| Reporting group values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
|---|---|--|--|
| Number of subjects | 11 | 50 | 51 |
| Age Categorical Units: participants | | | |
| 18 - <65 years | 5 | 20 | 23 |
| 65 - <85 years | 6 | 30 | 28 |
| Age Continuous Units: years | | | |
| arithmetic mean | 63.5 | 64.3 | 64.2 |
| standard deviation | ± 8.77 | ± 10.91 | ± 9.90 |
| Sex: Female, Male Units: participants | | | |
| Female | 5 | 21 | 21 |
| Male | 6 | 29 | 30 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 9 | 39 | 35 |
| Black or African American | 0 | 1 | 1 |
| Asian | 2 | 9 | 15 |
| Unknown | 0 | 1 | 0 |

| Reporting group values | Arm 3: gemcitabine/nab-paclitaxel | Total | |
|--|-----------------------------------|-------|--|
| Number of subjects | 52 | 164 | |
| Age Categorical Units: participants | | | |
| 18 - <65 years | 23 | 71 | |
| 65 - <85 years | 29 | 93 | |

| | | | |
|---|----------------|-----|--|
| Age Continuous Units: years arithmetic mean standard deviation | 64.8 ± 8.25 | - | |
| Sex: Female, Male Units: participants | | | |
| Female | 20 | 67 | |
| Male | 32 | 97 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 33 | 116 | |
| Black or African American | 3 | 5 | |
| Asian | 15 | 41 | |
| Unknown | 1 | 2 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the safety run-in part | |
| Reporting group title | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the randomized part | |
| Reporting group title | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
| Reporting group description: NIS793 2100 mg every 2 weeks i.v. with standard of care chemotherapy in the randomized part | |
| Reporting group title | Arm 3: gemcitabine/nab-paclitaxel |
| Reporting group description: Standard of care chemotherapy in the randomized part | |

Primary: Safety run-in part: Number of participants with Dose-Limiting Toxicities (DLTs)

| | |
|---|---|
| End point title | Safety run-in part: Number of participants with Dose-Limiting Toxicities (DLTs) ^{[1][2]} |
| End point description: A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value of Common Terminology Criteria for Adverse Events (CTCAE) grade ≥ 3 where the relationship to study treatment cannot be ruled out and is not clearly related solely to disease, disease progression, inter-current illness or concomitant medications, which occurs within the DLT evaluation period. The DLT evaluation period is the first 28 days of treatment with NIS793 with spartalizumab in combination with gemcitabine/nab-paclitaxel. Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher. | |
| End point type | Primary |
| End point timeframe: First cycle of treatment (28 days) | |

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: No statistical analysis were planned for this endpoint.

[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: This endpoint is applicable to the Safety run-in part only.

| | | | | |
|-----------------------------|---|--|--|--|
| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: participants | | | | |
| Any DLT | 1 | | | |
| - Colitis | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Safety run-in part: Number of participants with AEs and SAEs during the on-treatment period

| | |
|-----------------|---|
| End point title | Safety run-in part: Number of participants with AEs and SAEs during the on-treatment period ^{[3][4]} |
|-----------------|---|

End point description:

Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (SAEs), including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. For CTCAE v5.0, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.

The on-treatment period is defined from the day of first administration of any study treatment up to 30 days after the date of the last actual administration of any study drug.

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

End point timeframe:

Up to approximately 0.8 years

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: No statistical analysis were planned for this endpoint.

[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: This endpoint is applicable to the Safety run-in part only.

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: participants | | | | |
| AEs | 11 | | | |
| Treatment-related AEs | 11 | | | |
| AEs with grade ≥ 3 | 11 | | | |
| Treatment-related AEs with grade ≥ 3 | 8 | | | |
| SAEs | 8 | | | |
| Treatment-related SAEs | 3 | | | |
| Fatal SAEs | 1 | | | |
| Treatment-related fatal SAEs | 0 | | | |

Statistical analyses

Primary: Safety run-in part: Number of participants with dose reductions and dose interruptions of NIS793, spartalizumab, gemcitabine and nab-paclitaxel

| | |
|-----------------|---|
| End point title | Safety run-in part: Number of participants with dose reductions and dose interruptions of NIS793, spartalizumab, gemcitabine and nab-paclitaxel ^{[5][6]} |
|-----------------|---|

End point description:

Number of participants with at least one dose reduction and at least one dose interruption of study drugs. Dose adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule.

No dose reductions were allowed for NIS793 and spartalizumab beyond the first 28 days period of Safety run-in part.

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

End point timeframe:

Up to approximately 0.7 years

Notes:

[5] - 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: No statistical analysis were planned for this endpoint.

[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: This endpoint is applicable to the Safety run-in part only.

| | | | | |
|---|---|--|--|--|
| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: participants | | | | |
| NIS793: ≥1 dose reduction or interruption | 5 | | | |
| NIS793: ≥1 dose reduction | 0 | | | |
| NIS793: ≥1 dose interruption | 5 | | | |
| Spartalizumab: ≥1 dose reduction or interruption | 3 | | | |
| Spartalizumab: ≥1 dose reduction | 0 | | | |
| Spartalizumab: ≥1 dose interruption | 3 | | | |
| Gemcitabine: ≥1 dose reduction or interruption | 9 | | | |
| Gemcitabine: ≥1 dose reduction | 2 | | | |
| Gemcitabine: ≥1 dose interruption | 9 | | | |
| Nab-paclitaxel: ≥1 dose reduction or interruption | 9 | | | |
| Nab-paclitaxel: ≥1 dose reduction | 3 | | | |
| Nab-paclitaxel: ≥1 dose interruption | 9 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Safety run-in part: Dose intensity of NIS793 and spartalizumab

| | |
|-----------------|--|
| End point title | Safety run-in part: Dose intensity of NIS793 and |
|-----------------|--|

End point description:

Dose intensity of NIS793 and spartalizumab was calculated as cumulative actual dose in milligrams divided by duration of exposure in days and multiplied by 28 days.

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

End point timeframe:

Cycle 1 and Cycle 3. The duration of each cycle was 28 days.

Notes:

[7] - 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: No statistical analysis were planned for this endpoint.

[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: This endpoint is applicable to the Safety run-in part only.

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg per cycle | | | | |
| arithmetic mean (standard deviation) | | | | |
| NIS793 - cycle 1 (n=11) | 3627.3 (± 980.91) | | | |
| NIS793 - cycle 3 (n=5) | 4200.0 (± 0.00) | | | |
| Spartalizumab - cycle 1 (n=11) | 400.0 (± 0.00) | | | |
| Spartalizumab - cycle 3 (n=5) | 400.0 (± 0.00) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Safety run-in part: Dose intensity of gemcitabine and nab-paclitaxel

| | |
|-----------------|---|
| End point title | Safety run-in part: Dose intensity of gemcitabine and nab-paclitaxel ^[9] ^[10] |
|-----------------|---|

End point description:

Dose intensity of gemcitabine and nab-paclitaxel was calculated as cumulative actual dose in milligrams/m² divided by duration of exposure in days and multiplied by 28 days.

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

End point timeframe:

Cycle 1 and Cycle 3. The duration of each cycle was 28 days.

Notes:

[9] - 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: No statistical analysis were planned for this endpoint.

[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: This endpoint is applicable to the Safety run-in part only.

| | | | | |
|--|---|--|--|--|
| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg per m ² per cycle | | | | |
| arithmetic mean (standard deviation) | | | | |
| Gemcitabine - cycle 1 (n=11) | 2425.4 (± 698.27) | | | |
| Gemcitabine - cycle 3 (n=5) | 2619.1 (± 508.19) | | | |
| Nab-paclitaxel - cycle 1 (n=11) | 303.3 (± 87.18) | | | |
| Nab-paclitaxel - cycle 3 (n=5) | 327.6 (± 63.65) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Randomized Part: Progression-Free Survival (PFS) per RECIST v1.1 – Bayesian model

| | |
|-----------------|---|
| End point title | Randomized Part: Progression-Free Survival (PFS) per RECIST v1.1 – Bayesian model ^[11] |
|-----------------|---|

End point description:

PFS was based on local review of tumor assessments, using Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 criteria. PFS is defined as the time from the date of randomization to the date of the first documented progression or death due to any cause. If a subject had not had an event, PFS was censored at the date of last adequate tumor assessment.

PFS was estimated using a Bayesian model. For each comparison (arm 1 versus arm 3 and arm 2 versus arm 3), PFS was modeled using a two-piece hazard model, with specifying hazard rates before and after the possible delayed effect for arms 1 and 2 and constant hazard rate for arm 3.

Results in the table as expressed as estimated posterior median hazard rate and one-sided 90% credible interval.

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

End point timeframe:

Up to approximately 2 years. Risk changing timepoint=approximately 0.3 years.

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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|--|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 51 | 52 | |
| Units: events (progression, death) per year | | | | |
| median (confidence interval 90%) | | | | |
| Hazard rate before the risk changing timepoint | 2.54 (0 to 3.34) | 1.23 (0 to 1.79) | 2.09 (0 to 2.53) | |
| Hazard rate after the risk changing timepoint | 1.46 (0 to 2.06) | 2.94 (0 to 3.86) | 2.09 (0 to 2.53) | |

Statistical analyses

| Statistical analysis title | Arm 2 vs. Arm 3 |
|---|--|
| Comparison groups | Arm 2: NIS793 + gemcitabine/nab-paclitaxel v Arm 3: gemcitabine/nab-paclitaxel |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | Bayesian two-piece hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.41 |
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| upper limit | 1.96 |

| Statistical analysis title | Arm 1 vs. Arm 3 |
|---|--|
| Comparison groups | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel v Arm 3: gemcitabine/nab-paclitaxel |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | Bayesian two-piece hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| upper limit | 1.04 |

Primary: Randomized Part: Progression-Free Survival (PFS) per RECIST v1.1 –

Kaplan-Meier curves and Cox model

| | |
|-----------------|--|
| End point title | Randomized Part: Progression-Free Survival (PFS) per RECIST v1.1 – Kaplan-Meier curves and Cox model ^[12] |
|-----------------|--|

End point description:

PFS was based on local review of tumor assessments, using RECIST 1.1 criteria. PFS is defined as the time from the date of randomization to the date of the first documented progression or death due to any cause. If a subject had not had an event, PFS was censored at the date of last adequate tumor assessment.

PFS was analyzed based on the Kaplan-Meier curves and the Cox model.

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

End point timeframe:

Up to approximately 2 years

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: This endpoint is applicable to the Randomized part only.

| | | | | |
|----------------------------------|--|--|-----------------------------------|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 51 | 52 | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.91 (3.06 to 6.93) | 5.52 (3.94 to 7.29) | 4.37 (3.55 to 7.20) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Arm 2 vs. Arm 3 |
| Comparison groups | Arm 2: NIS793 + gemcitabine/nab-paclitaxel v Arm 3: gemcitabine/nab-paclitaxel |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.38 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| upper limit | 1.44 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Arm 1 vs. Arm 3 |
| Comparison groups | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel v Arm 3: gemcitabine/nab-paclitaxel |

| | |
|---|-------------------|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.46 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.02 |
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| upper limit | 1.37 |

Secondary: Randomized Part: Number of participants with AEs and SAEs during the on-treatment period

| | |
|-----------------|--|
| End point title | Randomized Part: Number of participants with AEs and SAEs during the on-treatment period ^[13] |
|-----------------|--|

End point description:

Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (SAEs), including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. For CTCAE v5.0, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.

The on-treatment period is defined from the day of first administration of any study treatment up to 30 days after the date of the last actual administration of any study drug.

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

End point timeframe:

Up to approximately 1.8 years

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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 49 | 45 | |
| Units: participants | | | | |
| AEs | 45 | 49 | 43 | |
| Treatment-related AEs | 45 | 45 | 38 | |
| AEs with grade ≥ 3 | 42 | 42 | 35 | |
| Treatment-related AEs with grade ≥ 3 | 34 | 37 | 24 | |
| SAEs | 32 | 26 | 26 | |
| Treatment-related SAEs | 19 | 12 | 12 | |
| Fatal SAEs | 3 | 1 | 4 | |
| Treatment-related fatal SAEs | 1 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Number of participants with dose reductions and dose interruptions of NIS793, spartalizumab, gemcitabine and nab-paclitaxel

| | |
|-----------------|--|
| End point title | Randomized Part: Number of participants with dose reductions and dose interruptions of NIS793, spartalizumab, gemcitabine and nab-paclitaxel ^[14] |
|-----------------|--|

End point description:

Number of participants with at least one dose reduction and at least one dose interruption of study drugs. Dose adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule.

No dose reductions were allowed for NIS793 and spartalizumab in the Randomized part.

Due to EudraCT system limitations, data fields in the table cannot be empty or contain letters (e.g. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

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

End point timeframe:

Up to approximately 1.7 years

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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|---|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 49 ^[15] | 45 ^[16] | |
| Units: participants | | | | |
| NIS793: ≥1 dose reduction or interruption | 35 | 31 | 999 | |
| NIS793: ≥1 dose reduction | 0 | 0 | 999 | |
| NIS793: ≥1 dose interruption | 35 | 31 | 999 | |
| Spartalizumab: ≥1 dose reduction or interruption | 21 | 999 | 999 | |
| Spartalizumab: ≥1 dose reduction | 0 | 999 | 999 | |
| Spartalizumab: ≥1 dose interruption | 21 | 999 | 999 | |
| Gemcitabine: ≥1 dose reduction or interruption | 38 | 41 | 32 | |
| Gemcitabine: ≥1 dose reduction | 25 | 23 | 19 | |
| Gemcitabine: ≥1 dose interruption | 35 | 36 | 29 | |
| Nab-paclitaxel: ≥1 dose reduction or interruption | 39 | 43 | 34 | |
| Nab-paclitaxel: ≥1 dose reduction | 26 | 27 | 19 | |
| Nab-paclitaxel: ≥1 dose interruption | 34 | 37 | 32 | |

Notes:

[15] - The dose reductions and interruptions of spartalizumab are not applicable.

[16] - The dose reductions and interruptions of spartalizumab and NIS793 are not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Dose intensity of NIS973 and spartalizumab

| | |
|--|---|
| End point title | Randomized Part: Dose intensity of NIS973 and |
| End point description: Dose intensity of NIS973 and spartalizumab was calculated as cumulative actual dose in milligrams divided by duration of exposure in days and multiplied by 28 days. Due to EudraCT system limitations, data fields in the table cannot be empty or contain letters (e.g. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'. | |
| End point type | Secondary |
| End point timeframe: Cycle 1 and Cycle 3. The duration of each cycle was 28 days | |

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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 46 | 49 ^[18] | | |
| Units: mg per cycle | | | | |
| arithmetic mean (standard deviation) | | | | |
| NIS793 - cycle 1 (n=46,49) | 3515.2 (± 995.32) | 3857.1 (± 784.22) | | |
| NIS793 - cycle 3 (n=26,42) | 3796.2 (± 844.03) | 3550.0 (± 982.59) | | |
| Spartalizumab - cycle 1 (n=46,0) | 400.0 (± 0.00) | 999 (± 999) | | |
| Spartalizumab - cycle 3 (n=24,0) | 400.0 (± 0.00) | 999 (± 999) | | |

Notes:

[18] - Dose intensity of spartalizumab is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Dose intensity of gemcitabine and nab-paclitaxel

| | |
|--|---|
| End point title | Randomized Part: Dose intensity of gemcitabine and nab-paclitaxel ^[19] |
| End point description: Dose intensity of gemcitabine and nab-paclitaxel was calculated as cumulative actual dose in | |

milligrams/m² divided by duration of exposure in days and multiplied by 28 days.

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

End point timeframe:

Cycle 1 and Cycle 3. The duration of each cycle was 28 days

Notes:

[19] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|--|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 49 | 45 | |
| Units: mg per m ² per cycle | | | | |
| arithmetic mean (standard deviation) | | | | |
| Gemcitabine - cycle 1 (n=46,49,45) | 2442.3 (± 675.34) | 2644.8 (± 543.43) | 2392.1 (± 651.00) | |
| Gemcitabine - cycle 3 (n=29,42,29) | 2293.9 (± 710.08) | 2426.5 (± 696.10) | 2445.3 (± 561.36) | |
| Nab-paclitaxel - cycle 1 (n=46,49,45) | 307.5 (± 84.91) | 330.7 (± 67.95) | 298.8 (± 80.96) | |
| Nab-paclitaxel - cycle 3 (n=29,42,29) | 286.2 (± 86.45) | 296.2 (± 88.06) | 299.1 (± 70.08) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Overall Response Rate (ORR) per RECIST v1.1

| | |
|-----------------|--|
| End point title | Randomized Part: Overall Response Rate (ORR) per RECIST v1.1 ^[20] |
|-----------------|--|

End point description:

ORR is the percentage of patients with a confirmed best overall response of complete response (CR) or partial response (PR), based on local investigator assessment per Response Evaluation Criteria for Solid Tumors (RECIST) v1.1.

For RECIST v1.1, CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

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

End point timeframe:

Up to approximately 1.7 years

Notes:

[20] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|-----------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 51 | 52 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 22.0 (11.5 to 36.0) | 31.4 (19.1 to 45.9) | 15.4 (6.9 to 28.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Time to Progression (TTP) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Randomized Part: Time to Progression (TTP) per RECIST |
|-----------------|---|

End point description:

TTP per RECIST v1.1 is defined as the time from the date of randomization to the date of event defined as the first documented progression per RECIST v1.1 or death due to underlying cancer. If a participant had no progression or death, the participant was censored at the date of last adequate tumor assessment.

DOR was analyzed using the Kaplan-Meier method.

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

End point timeframe:

Up to approximately 1.7 years

Notes:

[21] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|----------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 51 | 52 | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.94 (3.55 to 7.03) | 5.59 (4.57 to 7.36) | 5.36 (3.68 to 8.61) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Duration of Response (DOR) per RECIST v1.1

| | |
|-----------------|---|
| End point title | Randomized Part: Duration of Response (DOR) per RECIST v1.1 ^[22] |
|-----------------|---|

End point description:

DOR per RECIST v1.1 is defined as the time from the first documented response of CR or PR to the date of the first documented progression or death. DOR only applies to patients with a best overall response of CR or PR by investigator assessment per RECIST v1.1. Participants continuing without progression or death were censored at the date of their last adequate tumor assessment.

DOR was analyzed using the Kaplan-Meier method.

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

End point timeframe:

Up to approximately 1.7 years

Notes:

[22] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|---|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 16 | 18 | 15 | |
| Units: months | | | | |
| arithmetic mean (confidence interval 95%) | 5.85 (2.43 to 9.43) | 4.32 (3.61 to 6.37) | 3.73 (1.84 to 12.91) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Change from baseline in PD-L1 expression

| | |
|-----------------|---|
| End point title | Randomized Part: Change from baseline in PD-L1 expression ^[23] |
|-----------------|---|

End point description:

The tumor expression of programmed cell death-ligand 1 (PD-L1) was measured by immunohistochemical methods. Results are expressed as absolute change from baseline in PD-L1 expression.

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

End point timeframe:

Baseline (Screening), on-treatment (anytime between Cycle 3 Day 2 and Day 4). The duration of each cycle was 28 days.

Notes:

[23] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|------------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 12 | 5 | |
| Units: PD-L1 positivity percentage | | | | |

| | | | | |
|--------------------------------------|------------------------|------------------------|-----------------------|--|
| arithmetic mean (standard deviation) | 7.625 (\pm 10.4193) | 7.917 (\pm 17.0572) | 4.000 (\pm 8.9443) | |
|--------------------------------------|------------------------|------------------------|-----------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Overall Survival (OS)

| | |
|-----------------|--|
| End point title | Randomized Part: Overall Survival (OS) ^[24] |
|-----------------|--|

End point description:

Overall survival is defined as the time from the date of randomization to the date of death due to any cause.

OS was analyzed using the Kaplan-Meier method.

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

End point timeframe:

Up to approximately 2 years

Notes:

[24] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|----------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 51 | 52 | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.7 (7.2 to 12.7) | 8.5 (7.7 to 9.9) | 10.1 (6.5 to 13.4) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Number of participants with anti-NIS793 antibodies

| | |
|-----------------|---|
| End point title | Randomized Part: Number of participants with anti-NIS793 antibodies ^[25] |
|-----------------|---|

End point description:

The immunogenicity (IG) against NIS793 was assessed in serum using a validated enhanced electrochemiluminescence immunoassay (ECLIA).

Patient anti-drug antibodies (ADA) status was defined as follows:

- ADA-negative at baseline: ADA-negative sample at baseline
- ADA-positive at baseline: ADA-positive sample at baseline
- ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline sample, all of which are ADA-negative samples
- ADA-inconclusive post-baseline = patient who does not qualify as ADA-positive or ADA-negative post-baseline

- Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample

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

End point timeframe:

Baseline (before first dose) and post-baseline (assessed throughout the treatment up to approximately 1.7 years)

Notes:

[25] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|---------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 44 | | |
| Units: participants | | | | |
| ADA-negative at baseline | 41 | 44 | | |
| ADA-positive at baseline | 0 | 0 | | |
| ADA-negative post-baseline | 41 | 44 | | |
| ADA- inconclusive post-baseline | 0 | 0 | | |
| Treatment-induced ADA-positive | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Change from baseline in CD8 expression

| | |
|-----------------|---|
| End point title | Randomized Part: Change from baseline in CD8 expression ^[26] |
|-----------------|---|

End point description:

The tumor expression of CD8 was measured by immunohistochemical methods. Results are expressed as absolute change from baseline in CD8 expression.

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

End point timeframe:

Baseline (Screening), on-treatment (anytime between Cycle 3 Day 2 and Day 4). The duration of each cycle was 28 days.

Notes:

[26] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3 | 14 | 6 | |

| | | | | |
|--|----------------|--------------|--------------|--|
| Units: percent marker area expression of CD8 | | | | |
| arithmetic mean (standard deviation) | 10.1 (± 11.01) | 1.4 (± 2.64) | 2.1 (± 1.82) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Number of participants with anti-spartalizumab antibodies

| | |
|-----------------|--|
| End point title | Randomized Part: Number of participants with anti-spartalizumab antibodies ^[27] |
|-----------------|--|

End point description:

The immunogenicity (IG) against spartalizumab was assessed in serum using a validated a validated homogenous enzyme-linked immunosorbent assay (ELISA).

Patient anti-drug antibodies (ADA) status was defined as follows:

- ADA-negative at baseline: ADA-negative sample at baseline
- ADA-inconclusive at baseline: patient who does not qualify as ADA-positive or ADA-negative at baseline
- ADA-positive at baseline: ADA-positive sample at baseline
- ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline sample, all of which are ADA-negative samples
- ADA-inconclusive post-baseline = patient who does not qualify as ADA-positive or ADA-negative post-baseline
- Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample

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

End point timeframe:

Cycle 1 and Cycle 3. The duration of each cycle was 28 days

Notes:

[27] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|---------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: participants | | | | |
| ADA-negative at baseline | 40 | | | |
| ADA- inconclusive at baseline | 1 | | | |
| ADA-positive at baseline | 0 | | | |
| ADA-negative post-baseline | 35 | | | |
| ADA- inconclusive post-baseline | 2 | | | |
| Treatment-induced ADA-positive | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Maximum observed serum concentration (Cmax) of NIS793

| | |
|-----------------|--|
| End point title | Randomized Part: Maximum observed serum concentration (Cmax) of NIS793 ^[28] |
|-----------------|--|

End point description:

Pharmacokinetic (PK) parameters were calculated based on NIS793 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

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

End point timeframe:

Cycle 1 and Cycle 3: pre-dose, 1, 24, 168 and 336 hours after the end of the infusion on Day 1. The duration of the infusion was 30 minutes. One cycle=28 days

Notes:

[28] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 42 | 39 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42,39) | 603000 (± 181000) | 622000 (± 192000) | | |
| Cycle 3 (n=21,31) | 821000 (± 235000) | 784000 (± 286000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NIS793

| | |
|-----------------|--|
| End point title | Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NIS793 ^[29] |
|-----------------|--|

End point description:

PK parameters were calculated based on NIS793 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.

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

End point timeframe:

Cycle 1 and Cycle 3: pre-dose, 1, 24, 168 and 336 hours after the end of the infusion on Day 1. The duration of the infusion was 30 minutes. One cycle=28 days

Notes:

[29] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 42 | 39 | | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42,39) | 84700000 (± 29300000) | 96000000 (± 26100000) | | |
| Cycle 3 (n=21,31) | 153000000 (± 52300000) | 151000000 (± 55000000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Trough serum concentration (Ctough) of NIS793

| | |
|-----------------|--|
| End point title | Randomized Part: Trough serum concentration (Ctough) of NIS793 ^[30] |
|-----------------|--|

End point description:

Ctough is defined as the concentration reached immediately before the next dose is administered. All drug concentrations below the lower limit of quantification were treated as zero for the calculation of PK parameters.

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

End point timeframe:

Cycle 1: pre-dose on Day 1. Cycle 3: pre-dose on Day 1 and Day 15 (combined). One cycle=28 days

Notes:

[30] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 26 | 34 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=26,34) | 137000 (± 51700) | 156000 (± 50100) | | |
| Cycle 3 (n=22,34) | 289000 (± 121000) | 291000 (± 126000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Maximum observed serum concentration (Cmax) of spartalizumab

| | |
|-----------------|---|
| End point title | Randomized Part: Maximum observed serum concentration (Cmax) of spartalizumab ^[31] |
|-----------------|---|

End point description:

PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

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

End point timeframe:

Cycle 1 and Cycle 3: pre-dose, 1, 24, 168 and 648 hours after the end of the infusion on Day 1. The duration of the infusion was 30 minutes. One cycle=28 days

Notes:

[31] - 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: This endpoint is applicable to the Randomized part only.

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42) | 109 (± 22.4) | | | |
| Cycle 3 (n=21) | 120 (± 38.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab

| | |
|-----------------|---|
| End point title | Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab ^[32] |
|-----------------|---|

End point description:

PK parameters were calculated based on spartalizumab serum concentrations by using non-

compartmental methods. The linear trapezoidal method was used for AUClast calculation.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1 and Cycle 3: pre-dose, 1, 24, 168 and 648 hours after the end of the infusion on Day 1. The duration of the infusion was 30 minutes. One cycle=28 days | |
| Notes: | |
| [32] - 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: This endpoint is applicable to the Randomized part only. | |

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: h*µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42) | 10800 (± 4900) | | | |
| Cycle 3 (n=21) | 3240 (± 1900) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Trough serum concentration (Ctrough) of spartalizumab

| | |
|--|--|
| End point title | Randomized Part: Trough serum concentration (Ctrough) of spartalizumab ^[33] |
| End point description: | |
| Ctrough is defined as the concentration reached immediately before the next dose is administered. All drug concentrations below the lower limit of quantification were treated as zero for the calculation of PK parameters. | |
| End point type | Secondary |
| End point timeframe: | |
| Cycle 2, 3 and 4: pre-dose on Day 1. One cycle=28 days | |
| Notes: | |
| [33] - 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: This endpoint is applicable to the Randomized part only. | |

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: µg/mL | | | | |

| | | | | |
|--------------------------------------|---------------|--|--|--|
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 (n=32) | 22.3 (± 8.67) | | | |
| Cycle 3 (n=21) | 31.9 (± 11.7) | | | |
| Cycle 4 (n=23) | 30.5 (± 14.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Maximum observed plasma concentration (Cmax) of gemcitabine

| | |
|-----------------|--|
| End point title | Randomized Part: Maximum observed plasma concentration (Cmax) of gemcitabine ^[34] |
|-----------------|--|

End point description:

PK parameters were calculated based on gemcitabine plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

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

End point timeframe:

Cycle 1 and Cycle 4: pre-dose, end of infusion, and 2, 3, 5 and 24 hours after the start of infusion on Day 1. The duration of the infusion was according to the product labelling and local guidance. One cycle=28 days

Notes:

[34] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|--------------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 42 | 40 | 44 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42,40,44) | 9830 (± 8580) | 12000 (± 6850) | 10600 (± 6170) | |
| Cycle 4 (n=23,28,24) | 7950 (± 5650) | 8830 (± 6150) | 7000 (± 4210) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of gemcitabine

| | |
|-----------------|---|
| End point title | Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of gemcitabine ^[35] |
|-----------------|---|

End point description:

PK parameters were calculated based on gemcitabine plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.

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

End point timeframe:

Cycle 1 and Cycle 4: pre-dose, end of infusion, and 2, 3, 5 and 24 hours after the start of infusion on Day 1. The duration of the infusion was according to the product labelling and local guidance. One cycle=28 days

Notes:

[35] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|--------------------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 42 | 40 | 44 | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=42,40,44) | 7270 (± 6950) | 9900 (± 6140) | 8040 (± 4490) | |
| Cycle 4 (n=23,28,24) | 5270 (± 4730) | 5980 (± 4410) | 4920 (± 2830) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Trough serum concentration (Ctough) of gemcitabine

| | |
|-----------------|---|
| End point title | Randomized Part: Trough serum concentration (Ctough) of gemcitabine ^[36] |
|-----------------|---|

End point description:

Ctough is defined as the concentration reached immediately before the next dose is administered. All drug concentrations below the lower limit of quantification were treated as zero for the calculation of PK parameters.

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

End point timeframe:

Cycle 4: pre-dose on Day 1. One cycle=28 days

Notes:

[36] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/na b-paclitaxel | Arm 2: NIS793 + gemcitabine/na b-paclitaxel | Arm 3: gemcitabine/na b-paclitaxel | |
|-----------------------------|---|---|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 24 | 30 | 23 | |

| | | | | |
|--------------------------------------|---------|---------|---------|--|
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Maximum observed plasma concentration (Cmax) of nab-paclitaxel

| | |
|-----------------|---|
| End point title | Randomized Part: Maximum observed plasma concentration (Cmax) of nab-paclitaxel ^[37] |
|-----------------|---|

End point description:

PK parameters were calculated based on nab-paclitaxel plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

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

End point timeframe:

Cycle 1 and Cycle 4: pre-dose, end of infusion, and 2, 3, 5 and 24 hours after the start of infusion on Day 1. The duration of the infusion was according to the product labelling and local guidance. One cycle=28 days

Notes:

[37] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|--------------------------------------|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 38 | 43 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=37,38,43) | 9990 (± 37100) | 4120 (± 3370) | 3490 (± 1760) | |
| Cycle 4 (n=19,28,24) | 4570 (± 4910) | 4050 (± 2410) | 2900 (± 1370) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of nab-paclitaxel

| | |
|-----------------|--|
| End point title | Randomized Part: Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of nab-paclitaxel ^[38] |
|-----------------|--|

End point description:

PK parameters were calculated based on nab-paclitaxel plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.

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

End point timeframe:

Cycle 1 and Cycle 4: pre-dose, end of infusion, and 2, 3, 5 and 24 hours after the start of infusion on Day 1. The duration of the infusion was according to the product labelling and local guidance. One cycle=28 days

Notes:

[38] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|--------------------------------------|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 38 | 43 | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 (n=37,38,43) | 15700 (± 52400) | 5080 (± 2820) | 4820 (± 2500) | |
| Cycle 4 (n=19,28,24) | 5960 (± 3650) | 5020 (± 3050) | 4250 (± 2550) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Part: Trough serum concentration (Ctrough) of nab-paclitaxel

| | |
|-----------------|---|
| End point title | Randomized Part: Trough serum concentration (Ctrough) of nab-paclitaxel ^[39] |
|-----------------|---|

End point description:

Ctrough is defined as the concentration reached immediately before the next dose is administered. All drug concentrations below the lower limit of quantification were treated as zero for the calculation of PK parameters.

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

End point timeframe:

Cycle 4: pre-dose on Day 1. One cycle=28 days

Notes:

[39] - 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: This endpoint is applicable to the Randomized part only.

| End point values | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel | |
|--------------------------------------|--|--|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 30 | 23 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 455 (± 1320) | 2.13 (± 10.4) | 3.25 (± 5.08) | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: All-Collected Deaths

| | |
|---|----------------------|
| End point title | All-Collected Deaths |
| End point description: | |
| On-treatment and post-treatment safety follow-up (FU) deaths were collected from first dose of study treatment to 90 days after last dose of NIS793, 150 days after last dose of spartalizumab and 30 days after last dose of gemcitabine and nab-paclitaxel, whichever was longer. | |
| Survival FU deaths were collected from 91 days after last dose of NIS793, 151 days after last dose of spartalizumab and 31 days after last dose of gemcitabine and nab-paclitaxel, whichever was longer, until end of study. | |
| All deaths refer to the sum of pre-treatment deaths, on-treatment and post-treatment safety FU deaths, and survival FU deaths. | |
| End point type | Post-hoc |
| End point timeframe: | |
| On-treatment and post-treatment safety FU deaths: up to approximately 1 year (run-in part) and 1.9 years (randomized part). Survival FU deaths: up to approximately 1.8 years (run-in part) and 2 years (randomized part) | |

| End point values | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel | Arm 3: gemcitabine/nab-paclitaxel |
|--|---|--|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 50 | 51 | 52 |
| Units: Participants | | | | |
| On/post-treatment safety FU deaths (n=11,50,51,52) | 5 | 18 | 19 | 4 |
| Survival FU deaths (n=6,28,30,41) | 5 | 15 | 22 | 35 |
| All deaths (n=11,50,51,52) | 10 | 33 | 41 | 39 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs: up to approximately 1 year (run-in part) and 1.9 years (randomized part).

Deaths: up to approximately 1.8 years (run-in part) and 2 years (randomized part).

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 | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
|-----------------------|---|

Reporting group description:

NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the safety run-in part

| | |
|-----------------------|--|
| Reporting group title | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel |
|-----------------------|--|

Reporting group description:

NIS793 2100 mg every 2 weeks i.v. with spartalizumab 400 mg every 4 weeks i.v and standard of care chemotherapy in the randomized part

| | |
|-----------------------|--|
| Reporting group title | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
|-----------------------|--|

Reporting group description:

NIS793 2100 mg every 2 weeks i.v. with standard of care chemotherapy in the randomized part

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Arm 3: gemcitabine/nab-paclitaxel |
|-----------------------|-----------------------------------|

Reporting group description:

Standard of care chemotherapy in the randomized part

| Serious adverse events | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 11 (72.73%) | 34 / 46 (73.91%) | 28 / 49 (57.14%) |
| number of deaths (all causes) | 10 | 33 | 41 |
| number of deaths resulting from adverse events | 1 | 2 | 4 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Chills | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |

| | | | |
|---|-----------------|-----------------|----------------|
| Gait inability | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 46 (6.52%) | 0 / 49 (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 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 5 / 46 (10.87%) | 3 / 49 (6.12%) |
| occurrences causally related to treatment / all | 2 / 2 | 8 / 8 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Orchitis noninfective | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Interstitial lung disease | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| 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 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial necrosis marker increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 condition abnormal | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Craniofacial fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Cardiac disorders | | | |
| Supraventricular tachycardia | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 | | | |
| Demyelinating polyneuropathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 46 (4.35%) | 6 / 49 (12.24%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 7 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood loss anaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 46 (4.35%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Haemolytic uraemic syndrome | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 lower | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| 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 pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 46 (4.35%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 46 (4.35%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 5 / 46 (10.87%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 6 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 perforation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Gastritis haemorrhagic | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 toxicity | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Pancreatitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 46 (4.35%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Gallbladder rupture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Hepatitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Bladder tamponade | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute kidney injury | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 46 (6.52%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Glucocorticoid deficiency | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Hypopituitarism | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 | | | |
| Degenerative bone disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Infections and infestations | | | |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acarodermatitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (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 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 0 / 49 (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 / 11 (0.00%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Campylobacter infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 46 (6.52%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 3 / 49 (6.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 46 (8.70%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 4 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 4 / 46 (8.70%) | 3 / 49 (6.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Relapsing fever | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| 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 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |
| Hypokalaemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 / 11 (0.00%) | 1 / 46 (2.17%) | 0 / 49 (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 |

| Serious adverse events | Arm 3: gemcitabine/nab- paclitaxel | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 45 (57.78%) | | |
| number of deaths (all causes) | 39 | | |
| number of deaths resulting from adverse events | 4 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour obstruction | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gait inability | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Orchitis noninfective | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary fibrosis | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary oedema | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory failure | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Investigations | | | | |
| Blood bilirubin increased | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Alanine aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|----------------|--|--|--|
| Gamma-glutamyltransferase increased | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial necrosis marker increased | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General physical condition abnormal | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| Femur fracture | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fall | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Craniofacial fracture | | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acetabulum fracture | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Head injury | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Demyelinating polyneuropathy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood loss anaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemolytic uraemic syndrome | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |

| | | | | |
|---|----------------|--|--|--|
| Abdominal pain lower | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea haemorrhagic | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal obstruction | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal perforation | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric haemorrhage | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis haemorrhagic | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal pain | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal toxicity | | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematemesis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 1 / 45 (2.22%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune-mediated enterocolitis | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Melaena | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Impaired gastric emptying | | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subileus | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gallbladder rupture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|--|--|
| Renal failure | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bladder tamponade | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Glucocorticoid deficiency | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypopituitarism | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Degenerative bone disease | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Back pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acarodermatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary sepsis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 pneumonia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Campylobacter infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Large intestine infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia bacterial | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 2 / 2 | | |
| Relapsing fever | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Run-in: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 1: NIS793 + spartalizumab + gemcitabine/nab-paclitaxel | Arm 2: NIS793 + gemcitabine/nab-paclitaxel |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 11 (100.00%) | 45 / 46 (97.83%) | 48 / 49 (97.96%) |
| Vascular disorders | | | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------------|------------------------|------------------------|
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 2 / 46 (4.35%) 2 | 2 / 49 (4.08%) 3 |
| Hypertension subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 3 / 46 (6.52%) 4 | 4 / 49 (8.16%) 4 |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 4 / 46 (8.70%) 4 | 6 / 49 (12.24%) 7 |
| Vein rupture subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 5 / 11 (45.45%) 5 | 12 / 46 (26.09%) 19 | 16 / 49 (32.65%) 36 |
| Chills subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 3 / 46 (6.52%) 4 | 2 / 49 (4.08%) 2 |
| Fatigue subjects affected / exposed occurrences (all) | 7 / 11 (63.64%) 8 | 23 / 46 (50.00%) 29 | 18 / 49 (36.73%) 22 |
| Mucosal inflammation subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 5 / 46 (10.87%) 5 | 4 / 49 (8.16%) 4 |
| Oedema subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 3 / 46 (6.52%) 5 | 0 / 49 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 4 / 11 (36.36%) 5 | 11 / 46 (23.91%) 15 | 15 / 49 (30.61%) 19 |
| Pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 2 / 46 (4.35%) 2 | 1 / 49 (2.04%) 1 |
| Pyrexia | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 7 / 11 (63.64%) 12 | 19 / 46 (41.30%) 36 | 11 / 49 (22.45%) 28 |
| Reproductive system and breast disorders Prostatomegaly subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Nasal dryness subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Pulmonary embolism subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 2 / 11 (18.18%) 3 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 11 / 46 (23.91%) 13 1 / 46 (2.17%) 1 3 / 46 (6.52%) 5 4 / 46 (8.70%) 4 | 3 / 49 (6.12%) 3 14 / 49 (28.57%) 17 8 / 49 (16.33%) 9 11 / 49 (22.45%) 12 3 / 49 (6.12%) 3 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 | 4 / 46 (8.70%) 4 3 / 46 (6.52%) 3 | 3 / 49 (6.12%) 3 4 / 49 (8.16%) 4 |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) | 4 / 11 (36.36%) 7 1 / 11 (9.09%) 2 | 14 / 46 (30.43%) 14 5 / 46 (10.87%) 6 | 10 / 49 (20.41%) 15 2 / 49 (4.08%) 2 |

| | | | |
|---------------------------------------|-----------------|------------------|------------------|
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 13 / 46 (28.26%) | 9 / 49 (18.37%) |
| occurrences (all) | 6 | 15 | 17 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 4 / 46 (8.70%) | 2 / 49 (4.08%) |
| occurrences (all) | 2 | 4 | 3 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 1 | 5 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 46 (6.52%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 3 | 1 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 46 (4.35%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 2 | 6 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 4 / 46 (8.70%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 4 | 3 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 1 / 46 (2.17%) | 1 / 49 (2.04%) |
| occurrences (all) | 5 | 1 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 5 / 46 (10.87%) | 3 / 49 (6.12%) |
| occurrences (all) | 3 | 6 | 3 |
| Tri-iodothyronine decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 8 / 46 (17.39%) | 10 / 49 (20.41%) |
| occurrences (all) | 1 | 16 | 14 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 46 (6.52%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 4 | 5 |
| Weight decreased | | | |

| | | | |
|--|----------------------|-----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 2 / 46 (4.35%) 3 | 6 / 49 (12.24%) 7 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 7 / 46 (15.22%) 20 | 8 / 49 (16.33%) 16 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 46 (2.17%) 1 | 1 / 49 (2.04%) 3 |
| Infusion related reaction | | | |
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 2 / 46 (4.35%) 3 | 0 / 49 (0.00%) 0 |
| Wound dehiscence | | | |
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 1 / 49 (2.04%) 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 2 / 46 (4.35%) 2 | 1 / 49 (2.04%) 2 |
| Dysgeusia | | | |
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 6 / 46 (13.04%) 6 | 5 / 49 (10.20%) 5 |
| Dizziness | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 46 (2.17%) 1 | 3 / 49 (6.12%) 5 |
| Hypoaesthesia | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 3 / 46 (6.52%) 3 | 3 / 49 (6.12%) 3 |
| Paraesthesia | | | |
| subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 3 | 4 / 46 (8.70%) 6 | 3 / 49 (6.12%) 4 |
| Neurotoxicity | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 46 (2.17%) 1 | 0 / 49 (0.00%) 0 |
| Neuropathy peripheral | | | |

| | | | |
|--------------------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 5 / 46 (10.87%) | 11 / 49 (22.45%) |
| occurrences (all) | 0 | 5 | 11 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 4 / 46 (8.70%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 6 | 2 |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 5 / 46 (10.87%) | 5 / 49 (10.20%) |
| occurrences (all) | 1 | 5 | 7 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 11 (45.45%) | 29 / 46 (63.04%) | 33 / 49 (67.35%) |
| occurrences (all) | 8 | 40 | 52 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 46 (8.70%) | 2 / 49 (4.08%) |
| occurrences (all) | 1 | 4 | 5 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 3 / 46 (6.52%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 5 / 11 (45.45%) | 11 / 46 (23.91%) | 9 / 49 (18.37%) |
| occurrences (all) | 8 | 24 | 16 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 7 / 46 (15.22%) | 4 / 49 (8.16%) |
| occurrences (all) | 6 | 7 | 7 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 46 (8.70%) | 9 / 49 (18.37%) |
| occurrences (all) | 1 | 4 | 9 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 46 (0.00%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 0 | 5 |
| Abdominal pain upper | | | |

| | | | |
|----------------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 46 (8.70%) | 8 / 49 (16.33%) |
| occurrences (all) | 1 | 4 | 10 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 16 / 46 (34.78%) | 16 / 49 (32.65%) |
| occurrences (all) | 1 | 18 | 22 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 2 | 0 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 1 | 4 |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 11 (45.45%) | 26 / 46 (56.52%) | 19 / 49 (38.78%) |
| occurrences (all) | 11 | 38 | 28 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 2 | 5 |
| Ileal perforation | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 46 (2.17%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 2 | 3 |
| Gingival swelling | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gingival hypertrophy | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 46 (2.17%) | 6 / 49 (12.24%) |
| occurrences (all) | 2 | 1 | 7 |
| Ileus | | | |

| | | | |
|--|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 46 (2.17%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 10 / 46 (21.74%) | 18 / 49 (36.73%) |
| occurrences (all) | 3 | 15 | 24 |
| Tongue disorder | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tongue coated | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 46 (2.17%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 1 | 4 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 7 / 11 (63.64%) | 20 / 46 (43.48%) | 27 / 49 (55.10%) |
| occurrences (all) | 9 | 28 | 42 |
| Hepatobiliary disorders | | | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disease | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 46 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 14 / 46 (30.43%) | 8 / 49 (16.33%) |
| occurrences (all) | 4 | 25 | 9 |
| Rash | | | |

| | | | |
|--|----------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 6 / 11 (54.55%) 7 | 13 / 46 (28.26%) 17 | 18 / 49 (36.73%) 24 |
| Rash macular subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| Onycholysis subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| Night sweats subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 2 / 49 (4.08%) 2 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 4 / 46 (8.70%) 5 | 3 / 49 (6.12%) 3 |
| Alopecia subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 3 | 11 / 46 (23.91%) 11 | 15 / 49 (30.61%) 15 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 3 / 46 (6.52%) 3 | 3 / 49 (6.12%) 3 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 3 | 10 / 46 (21.74%) 15 | 1 / 49 (2.04%) 1 |
| Skin toxicity subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 3 / 46 (6.52%) 4 | 1 / 49 (2.04%) 1 |
| Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 46 (0.00%) 0 | 5 / 49 (10.20%) 5 |
| Neck pain | | | |

| | | | |
|---|----------------------|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 46 (2.17%) 1 | 1 / 49 (2.04%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 3 / 46 (6.52%) 4 | 1 / 49 (2.04%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 6 / 46 (13.04%) 7 | 5 / 49 (10.20%) 6 |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 4 / 46 (8.70%) 5 | 5 / 49 (10.20%) 7 |
| Infections and infestations | | | |
| Pneumonia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 46 (0.00%) 0 | 2 / 49 (4.08%) 2 |
| Infection subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 2 / 46 (4.35%) 2 | 0 / 49 (0.00%) 0 |
| COVID-19 subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 13 / 46 (28.26%) 13 | 6 / 49 (12.24%) 6 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 7 / 46 (15.22%) 11 | 6 / 49 (12.24%) 6 |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 8 / 46 (17.39%) 12 | 6 / 49 (12.24%) 9 |
| Hypochloraemia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 46 (0.00%) 0 | 0 / 49 (0.00%) 0 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 1 / 46 (2.17%) 2 | 1 / 49 (2.04%) 1 |
| Decreased appetite | | | |

| | | | |
|-----------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 4 / 11 (36.36%) | 10 / 46 (21.74%) | 17 / 49 (34.69%) |
| occurrences (all) | 7 | 11 | 25 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 4 / 46 (8.70%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 4 | 1 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 9 / 46 (19.57%) | 7 / 49 (14.29%) |
| occurrences (all) | 4 | 12 | 9 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 46 (2.17%) | 2 / 49 (4.08%) |
| occurrences (all) | 1 | 1 | 6 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 4 / 46 (8.70%) | 2 / 49 (4.08%) |
| occurrences (all) | 1 | 6 | 2 |

| Non-serious adverse events | Arm 3: gemcitabine/nab- paclitaxel | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 45 (88.89%) | | |
| Vascular disorders | | | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 4 | | |
| Hypotension | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 4 | | |
| Vein rupture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |

| | | | |
|--|------------------|--|--|
| <p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Chills</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucosal inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | 11 / 45 (24.44%) | | |
| | 22 | | |
| | 5 / 45 (11.11%) | | |
| | 5 | | |
| | 14 / 45 (31.11%) | | |
| | 18 | | |
| | 1 / 45 (2.22%) | | |
| | 1 | | |
| <p>Reproductive system and breast disorders</p> <p>Prostatomegaly</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Respiratory, thoracic and mediastinal disorders</p> <p>Nasal dryness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> | 2 / 45 (4.44%) | | |
| | 2 | | |
| | 8 / 45 (17.78%) | | |
| | 10 | | |
| | 1 / 45 (2.22%) | | |
| | 3 | | |
| | 14 / 45 (31.11%) | | |
| | 30 | | |
| <p>Reproductive system and breast disorders</p> <p>Prostatomegaly</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Respiratory, thoracic and mediastinal disorders</p> <p>Nasal dryness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> | 0 / 45 (0.00%) | | |
| | 0 | | |
| | 1 / 45 (2.22%) | | |
| | 1 | | |
| | 1 / 45 (2.22%) | | |
| | 1 | | |
| | | | |
| | | | |

| | | | |
|---------------------------------------|------------------|--|--|
| subjects affected / exposed | 7 / 45 (15.56%) | | |
| occurrences (all) | 7 | | |
| Cough | | | |
| subjects affected / exposed | 12 / 45 (26.67%) | | |
| occurrences (all) | 12 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | | |
| occurrences (all) | 7 | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 10 / 45 (22.22%) | | |
| occurrences (all) | 13 | | |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 3 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | | |
| occurrences (all) | 11 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 4 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood lactate dehydrogenase increased | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 2 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 3 | | |
| Tri-iodothyronine decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 9 / 45 (20.00%) | | |
| occurrences (all) | 10 | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 5 | | |
| Weight decreased | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences (all) | 5 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 9 / 45 (20.00%) | | |
| occurrences (all) | 21 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Wound dehiscence | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 4 | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 4 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 6 / 45 (13.33%) | | |
| occurrences (all) | 9 | | |
| Neurotoxicity | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 5 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences (all) | 5 | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 5 | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 20 / 45 (44.44%) | | |
| occurrences (all) | 33 | | |
| Leukopenia | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 5 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 3 | | |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 9 / 45 (20.00%) | | |
| occurrences (all) | 26 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 13 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 6 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences (all) | 6 | | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 12 / 45 (26.67%) | | |
| occurrences (all) | 13 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry mouth | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |

| | | | |
|----------------------------------|------------------|--|--|
| Diarrhoea | | | |
| subjects affected / exposed | 18 / 45 (40.00%) | | |
| occurrences (all) | 28 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | | |
| occurrences (all) | 5 | | |
| Ileal perforation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival swelling | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival hypertrophy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ileus | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 12 / 45 (26.67%) | | |
| occurrences (all) | 14 | | |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tongue coated | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|------------------------|--|--|
| Rectal haemorrhage subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Nausea subjects affected / exposed occurrences (all) | 20 / 45 (44.44%) 31 | | |
| Hepatobiliary disorders | | | |
| Immune-mediated hepatitis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Hepatobiliary disease subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | | |
| Rash subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 5 | | |
| Rash macular subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Onycholysis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Night sweats subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Erythema subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | | |
| Alopecia | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash maculo-papular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin toxicity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 45 (15.56%)</p> <p>7</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>0 / 45 (0.00%)</p> <p>0</p> <p>0 / 45 (0.00%)</p> <p>0</p> | | |
| <p>Renal and urinary disorders</p> <p>Haematuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 45 (0.00%)</p> <p>0</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 45 (4.44%)</p> <p>2</p> <p>1 / 45 (2.22%)</p> <p>1</p> <p>4 / 45 (8.89%)</p> <p>4</p> <p>2 / 45 (4.44%)</p> <p>2</p> <p>8 / 45 (17.78%)</p> <p>11</p> | | |
| <p>Infections and infestations</p> <p>Pneumonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Infection</p> | <p>3 / 45 (6.67%)</p> <p>3</p> | | |

| | | | |
|------------------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences (all) | 6 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 9 / 45 (20.00%) | | |
| occurrences (all) | 12 | | |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 15 / 45 (33.33%) | | |
| occurrences (all) | 17 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 20 July 2020 | Amendment 1 introduced changes to address Health Authorities request to incorporate grade 3 diarrhea lasting for >72 hours as a DLT. |
| 31 August 2020 | Amendment 2 introduced changes to address Health Authorities request to state that sexually active males have to use a condom while taking study treatment and for 180 days after stopping treatment and to include instruction to follow contraception recommendations and other precautionary measures required by locally approved SmPC of gemcitabine and nab-paclitaxel. |
| 16 April 2021 | Amendment 3 was made to address the following: <ul style="list-style-type: none">• Additional precautionary measures were implemented to enhance cardiovascular and renal risks mitigation.• Additional clarification on the mitigation of risks already described in the NIS793 Investigator Brochure including exclusion criterion related to bleeding risk was added and drug-induced liver injury (DILI) was included in the dose modification recommendation.• Primary estimands were revised and secondary estimands related to efficacy objectives (anti-tumor response, overall survival) were introduced.• In order to mitigate the risks for participant safety and data integrity due to disruptions (e.g. COVID-19), disruption proofing language was added throughout the protocol.• Maximum permitted duration of study treatment interruption or delay was extended to 12 weeks to account for potential immune related toxicity and allow more time for recovery in case of toxicity.• For consistency between both study treatments, spartalizumab and NIS793, the 2h observation period was aligned to the first cycle. |
| 18 April 2022 | Amendment 4 was made to allow for potential interim analysis (IA) where statistical analyses by treatment arm can be conducted. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported