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
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 (≤ 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/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 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/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	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/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.

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	64.8		
standard deviation	± 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/nab-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

No statistical analyses for this end point

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 NIS973 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/m^2 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/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: 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/m^2 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/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: 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/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%)	3.94 (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/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	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/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	4	12	5	
Units: PD-L1 positivity percentage				

arithmetic mean (standard deviation)	7.625 (± 10.4193)	7.917 (± 17.0572)	4.000 (± 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/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%)	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/nab-paclitaxel	Arm 2: NIS793 + gemcitabine/nab-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/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	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/nab-paclitaxel	Arm 2: NIS793 + gemcitabine/nab-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/nab-paclitaxel	Arm 2: NIS793 + gemcitabine/nab-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 (Ctrough) of NIS793

End point title	Randomized Part: Trough serum concentration (Ctrough) of NIS793[30]

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 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/nab-paclitaxel	Arm 2: NIS793 + gemcitabine/nab-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/nab-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/nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: h*µg/mL				
arithmetic mean (standard deviation)				
Cycle 1 (n=42) Cycle 3 (n=21)	10800 (± 4900) 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/nab-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/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	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/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	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 (Ctrough) of gemcitabine

End point title	Randomized Part: Trough serum concentration (Ctrough) of gemcitabine[36]

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:

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

subjects affected / exposed	7 / 11 (63.64%)	19 / 46 (41.30%)	11 / 49 (22.45%)
occurrences (all)	12	36	28
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 46 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	3
Epistaxis			
subjects affected / exposed	2 / 11 (18.18%)	11 / 46 (23.91%)	14 / 49 (28.57%)
occurrences (all)	3	13	17
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 46 (2.17%)	8 / 49 (16.33%)
occurrences (all)	1	1	9
Cough			
subjects affected / exposed	1 / 11 (9.09%)	3 / 46 (6.52%)	11 / 49 (22.45%)
occurrences (all)	1	5	12
Pulmonary embolism			
subjects affected / exposed	1 / 11 (9.09%)	4 / 46 (8.70%)	3 / 49 (6.12%)
occurrences (all)	1	4	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	4 / 46 (8.70%)	3 / 49 (6.12%)
occurrences (all)	1	4	3
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	3 / 46 (6.52%)	4 / 49 (8.16%)
occurrences (all)	0	3	4
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 11 (36.36%)	14 / 46 (30.43%)	10 / 49 (20.41%)
occurrences (all)	7	14	15
Amylase increased			
subjects affected / exposed	1 / 11 (9.09%)	5 / 46 (10.87%)	2 / 49 (4.08%)
occurrences (all)	2	6	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	2 / 11 (18.18%)	2 / 46 (4.35%)	6 / 49 (12.24%)
occurrences (all)	2	3	7
Neutrophil count decreased			
subjects affected / exposed	2 / 11 (18.18%)	7 / 46 (15.22%)	8 / 49 (16.33%)
occurrences (all)	2	20	16
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 11 (9.09%)	1 / 46 (2.17%)	1 / 49 (2.04%)
occurrences (all)	1	1	3
Infusion related reaction			
subjects affected / exposed	1 / 11 (9.09%)	2 / 46 (4.35%)	0 / 49 (0.00%)
occurrences (all)	1	3	0
Wound dehiscence			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 11 (9.09%)	2 / 46 (4.35%)	1 / 49 (2.04%)
occurrences (all)	1	2	2
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)	6 / 46 (13.04%)	5 / 49 (10.20%)
occurrences (all)	1	6	5
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 46 (2.17%)	3 / 49 (6.12%)
occurrences (all)	0	1	5
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 46 (6.52%)	3 / 49 (6.12%)
occurrences (all)	0	3	3
Paraesthesia			
subjects affected / exposed	2 / 11 (18.18%)	4 / 46 (8.70%)	3 / 49 (6.12%)
occurrences (all)	3	6	4
Neurotoxicity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 46 (2.17%)	0 / 49 (0.00%)
occurrences (all)	0	1	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	6 / 11 (54.55%)	13 / 46 (28.26%)	18 / 49 (36.73%)
occurrences (all)	7	17	24
Rash macular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Onycholysis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	2 / 49 (4.08%)
occurrences (all)	1	0	2
Erythema			
subjects affected / exposed	1 / 11 (9.09%)	4 / 46 (8.70%)	3 / 49 (6.12%)
occurrences (all)	1	5	3
Alopecia			
subjects affected / exposed	3 / 11 (27.27%)	11 / 46 (23.91%)	15 / 49 (30.61%)
occurrences (all)	3	11	15
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	3 / 46 (6.52%)	3 / 49 (6.12%)
occurrences (all)	0	3	3
Rash maculo-papular			
subjects affected / exposed	2 / 11 (18.18%)	10 / 46 (21.74%)	1 / 49 (2.04%)
occurrences (all)	3	15	1
Skin toxicity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 46 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)	3 / 46 (6.52%)	1 / 49 (2.04%)
occurrences (all)	0	4	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 46 (0.00%)	5 / 49 (10.20%)
occurrences (all)	0	0	5
Neck pain			

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

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

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	0 / 45 (0.00%)		
occurrences (all)	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			

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

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: • Additional precautionary measures were implemented to enhance cardio-vascular 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