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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Nisevokitug/NIS793

Trial Indication(s)

Metastatic pancreatic ductal adenocarcinoma (mPDAC)

Protocol Number

CNIS793B12301

Protocol Title

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

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

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Study Start/End Dates

Study Start Date: September 30, 2021 (Actual)
Primary Completion Date: August 13, 2024 (Actual)
Study Completion Date: August 13, 2024 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a randomized, double-blind, multicenter, two-group, phase III study that consisted of two parts: a Safety Run-in part and a Randomized part. The open-label Safety Run-in part was conducted to confirm the recommended phase 3 dose (RP3D) of NIS793 in combination with gemcitabine and nab-paclitaxel.

The randomized part randomized participants 1:1 to one of the two treatment groups:

- Investigational group (Arm A); combination of NIS793, gemcitabine and nab-paclitaxel
- Control group (Arm B): combination of placebo, gemcitabine and nab-paclitaxel

Centers

114 centers in 27 countries: Australia(2), Japan(6), United States(10), Belgium(4), Germany(7), Spain(6), Korea, Republic of(3), Russia(2), Israel(3), Czech Republic(4), United Kingdom(5), Canada(3), Italy(4), Norway(2), Slovakia (Slovak Republic)(3), Taiwan(3), Finland(2), Switzerland(3), Turkey(4), France(9), Hungary(3), Greece(2), Netherlands(1), Brazil(4), Sweden(2), China(16), Singapore(1)

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Objectives:

Primary objective and endpoints

Objectives	Endpoints
Primary objectives	**Endpoints for primary objectives**
• **Safety run-in part:** To confirm the RP3D of NIS793 in combination with gemcitabine and nab-paclitaxel.	• **Safety run-in part**: Incidence of drug limiting toxicities (DLTs) during the first cycle (4 weeks) of treatment
• **Randomized part**: To compare OS in participants with mPDAC treated as the first line treatment with the combination of NIS793, gemcitabine and nab-paclitaxel to the combination of placebo with gemcitabine and nab-paclitaxel.	• **Randomized part**: Overall Survival (OS)

Secondary objectives and endpoints

Secondary objectives	Endpoints for secondary objectives
Safety run-in part: • To evaluate safety and tolerability of NIS793 in combination with gemcitabine and nab-paclitaxel	**Safety run-in part:** • Safety: Incidence and severity of AEs including changes in laboratory parameters, vital signs, body weight and cardiac assessments • Tolerability: Dose interruptions, reductions and dose intensity
• Pharmacokinetics (PK) of NIS793 in combination with gemcitabine and nab-paclitaxel	• PK parameters including e.g. Cmax and Ctrough for NIS793 in combination with gemcitabine and nab-paclitaxel

Secondary objectives	Endpoints for secondary objectives
• Preliminary anti-tumor activity of NIS793 in combination with gemcitabine and nab-paclitaxel	• Progression-free survival (PFS), overall response rate (ORR), disease control rate (DCR), duration of response (DOR) and time to response (TTR) by Investigator's assessment per RECIST 1.1
Randomized part: • To evaluate the efficacy (PFS, ORR, DCR, DOR, TTR) in participants treated as the first line treatment of NIS793 in combination with gemcitabine and nab-paclitaxel versus placebo plus gemcitabine and nab-paclitaxel	**Randomized part:** • PFS, ORR, DCR, DOR and TTR by investigator's assessment per RECIST 1.1
• To evaluate safety and tolerability in each treatment group	• Incidence and severity of AEs and SAEs, changes in laboratory parameters, vital signs, body weight and cardiac assessments; dose interruptions, reductions and dose intensity
• To explore pharmacokinetics (PK) of NIS793 in combination with gemcitabine and nab-paclitaxel	• For participants with intense PK sampling enrolled in China, NIS793 serum concentrations over time and derived PK parameters (e.g. Cmax, AUC) • For participants without intensive PK sampling, PK parameters including Cmax, Ctrough and $Ctrough_{ss}$ for NIS793
• To characterize the incidence of immunogenicity of NIS793 in combination with gemcitabine/nab-paclitaxel	• Anti-drug antibodies (ADA) prevalence at baseline and ADA incidence on-treatment

Test Product (s), Dose(s), and Mode(s) of Administration

The safety run-in part started with one treatment regimen – NIS793 (2100 mg intravenous (i.v.) every 2 weeks (Q2W)) in combination with gemcitabine and nab-paclitaxel during the drug limiting toxicities (DLT) assessment period.

The study treatment was administered as a 28-day treatment cycle. NIS793 was administered at a flat dose as confirmed in the Safety Run-in part on day 1 and 15 (e.g., 2100 mg i.v.). Gemcitabine (1000 mg/m² on days 1, 8 and 15) and nab-paclitaxel (125 mg/m² on days 1, 8 and 15) were administered as per label.

As of 7-Jul-2023, the administration of NIS793/placebo was stopped for all subjects following the recommendation from Data Monitoring Committee (DMC).

The study treatment is the combination of NIS793, gemcitabine and nab-paclitaxel versus the combination of placebo, gemcitabine and nab-paclitaxel.

Statistical Methods

Safety run-in part

Efficacy: The primary endpoint for the safety run-in part was the incidence of DLT during the first 28 days. A Bayesian logistic regression model (BLRM) using the escalation with the overdose control (EWOC) criteria to evaluate the risk of DLT was used to confirm the dose of RP3D.

Pharmacokinetics: Summary statistics (arithmetic mean, geometric mean, SD, arithmetic CV, geometric CV, median, minimum and maximum) were presented by treatment and visit/sampling timepoints. Concentrations below the lower limit of quantification (LLOQ) were treated as zero in summary statistics.

Randomized part:

Efficacy: The OS distribution (primary endpoint) was estimated using the KM method, and KM curves, medians and two-sided 95% CIs of the medians were presented for each treatment group. The hazard ratio (HR) for OS was calculated, along with its two-sided 95% CI, from a stratified Cox model using the same stratification factors as for the log-rank test. Progression free survival, ORR, DCR, TTR and DOR by Investigator's assessment per RECIST 1.1 (secondary endpoints) were evaluated and summarized by dose cohort.

Safety: AE summaries include all AEs occurring during on-treatment period. AEs were summarized by number and percentage of participants having at least one AE, having at least one AE in each primary system organ class (SOC) and for each preferred term (PT) using MedDRA coding by treatment group. AESI groupings were defined using MedDRA terms, SMQs (standardized MedDRA queries), HLGTs (high level group terms), HLT (high level terms) and PTs. Summaries of these AESIs were provided by treatment group. Separate summaries for on-treatment and all deaths were produced by treatment group, SOC and PT. All deaths were listed, post treatment deaths were flagged. All laboratory data were listed

by treatment group, participant, and visit/time and if normal ranges were available, abnormalities were flagged. Summary statistics were provided by treatment and visit/time.

Pharmacokinetics: Descriptive statistics (n, m (number of non-zero concentrations), arithmetic mean, CV% mean, SD, median, geometric mean, CV% geo-mean, minimum and maximum) for NIS793 concentration were presented at each scheduled time point. For Chinese participants with more intensive PK sampling schedule in the randomized part, the descriptive statistics (n, mean, CV%, SD, median, geometric mean, geometric CV%, minimum and maximum) were presented by treatment for PK parameters. For Chinese participants without intensive PK sampling schedule and global participants, for which only sparse PK samples were planned and collected, the descriptive statistics (n, mean, CV%, SD, median, geometric mean, geometric CV%, minimum and maximum) were presented by treatment for PK parameters at appropriate timepoints.

Immunogenicity: Incidence of anti-NIS793 antibody by treatment groups for the randomized part were summarized and presented

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

Applicable for both Safety run-in and Randomized part

• Participants aged ≥18 years with histologically or cytologically confirmed (based on local assessment and per local guidelines) mPDAC eligible for treatment in the first line setting and not amenable for potentially curative surgery

• Presence of at least one measurable lesion assessed by Computerized Tomography (CT) and/or Magnetic Resonance Imaging (MRI) according to RECIST 1.1

• Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1

• Adequate organ function (assessed by central laboratory for eligibility)

• Participants must have recovered from treatment-related toxicities of prior anticancer therapies to grade ≤ 1 (CTCAE v 5.0) at time of screening, except alopecia.

Key Main Exclusion Criteria:

Applicable for both Safety run-in and Randomized part

• Previous systemic anti-cancer treatment for metastatic PDAC

• Pancreatic neuroendocrine (islet) or acinar tumors

• Participants with known status of microsatellite instability-high (MSI-H) or mismatch repair-deficient pancreatic cancer (if status is not already available, testing is not required at screening).

• Participant has not recovered from a major surgery performed prior to start of study treatment or has had a major surgery within 4 weeks prior to start of study treatment.

• Radiation therapy or brain radiotherapy ≤ 4 weeks prior to start of study treatment (palliative radiotherapy to bone lesions allowed > 2 weeks prior to start of study treatment).

• Impaired cardiac function or clinically significant cardio-vascular disease

• Use of hematopoietic growth factors or transfusion support ≤ 2 weeks prior to start of study treatment.

• Participant has conditions that are considered to have a high risk of clinically significant gastrointestinal tract bleeding or any other condition associated with or history of significant bleeding.

• Serious non-healing wounds.

• Pregnant or breast-feeding women

• Women of childbearing potential, unless willing to use highly effective contraception methods during treatment and after stopping study treatments as indicated

• Pre-existing peripheral neuropathy > grade 1 (CTCAE v5.0)

Other Inclusion/Exclusion criteria may apply.

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Participant Flow Table

Overall Study

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)	Total
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	
Started	21	245	245	511
Entered post treatment follow-up	18	192	200	410
Completed	0	0	0	0
Not Completed	21	245	245	511
Progressive disease	17	148	149	314
Physician Decision	2	20	24	46
Adverse Event	1	25	24	50
Lost to Follow-up	1	0	0	1
Death	0	16	8	24
Guardian decision	0	1	0	1
Sponsor decision	0	9	16	25
Participant decision	0	25	24	49
Participants not treated due to Protocol deviation	0	1	0	1

Baseline Characteristics

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)	Total
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	
Number of Participants [units: participants]	21	245	245	511
Baseline Analysis Population Description				
Age, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
<= 65 years	13	130	125	268
Between 65 and 75 years	7	97	91	195
>= 75 years	1	18	29	48
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Female	6	109	99	214
Male	15	136	146	297

Race (NIH/OMB)
(units: Participants)
Analysis Population Type: Participants
Count of Participants (Not Applicable)

American Indian or Alaska Native	0	3	0	3
Asian	2	87	87	176
Native Hawaiian or Other Pacific Islander	0	1	0	1
Black or African American	0	9	6	15
White	19	137	143	299
More than one race	0	1	0	1
Unknown or Not Reported	0	7	9	16

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Primary Outcome Result(s)

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

Description	A dose-limiting toxicity (DLT) was defined as an adverse event or abnormal laboratory value assessed as unrelated to disease, disease progression, inter-current illness, or concomitant medications that occurred within the first cycle (i.e., 28 days or 4 weeks) of the treatment with NIS793 in combination with gemcitabine/nab-paclitaxel. The National Cancer Institute Common Terminology Criteria for Adverse events (NCI CTCAE) version 5 was used for all grading.
Time Frame	Up to 4 weeks
Analysis Population Description	Dose-Determining Set (DDS) - The DDS consisted of all participants in the safety run-in part who met the minimum exposure criterion and had sufficient safety evaluations after 4 weeks of treatment or experienced a DLT during the first 4 weeks of treatment.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	18
Safety run-in part: Percentage of participants with dose limiting toxicities (DLTs) during the first cycle (4 weeks) of treatment. (units: Participants)	**Count of Participants (Not Applicable)**
	0 (%)

Randomized part: Overall Survival (OS)

Description	Overall Survival (OS) was defined as the time from date of randomization/start of treatment to date of death due to any cause. If a patient was not known to have died, survival was censored at the date of last known date patient alive.
Time Frame	From randomization up to death, assessed up to approximately 34 months
Analysis Population Description	The Full Analysis Set (FAS) in the Randomized Part included all participants assigned study treatment by randomization and were analyzed according to the treatment they were assigned during the randomization procedure.

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	245	245
Randomized part: Overall Survival (OS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	9.2 (8.1 to 10.5)	11.2 (9.6 to 12.1)

Secondary Outcome Result(s)

Percentage of participants with Adverse Events (AEs)

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of a medicinal (investigational) product. Treatment emergent Adverse Event (TEAEs) in this study are events that started after the first dose of study treatment and until 30 days after last dose of SOC chemotherapies and up to 90 days after NIS793, whichever is later.
Time Frame	Up to approximately 32 months
Analysis Population Description	The Safety Set (SAF) in the Run-in part included all participants who received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment(s) they received. In the Randomized Part, the SAF included all participants who received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment they received, either the randomized treatment assigned or the first treatment received.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and

	stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	239	241
Percentage of participants with Adverse Events (AEs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Adverse Events (AEs)	21 (100%)	239 (100%)	239 (99.17%)
Serious Adverse Events (SAEs)	13 (61.9%)	144 (60.25%)	110 (45.64%)
Fatal SAEs	0 (%)	12 (5.02%)	8 (3.32%)
AEs leading to discontinuation	2 (9.52%)	46 (19.25%)	50 (20.75%)
AEs leading to dose adjustment/interruption	16 (76.19%)	205 (85.77%)	208 (86.31%)
AEs requiring additional therapy	21 (100%)	231 (96.65%)	227 (94.19%)

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

Description	No dose reductions were allowed for NIS793 in the Randomized part and beyond the first 28 days period of the Safety Run-in part. Increasing the dosing interval from every 2 weeks (Q2W) to every 2 weeks (Q4W) was allowed. Dose interruption for NIS793 was permitted if adverse drug reaction was suspected to be related to NIS793. If NIS793 was interrupted or delayed for > 8 weeks due to toxicity that was suspected to be related to treatment, study treatment was permanently discontinued.
Time Frame	Up to approximately 32 months
Analysis Population Description	The Safety Set (SAF) in the Run-in part included all participants who received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment(s) they received. In the Randomized Part, the SAF included all participants who received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment they received, either the randomized treatment assigned or the first treatment received.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	239	241
Percentage of participants with dose interruptions and dose reductions of NIS793 in combination with gemcitabine and nab-paclitaxel (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
With no dose interruption	5 (23.81%)	92 (38.49%)	82 (34.02%)
With at least one dose interruption	16 (76.19%)	147 (61.51%)	159 (65.98%)
With no dose reduction	21 (100%)	237 (99.16%)	241 (100%)
With at least one dose reduction	0 (%)	2 (.84%)	0 (%)

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

Description	Dose intensity was computed as the ratio of actual cumulative dose received and actual duration of exposure.
Time Frame	Up to approximately 32 months
Analysis Population Description	The Safety Set (SAF) in the Run-in part included all participants who received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment(s) they received. In the Randomized Part, the SAF included all participants who

received at least one dose of study treatment, including incomplete infusions, and were analyzed according to the treatment they received, either the randomized treatment assigned or the first treatment received.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	239	241
Dose intensity of NIS793 in combination with gemcitabine and nab-paclitaxel (units: mg/cycle)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	3669.2 ± 528.07	3134.1 ± 573.15	3183.4 ± 593.92

Progression-Free Survival (PFS)

Description	Progression-Free Survival (PFS) was defined as the time from the enrollment (run-in part) or randomization (randomized part) to the date of the first documented disease progression based on local investigator assessment as per RECIST 1.1 or date of death due to any cause, whichever occurs first. PFS was censored if no PFS event was observed before the analysis cut-off date. The censoring date was the date of the last adequate tumor assessment prior to the analysis cut-off.
Time Frame	From enrollment (run-in part) or randomization (randomized part) up to disease progression or death, assessed up to approximately 34 months
Analysis Population Description	The Full Analysis Set (FAS) in the Safety Run-in Part included all participants who received any study drug and were analyzed according to the treatment(s) received, following the intent-to-treat (ITT) principle. In the Randomized Part, the FAS included all participants assigned study treatment by randomization and were analyzed according to the treatment they were assigned during the randomization procedure.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)

Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	245	245
Progression-Free Survival (PFS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	5.4 (3.6 to 7.3)	4.6 (3.7 to 5.4)	5.4 (5.3 to 6.6)

Overall Response Rate (ORR)

Description	Overall Response Rate (ORR) was defined as the proportion of participants with a Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR) as per local review. ORR was evaluated according to RECIST 1.1. The BOR was determined from response assessments undertaken while on treatment.
Time Frame	Up to approximately 34 months
Analysis Population Description	The Full Analysis Set (FAS) in the Safety Run-in Part included all participants who received any study drug and were analyzed according to the treatment(s) received, following the intent-to-treat (ITT) principle. In the Randomized Part, the FAS included all participants assigned study treatment by randomization and were analyzed according to the treatment they were assigned during the randomization procedure.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	**Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)**	**Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)**
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)

	(gemcitabine+ nab-paclitaxel) per investigator assessment.		
Number of Participants Analyzed [units: participants]	21	245	245
Overall Response Rate (ORR) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	19.0 (5.4 to 41.9)	21.6 (16.6 to 27.3)	25.3 (20.0 to 31.2)

Disease Control Rate (DCR)

Description	Disease Control Rate (DCR) was defined as the proportion of participants with Best Overall Response (BOR) of Complete Response (CR) or Partial Response (PR), or Stable Disease (SD) or Non-CR/Non-progressive disease as per local review. DCR was evaluated according to RECIST 1.1.
Time Frame	Up to approximately 34 months
Analysis Population Description	The Full Analysis Set (FAS) in the Safety Run-in Part included all participants who received any study drug and were analyzed according to the treatment(s) received, following the intent-to-treat (ITT) principle. In the Randomized Part, the FAS included all participants assigned study treatment by randomization and were analyzed according to the treatment they were assigned during the randomization procedure.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	**Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)**	**Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)**
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	245	245
Disease Control Rate (DCR) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**

	76.2 (52.8 to 91.8)	66.9 (60.7 to 72.8)	72.2 (66.2 to 77.8)

Duration of Response (DOR)

Description	Duration of Response (DOR) was defined as the duration of time between the date of first documented response (CR or PR) and the date of first documented progression or death due to any cause.
Time Frame	Up to approximately 34 months
Analysis Population Description	Full Analysis Set (FAS) - Only participants with first documented response (CR or PR) included

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	**Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)**	**Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)**
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	4	53	62
Duration of Response (DOR) (units: Months)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	8.6 (3.5 to NA)[1]	6.2 (4.7 to 7.4)	5.6 (5.0 to 7.2)

[1] NA: Not estimable due to insufficient number of participants with events

Time to Response (TTR)

Description	Time to Response (TTR) was defined as the duration of time between the date of enrollment (run-in part) or randomization (randomized part) and the date of first documented response of either CR or PR as per local review, which was subsequently confirmed. TTR was evaluated

	according to RECIST 1.1. Participants without a confirmed CR or PR were censored at the time of PFS event (i.e., disease progression or death due to any cause) for participants with a PFS event (i.e., disease progression or death due to any cause), or at the date of the last adequate tumor assessment for participants without a PFS event.
Time Frame	From enrollment (run-in part) or randomization (randomized part) up to first documented response, assessed up to approximately 34 months
Analysis Population Description	The Full Analysis Set (FAS) in the Safety Run-in Part included all participants who received any study drug and were analyzed according to the treatment(s) received, following the intent-to-treat (ITT) principle. In the Randomized Part, the FAS included all participants assigned study treatment by randomization and were analyzed according to the treatment they were assigned during the randomization procedure.

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)	**Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)**	**Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel)**
Arm/Group Description	Participants received a combination of NIS793, gemcitabine and nab-paclitaxel. Note: As of 7-Jul-2023, treatment with NIS793/placebo was stopped. Study participants were allowed to continue with standard of care (SoC) chemotherapy (gemcitabine+ nab-paclitaxel) per investigator assessment.	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)	Participants received a combination of placebo, gemcitabine and nab-paclitaxel: • Placebo for NIS793 (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	21	245	245
Time to Response (TTR) (units: Months)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	NA (NA to NA)[1]	NA (NA to NA)[1]	NA (NA to NA)[1]

[1] NA: Not estimable due to number of events censored

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

Description	Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Ctrough was listed and summarized using descriptive statistics.
Time Frame	Cycles 1 and 3 Day 1 (0 hour (pre-dose) and 1 hour) and Day 15 (0 hour (pre-dose)), Cycles 2, 4, 6 and 12 Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.

Analysis Population Description	Pharmacokinetic Analysis Set - Participants with corresponding evaluable PK parameters

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	19
Safety run-in part: Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean ± Standard Deviation**
Cycle 1 Day 1: 0 hour (pre-dose)	0.00 ± 0.00
Cycle 1 Day 1: 1 hour	577000 ± 172000
Cycle 1 Day 15: 0 hour (pre-dose)	230000 ± 250000
Cycle 2 Day 1: 0 hour (pre-dose)	207000 ± 82400
Cycle 3 Day 1: 0 hour (pre-dose)	300000 ± 123000
Cycle 3 Day 1: 1 hour	771000 ± 225000
Cycle 3 Day 15: 0 hour (pre-dose)	309000 ± 130000
Cycle 4 Day 1: 0 hour (pre-dose)	370000 ± 148000
Cycle 6 Day 1: 0 hour (pre-dose)	425000 ± 86800
Cycle 12 Day 1: 0 hour (pre-dose)	553000 ± NA[1]

[1] NA: Not estimable due to insufficient number of participants with events

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

Description	Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Cmax was listed and summarized using descriptive statistics.
Time Frame	Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.

Analysis Population Description	Pharmacokinetic Analysis Set - Participants with corresponding evaluable PK parameters

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	19
Safety run-in part: Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean ± Standard Deviation**
Cycle 1 Day 1	549000 ± 193000
Cycle 3 Day 1	837000 ± 394000

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

Description	Venous whole blood samples were collected for activity-based pharmacokinetics characterization. Tmax was listed and summarized using descriptive statistics.
Time Frame	Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Participants with corresponding evaluable PK parameters

	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel : • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	19

Safety run-in part: Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: Hour)	**Median** **(Full Range)**
Cycle 1 Day 1	1.12 (0.583 to 5.00)
Cycle 3 Day 1	0.883 (0.5 to 4.17)

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

Description	In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Ctrough was summarized using descriptive statistics.
Time Frame	Cycle 1 Day 15, Cycle 3 Day 1, Cycle 3 Day 15, Cycle 4 Day 1 and Cycle 6 Day 1: 0 hour (pre-dose). 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Chinese participants with intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	24
Randomized part (Chinese participants with intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean** **± Standard Deviation**
Cycle 1 Day 15: 0 hour (pre-dose)	149000 ± 36400
Cycle 3 Day 1: 0 hour (pre-dose)	366000 ± 114000
Cycle 3 Day 15: 0 hour (pre-dose)	380000 ± 187000

Cycle 4 Day 1: 0 hour (pre-dose)	371000 ± 131000
Cycle 6 Day 1: 0 hour (pre-dose)	493000 ± 221000

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

Description	In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Cmax was summarized using descriptive statistics.
Time Frame	Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Chinese participants with intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	24
Randomized part (Chinese participants with intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean ± Standard Deviation**
Cycle 1 Day 1	691000 ± 113000
Cycle 3 Day 1	978000 ± 131000

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

Description	In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in

	Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and Tmax was summarized using descriptive statistics.
Time Frame	Cycles 1 and 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Chinese participants with intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	24
Randomized part (Chinese participants with intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: Hour)	**Median (Full Range)**
Cycle 1 Day 1	1.52 (0.583 to 7.00)
Cycle 3 Day 1	3.98 (0.567 to 7.75)

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

Description	In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected for activity-based pharmacokinetics characterization and AUClast was summarized using descriptive statistics.
Time Frame	Cycles 1 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Chinese participants with intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	23
Randomized part (Chinese participants with intensive PK sampling): Area under the curve from time zero to the last measurable concentration sampling time (AUClast) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: h*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
	48900000 (104.3%)

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

Description	In the randomized part, participants enrolled for treatment in China were assigned to more intensive PK sampling (taken into account the ability of clinical sites to comply with the instructions in the laboratory manual concerning the preparation of serum samples) to assess PK of NIS793 in Chinese participants. Venous whole blood samples were collected and AUCtau was summarized using descriptive statistics.
Time Frame	Cycles 3 Day 1: 0 hour (pre-dose) and 1 hour. 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Chinese participants with intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	7
Randomized part (Chinese participants with intensive PK sampling): Area under the curve calculated to the end of a dosing interval (tau) at steady-state (AUCtau) of NIS793 in combination with gemcitabine and nab-	**Geometric Mean (Geometric Coefficient of Variation)**

paclitaxel (units: h*ng/mL)	
	159000000 (25.5%)

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

Description	For participants without intensive PK sampling, venous whole blood samples were collected for activity-based pharmacokinetics characterization. Ctrough was listed and summarized using descriptive statistics.
Time Frame	Cycles 2, 3, 4, 6 and 12 Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Participants without intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	175
Randomized part (participants without intensive PK sampling): Trough Concentration (Ctrough) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean** **± Standard Deviation**
Cycle 2 Day 1: 0 hour (pre-dose)	249000 ± 105000
Cycle 3 Day 1: 0 hour (pre-dose)	331000 ± 133000
Cycle 4 Day 1: 0 hour (pre-dose)	335000 ± 138000
Cycle 6 Day 1: 0 hour (pre-dose)	334000 ± 136000
Cycle 12 Day 1: 0 hour (pre-dose)	302000 ± 63600

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

Description	For Chinese participants without intensive PK sampling schedule and global participants in the randomized part, for which only sparse PK samples were collected for activity-based pharmacokinetics characterization, Cmax was listed and summarized using descriptive statistics.
Time Frame	Cycles 1 and 3: Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Participants without intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	175
Randomized part (participants without intensive PK sampling): Maximum concentration (Cmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: ng/mL)	**Mean ± Standard Deviation**
Cycle 1 Day 1: 0 hour (pre-dose)	625000 ± 185000
Cycle 3 Day 1: 0 hour (pre-dose)	807000 ± 228000

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

Description	For Chinese participants without intensive PK sampling schedule and global participants in the randomized part, for which only sparse PK samples were collected for activity-based pharmacokinetics characterization, Tmax was listed and summarized using descriptive statistics.
Time Frame	Cycles 1 and 3: Day 1 (0 hour (pre-dose)). 1 cycle = 28 days.
Analysis Population Description	Pharmacokinetic Analysis Set - Participants without intensive PK sampling with corresponding evaluable PK parameters

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)

Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	175
Randomized part (participants without intensive PK sampling): Time to reach maximum concentration (Tmax) of NIS793 in combination with gemcitabine and nab-paclitaxel (units: Hour)	**Median (Full Range)**
Cycle 1 Day 1: 0 hour (pre-dose)	1.08 (0.5 to 5.17)
Cycle 3 Day 1: 0 hour (pre-dose)	0.833 (0.5 to 2.83)

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

Description	Anti-drug antibodies (ADA) against NIS793 prevalence at baseline refers to the proportion of subjects who have developed antibodies against the drug NIS793 before starting treatment. This is calculated by dividing the number of subjects with ADA-positive samples at baseline by the total number of subjects whose baseline samples were tested for ADA.
Time Frame	Baseline
Analysis Population Description	For the randomized part, the immunogenicity (IG) incidence set included all participants in the IG prevalence set with a determinant baseline IG sample.

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	196
Randomized part: Anti-drug antibodies (ADA) against NIS793 prevalence at baseline (units: Participants)	**Count of Participants (Not Applicable)**
ADA-negative sample at baseline	196 (100%)

ADA-positive sample at baseline	0 (%)

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

Description	Anti-drug antibodies (ADA) against NIS793 incidence on treatment refers to the proportion of participants who developed antibodies against the drug NIS793 during the treatment period. This can be categorized into two types: 1) Treatment-induced ADA positive: Participants who were ADA-negative at baseline but became ADA-positive after starting the treatment. 2) Treatment-boosted ADA positive: Participants who were ADA-positive at baseline and showed a significant increase in ADA titer during the treatment.
Time Frame	From date of first study drug intake up to approximately 34 months
Analysis Population Description	For the randomized part, the immunogenicity (IG) incidence set included all participants in the IG prevalence set with a determinant baseline IG sample and at least one determinant post-baseline IG sample.

	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel)
Arm/Group Description	Participants received a combination of NIS793, Gemcitabine and Nab-paclitaxel: • NIS793 at 2100 mg (Days 1 and 15) • Gemcitabine at 1000 mg/m² (Days 1, 8 and 15) • Nab-paclitaxel at 125 mg/m² (Days 1, 8 and 15)
Number of Participants Analyzed [units: participants]	196
Randomized part: Anti-drug antibodies (ADA) against NIS793 incidence on treatment (units: Participants)	**Count of Participants (Not Applicable)**
Treatment-boosted ADA-positive	0 (%)
Treatment-induced ADA-positive	0 (%)
ADA-negative	196 (100%)

Other Pre-Specified Outcome Result(s)

No data identified.

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Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Time Frame	Adverse Events (AEs) were collected from first dose of study medication until end of extended follow-up phase (end of study), assessed up to approximately 34 months. Deaths were recorded from study start date until end of post-treatment follow-up (end of study), assessed up to approximately 34 months. On-treatment period (up to 30 days after last dose) and post-treatment follow-up phase (thereafter) are reported separately.
Additional Description	The total number at risk in the post-treatment follow-up (efficacy follow-up period or survival follow-up period) included patients who entered this period. All-cause Mortality was assessed for all participants enrolled in the study, while Serious and Other Adverse Events were assessed for all participants who received at least one dose of the study medication.
Source Vocabulary for Table Default	MedDRA (20.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Safety run-in: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 21	**Safety run-in: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 18**	**Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 239**	**Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 192**	**Randomized Arm B: Placebo + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 241**	**Randomized Arm B: Placebo + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 200**
Arm/Group Description	Safety run-in part: NIS793 plus (Gemcitabine and	Safety run-in part: NIS793 plus (Gemcitabine and	Randomized part (Arm A): NIS793 plus (Gemcitabine	Randomized part (Arm A): NIS793 plus (Gemcitabine	Randomized part (Arm B): Placebo plus (Gemcitabine	Randomized part (Arm B): Placebo plus (Gemcitabine

	Nab-paclitaxel) - Events up to 30 days safety follow-up	Nab-paclitaxel) - Events in the post-treatment follow-up phase	and Nab-paclitaxel) - Events up to 30 days safety follow-up	and Nab-paclitaxel) - Events in the post-treatment follow-up phase	and Nab-paclitaxel) - Events up to 30 days safety follow-up	and Nab-paclitaxel) - Events in the post-treatment follow-up phase
Total Number Affected	0	18	24	135	16	132
Total Number At Risk	21	18	239	192	241	200

Serious Adverse Events

Time Frame	Adverse Events (AEs) were collected from first dose of study medication until end of extended follow-up phase (end of study), assessed up to approximately 34 months. Deaths were recorded from study start date until end of post-treatment follow-up (end of study), assessed up to approximately 34 months. On-treatment period (up to 30 days after last dose) and post-treatment follow-up phase (thereafter) are reported separately.
Additional Description	The total number at risk in the post-treatment follow-up (efficacy follow-up period or survival follow-up period) included patients who entered this period. All-cause Mortality was assessed for all participants enrolled in the study, while Serious and Other Adverse Events were assessed for all participants who received at least one dose of the study medication.
Source Vocabulary for Table Default	MedDRA (20.1)
Collection Approach for Table Default	Systematic Assessment

	Safety run-in: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last	**Safety run-in: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 18**	**Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last**	**Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 192**	**Randomized Arm B: Placebo + Gem/Nab-paclitaxel, treatment up to 30 days post last**	**Randomized Arm B: Placebo + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 200**

	dose N = 21		dose N = 239		dose N = 241	
Arm/Group Description	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase
Total # Affected by any Serious Adverse Event	13	2	144	21	110	28
Total # at Risk by any Serious Adverse Event	21	18	239	192	241	200
Blood and lymphatic system disorders						
Anaemia	1 (4.76%)	0 (0.00%)	13 (5.44%)	1 (0.52%)	3 (1.24%)	0 (0.00%)
Atypical haemolytic uraemic syndrome	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood loss anaemia	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Coagulopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Disseminated intravascular coagulation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	4 (1.66%)	0 (0.00%)
Leukocytosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancytopenia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombotic microangiopathy	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Cardiac disorders						
Acute myocardial infarction	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Atrial fibrillation	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac arrest	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Cardiac disorder	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Cardiac valve disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Cardiopulmonary failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Coronary artery disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Heart failure with preserved ejection fraction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Myocardial infarction	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Palpitations	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ventricular fibrillation	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders						
Papilloedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Retinal ischaemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Retinal vasculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Gastrointestinal disorders						
Abdominal distension	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	8 (3.32%)	1 (0.50%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	1 (0.41%)	0 (0.00%)
Acute abdomen	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Diarrhoea	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	6 (2.49%)	1 (0.50%)
Duodenal obstruction	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Duodenal stenosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Duodenal ulcer	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Gastric haemorrhage	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Gastric perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Gastric stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Gastrointestinal haemorrhage	1 (4.76%)	0 (0.00%)	4 (1.67%)	1 (0.52%)	1 (0.41%)	0 (0.00%)
Gastrointestinal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Gastrointestinal toxicity	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematemesis	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Haematochezia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemorrhoidal haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ileus	0 (0.00%)	0 (0.00%)	2 (0.84%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Impaired gastric emptying	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intestinal obstruction	0 (0.00%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ischaemic enteritis	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Large intestinal obstruction	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lower gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malignant ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Malignant gastrointestinal obstruction	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Melaena	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Obstruction gastric	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatitis	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Portal hypertensive gastropathy	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rectal haemorrhage	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Small intestinal haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	1 (0.41%)	0 (0.00%)
Small intestinal perforation	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Upper gastrointestinal haemorrhage	1 (4.76%)	0 (0.00%)	8 (3.35%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Vomiting	2 (9.52%)	0 (0.00%)	5 (2.09%)	0 (0.00%)	3 (1.24%)	2 (1.00%)
General disorders and administration site conditions						
Asthenia	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Condition aggravated	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Death	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (4.76%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	4 (1.66%)	0 (0.00%)
General physical health deterioration	0 (0.00%)	0 (0.00%)	6 (2.51%)	3 (1.56%)	2 (0.83%)	1 (0.50%)
Generalised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Pain	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	1 (4.76%)	0 (0.00%)	11 (4.60%)	0 (0.00%)	11 (4.56%)	2 (1.00%)
Hepatobiliary disorders						
Autoimmune hepatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Bile duct stenosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Biliary obstruction	0 (0.00%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	5 (2.07%)	0 (0.00%)
Cholangitis	0 (0.00%)	0 (0.00%)	7 (2.93%)	1 (0.52%)	6 (2.49%)	0 (0.00%)
Cholangitis acute	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholecystitis	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Cholecystitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	2 (0.83%)	0 (0.00%)
Gallbladder fistula	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hepatic function abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hepatobiliary disease	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Jaundice	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Jaundice cholestatic	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Liver disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Malignant biliary obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Portal vein thrombosis	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations						
Abdominal abscess	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Abdominal infection	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	2 (0.83%)	1 (0.50%)
Anal abscess	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Appendicitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.24%)	0 (0.00%)
Bacteraemia	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	2 (0.83%)	1 (0.50%)
Bacterial infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Biliary tract infection	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	5 (2.07%)	0 (0.00%)
Cellulitis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Cholangitis infective	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Clostridium difficile colitis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Clostridium difficile infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
COVID-19 pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Device related infection	1 (4.76%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Device related sepsis	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Erysipelas	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Escherichia infection	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Escherichia sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Escherichia urinary tract infection	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye infection	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Febrile infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	1 (0.41%)	0 (0.00%)
Focal peritonitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Gastroenteritis	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Giardiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hepatic infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	2 (0.83%)	1 (0.50%)
Liver abscess	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Lower respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Nail infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Oesophageal candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Oropharyngitis fungal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Pancreas infection	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Penile infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Peritonitis	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Pneumococcal infection	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	1 (4.76%)	0 (0.00%)	7 (2.93%)	0 (0.00%)	7 (2.90%)	0 (0.00%)
Pneumonia bacterial	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyelonephritis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinovirus infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Sepsis	0 (0.00%)	0 (0.00%)	5 (2.09%)	1 (0.52%)	7 (2.90%)	2 (1.00%)
Septic shock	0 (0.00%)	0 (0.00%)	5 (2.09%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Sinusitis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	4 (1.67%)	1 (0.52%)	4 (1.66%)	0 (0.00%)
Urosepsis	1 (4.76%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Injury, poisoning and procedural complications						
Anastomotic ulcer	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Femur fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Fractured sacrum	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic rupture	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hip fracture	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Spinal fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Vascular pseudoaneurysm ruptured	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Wound dehiscence	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations						

Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Amylase increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	1 (0.50%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders						
Decreased appetite	0 (0.00%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	2 (0.83%)	1 (0.50%)
Dehydration	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	3 (1.24%)	0 (0.00%)
Diabetic ketoacidosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Failure to thrive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoalbuminaemia	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hypoglycaemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Hypophosphataemia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malnutrition	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Metabolic acidosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders						
Back pain	1 (4.76%)	0 (0.00%)	4 (1.67%)	1 (0.52%)	3 (1.24%)	0 (0.00%)
Muscular weakness	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Myalgia	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Osteoporotic fracture	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pathological fracture	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sarcopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Oesophageal adenocarcinoma	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Transitional cell carcinoma	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour associated fever	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour haemorrhage	1 (4.76%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders						
Cerebral haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebral infarction	1 (4.76%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebrovascular accident	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Coma	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Dysstasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Encephalopathy	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Facial paralysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Haemorrhage intracranial	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Metabolic encephalopathy	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Motor dysfunction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Neuropathy peripheral	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neurotoxicity	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Putamen haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Seizure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.50%)
Syncope	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Transient ischaemic attack	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	1 (0.50%)
Product issues						
Device dislocation	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Device occlusion	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stent malfunction	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders						
Delirium	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Renal and urinary disorders						
Acute kidney injury	0 (0.00%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Calculus urinary	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	1 (4.76%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Nephrolithiasis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	3 (1.24%)	1 (0.50%)
Epistaxis	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemoptysis	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hiccups	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hydrothorax	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Interstitial lung disease	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiogenic pulmonary oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Pneumonitis	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	3 (1.24%)	0 (0.00%)
Pneumothorax	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary embolism	1 (4.76%)	0 (0.00%)	4 (1.67%)	2 (1.04%)	4 (1.66%)	0 (0.00%)
Respiratory distress	0 (0.00%)	0 (0.00%)	1 (0.42%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Respiratory failure	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Rash	0 (0.00%)	0 (0.00%)	2 (0.84%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders						
Aortic dissection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.52%)	0 (0.00%)	0 (0.00%)
Deep vein thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	1 (0.50%)
Distributive shock	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Embolism	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypotension	0 (0.00%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	4 (1.66%)	1 (0.50%)
Orthostatic hypotension	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral vein thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Shock haemorrhagic	0 (0.00%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	1 (0.41%)	0 (0.00%)
Thrombophlebitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.41%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse Events (AEs) were collected from first dose of study medication until end of extended follow-up phase (end of study), assessed up to approximately 34 months. Deaths were recorded from study start date until end of post-treatment follow-up (end of study), assessed up to approximately 34 months. On-treatment period (up to 30 days after last dose) and post-treatment follow-up phase (thereafter) are reported separately.
Additional Description	The total number at risk in the post-treatment follow-up (efficacy follow-up period or survival follow-up period) included patients who entered this period. All-cause Mortality was assessed for all participants enrolled in the study, while Serious and Other Adverse Events were assessed for all participants who received at least one dose of the study medication.
Source Vocabulary for Table Default	MedDRA (20.1)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Safety run-in: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 21	Safety run-in: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 18	Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 239	Randomized Arm A: NIS793 + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 192	Randomized Arm B: Placebo + Gem/Nab-paclitaxel, treatment up to 30 days post last dose N = 241	Randomized Arm B: Placebo + Gem/Nab-paclitaxel, post-treatment follow-up phase N = 200
Arm/Group Description	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Safety run-in part: NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Randomized part (Arm A): NIS793 plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel) - Events up to 30 days safety follow-up	Randomized part (Arm B): Placebo plus (Gemcitabine and Nab-paclitaxel) - Events in the post-treatment follow-up phase
Total # Affected by any Other Adverse Event	21	6	228	29	236	36
Total # at Risk by any Other Adverse Event	21	18	239	192	241	200
Blood and lymphatic system disorders						
Anaemia	14 (66.67%)	0 (0.00%)	165 (69.04%)	16 (8.33%)	143 (59.34%)	10 (5.00%)
Leukopenia	2 (9.52%)	0 (0.00%)	15 (6.28%)	0 (0.00%)	29 (12.03%)	0 (0.00%)
Neutropenia	5 (23.81%)	0 (0.00%)	49 (20.50%)	0 (0.00%)	66 (27.39%)	1 (0.50%)
Thrombocytopenia	3 (14.29%)	0 (0.00%)	36 (15.06%)	1 (0.52%)	32 (13.28%)	2 (1.00%)
Gastrointestinal disorders						
Abdominal distension	2 (9.52%)	0 (0.00%)	9 (3.77%)	0 (0.00%)	7 (2.90%)	0 (0.00%)
Abdominal pain	8 (38.10%)	1 (5.56%)	25 (10.46%)	0 (0.00%)	28 (11.62%)	1 (0.50%)
Abdominal pain upper	1 (4.76%)	0 (0.00%)	13 (5.44%)	2 (1.04%)	12 (4.98%)	1 (0.50%)
Constipation	7 (33.33%)	0 (0.00%)	47 (19.67%)	2 (1.04%)	57 (23.65%)	1 (0.50%)
Diarrhoea	9 (42.86%)	1 (5.56%)	70 (29.29%)	2 (1.04%)	80 (33.20%)	2 (1.00%)

Gingival bleeding	3 (14.29%)	0 (0.00%)	9 (3.77%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemorrhoids	1 (4.76%)	0 (0.00%)	14 (5.86%)	0 (0.00%)	3 (1.24%)	0 (0.00%)
Mouth ulceration	2 (9.52%)	0 (0.00%)	5 (2.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	12 (57.14%)	0 (0.00%)	89 (37.24%)	1 (0.52%)	86 (35.68%)	5 (2.50%)
Rectal haemorrhage	2 (9.52%)	0 (0.00%)	8 (3.35%)	0 (0.00%)	3 (1.24%)	0 (0.00%)
Stomatitis	0 (0.00%)	0 (0.00%)	25 (10.46%)	0 (0.00%)	8 (3.32%)	0 (0.00%)
Vomiting	4 (19.05%)	0 (0.00%)	57 (23.85%)	1 (0.52%)	53 (21.99%)	0 (0.00%)
General disorders and administration site conditions						
Asthenia	2 (9.52%)	0 (0.00%)	39 (16.32%)	0 (0.00%)	45 (18.67%)	4 (2.00%)
Chills	1 (4.76%)	0 (0.00%)	13 (5.44%)	0 (0.00%)	13 (5.39%)	1 (0.50%)
Fatigue	12 (57.14%)	0 (0.00%)	76 (31.80%)	2 (1.04%)	78 (32.37%)	5 (2.50%)
Malaise	1 (4.76%)	0 (0.00%)	21 (8.79%)	1 (0.52%)	15 (6.22%)	0 (0.00%)
Mucosal inflammation	0 (0.00%)	0 (0.00%)	11 (4.60%)	0 (0.00%)	13 (5.39%)	0 (0.00%)
Oedema peripheral	4 (19.05%)	0 (0.00%)	36 (15.06%)	0 (0.00%)	66 (27.39%)	3 (1.50%)
Pyrexia	5 (23.81%)	1 (5.56%)	75 (31.38%)	2 (1.04%)	63 (26.14%)	3 (1.50%)
Infections and infestations						
COVID-19	1 (4.76%)	0 (0.00%)	20 (8.37%)	0 (0.00%)	23 (9.54%)	0 (0.00%)
Urinary tract infection	3 (14.29%)	0 (0.00%)	28 (11.72%)	1 (0.52%)	17 (7.05%)	2 (1.00%)
Investigations						
Alanine aminotransferase increased	4 (19.05%)	0 (0.00%)	59 (24.69%)	3 (1.56%)	63 (26.14%)	4 (2.00%)
Amylase increased	2 (9.52%)	0 (0.00%)	9 (3.77%)	2 (1.04%)	7 (2.90%)	0 (0.00%)
Aspartate aminotransferase increased	4 (19.05%)	0 (0.00%)	54 (22.59%)	1 (0.52%)	56 (23.24%)	5 (2.50%)

Blood alkaline phosphatase increased	3 (14.29%)	0 (0.00%)	20 (8.37%)	3 (1.56%)	21 (8.71%)	3 (1.50%)
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	19 (7.95%)	3 (1.56%)	14 (5.81%)	4 (2.00%)
Blood lactate dehydrogenase increased	2 (9.52%)	0 (0.00%)	6 (2.51%)	0 (0.00%)	7 (2.90%)	2 (1.00%)
Gamma-glutamyltransferase increased	3 (14.29%)	0 (0.00%)	27 (11.30%)	4 (2.08%)	25 (10.37%)	2 (1.00%)
Lipase increased	3 (14.29%)	0 (0.00%)	15 (6.28%)	1 (0.52%)	11 (4.56%)	0 (0.00%)
Lymphocyte count decreased	2 (9.52%)	0 (0.00%)	17 (7.11%)	2 (1.04%)	8 (3.32%)	0 (0.00%)
Neutrophil count decreased	3 (14.29%)	0 (0.00%)	63 (26.36%)	0 (0.00%)	78 (32.37%)	0 (0.00%)
Platelet count decreased	4 (19.05%)	0 (0.00%)	52 (21.76%)	3 (1.56%)	70 (29.05%)	2 (1.00%)
Weight decreased	6 (28.57%)	1 (5.56%)	44 (18.41%)	4 (2.08%)	34 (14.11%)	3 (1.50%)
White blood cell count decreased	2 (9.52%)	0 (0.00%)	48 (20.08%)	1 (0.52%)	63 (26.14%)	0 (0.00%)
White blood cell count increased	3 (14.29%)	0 (0.00%)	3 (1.26%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Metabolism and nutrition disorders						
Decreased appetite	8 (38.10%)	0 (0.00%)	66 (27.62%)	4 (2.08%)	63 (26.14%)	4 (2.00%)
Hyperglycaemia	1 (4.76%)	0 (0.00%)	12 (5.02%)	1 (0.52%)	20 (8.30%)	1 (0.50%)
Hypoalbuminaemia	1 (4.76%)	0 (0.00%)	39 (16.32%)	3 (1.56%)	24 (9.96%)	6 (3.00%)
Hypocalcaemia	2 (9.52%)	0 (0.00%)	30 (12.55%)	3 (1.56%)	13 (5.39%)	0 (0.00%)
Hypokalaemia	4 (19.05%)	0 (0.00%)	28 (11.72%)	5 (2.60%)	24 (9.96%)	2 (1.00%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	12 (5.02%)	0 (0.00%)	9 (3.73%)	1 (0.50%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	26 (10.88%)	6 (3.13%)	14 (5.81%)	0 (0.00%)
Hypophosphataemia	3 (14.29%)	0 (0.00%)	35 (14.64%)	2 (1.04%)	6 (2.49%)	0 (0.00%)
Iron deficiency	4 (19.05%)	0 (0.00%)	5 (2.09%)	0 (0.00%)	4 (1.66%)	0 (0.00%)

Musculoskeletal and connective tissue disorders						
Arthralgia	0 (0.00%)	0 (0.00%)	16 (6.69%)	0 (0.00%)	18 (7.47%)	0 (0.00%)
Back pain	4 (19.05%)	3 (16.67%)	18 (7.53%)	0 (0.00%)	19 (7.88%)	0 (0.00%)
Joint swelling	3 (14.29%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Myalgia	0 (0.00%)	0 (0.00%)	17 (7.11%)	0 (0.00%)	17 (7.05%)	1 (0.50%)
Pain in extremity	1 (4.76%)	0 (0.00%)	18 (7.53%)	0 (0.00%)	15 (6.22%)	0 (0.00%)
Nervous system disorders						
Dizziness	2 (9.52%)	0 (0.00%)	15 (6.28%)	0 (0.00%)	16 (6.64%)	0 (0.00%)
Dysgeusia	2 (9.52%)	0 (0.00%)	20 (8.37%)	0 (0.00%)	21 (8.71%)	0 (0.00%)
Headache	4 (19.05%)	0 (0.00%)	17 (7.11%)	0 (0.00%)	17 (7.05%)	0 (0.00%)
Neuropathy peripheral	1 (4.76%)	0 (0.00%)	31 (12.97%)	0 (0.00%)	35 (14.52%)	0 (0.00%)
Paraesthesia	2 (9.52%)	0 (0.00%)	10 (4.18%)	0 (0.00%)	10 (4.15%)	0 (0.00%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	22 (9.21%)	0 (0.00%)	36 (14.94%)	1 (0.50%)
Psychiatric disorders						
Delirium	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.83%)	0 (0.00%)
Insomnia	3 (14.29%)	0 (0.00%)	18 (7.53%)	1 (0.52%)	26 (10.79%)	1 (0.50%)
Renal and urinary disorders						
Dysuria	2 (9.52%)	0 (0.00%)	4 (1.67%)	0 (0.00%)	5 (2.07%)	0 (0.00%)
Haematuria	1 (4.76%)	0 (0.00%)	14 (5.86%)	1 (0.52%)	4 (1.66%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Cough	2 (9.52%)	0 (0.00%)	23 (9.62%)	0 (0.00%)	26 (10.79%)	0 (0.00%)
Dyspnoea	1 (4.76%)	0 (0.00%)	18 (7.53%)	1 (0.52%)	18 (7.47%)	1 (0.50%)
Epistaxis	7 (33.33%)	0 (0.00%)	66 (27.62%)	1 (0.52%)	20 (8.30%)	0 (0.00%)

Skin and subcutaneous tissue disorders						
Alopecia	9 (42.86%)	0 (0.00%)	83 (34.73%)	0 (0.00%)	71 (29.46%)	1 (0.50%)
Pruritus	2 (9.52%)	1 (5.56%)	28 (11.72%)	1 (0.52%)	18 (7.47%)	0 (0.00%)
Rash	6 (28.57%)	0 (0.00%)	67 (28.03%)	0 (0.00%)	45 (18.67%)	0 (0.00%)
Rash maculo-papular	1 (4.76%)	0 (0.00%)	13 (5.44%)	0 (0.00%)	8 (3.32%)	0 (0.00%)
Rash papular	2 (9.52%)	0 (0.00%)	1 (0.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders						
Hypertension	1 (4.76%)	0 (0.00%)	11 (4.60%)	0 (0.00%)	13 (5.39%)	1 (0.50%)
Hypotension	2 (9.52%)	0 (0.00%)	12 (5.02%)	0 (0.00%)	12 (4.98%)	1 (0.50%)

Other Relevant Findings

None

Conclusion:

Based on the analysis of unblinded clinical data results, it was observed that there were higher number of deaths in the experimental treatment group (NIS793 with gemcitabine/nab-paclitaxel) when compared to placebo group. Consequently, DMC decided to halt the NIS793 study treatment. Actions were classified as an urgent safety measure (USM) due to the unfavorable benefit-risk observed from review of the available data by DMC.

The experimental arm NIS793 with standard-of-care (gemcitabine/nab-paclitaxel) did not result in improved efficacy in this difficult to treat population of metastatic PDAC when compared to the placebo group. The safety results are similar to the known safety profile of NIS793.

NOVARTIS

Date of Clinical Trial Report

01-April-2025