# Clinical trial results:
# Nab-paclitaxel (Abraxane) Plus Gemcitabine in Subjects With Locally Advanced Pancreatic Cancer (LAPC): An International, Open-label, Multi-center, Phase 2 Study (LAPACT).

## Summary

| | |
|---|---|
| EudraCT number | 2014-001408-23 |
| Trial protocol | IT ES |
| Global end of trial date | 21 November 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 29 March 2019 |
| First version publication date | 29 March 2019 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ABI-007-PANC-007 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02301143 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Celgene Corporation |
| Sponsor organisation address | 86 Morris Avenue, Summit, United States, 07901 |
| Public contact | Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com |
| Scientific contact | Teng Jin Ong, Celgene Corporation, 01 908-673-9586, TOng@Celgene.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 | 28 January 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 November 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 November 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the time to treatment failure (TTF) in locally advanced pancreatic cancer (LAPC) subjects treated with nab-paclitaxel plus gemcitabine as induction therapy followed by Investigator's Choice of treatment

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection, Archiving of Essential Documents

Background therapy:

Six cycles of nab-Paclitaxel 125 mg/m2 intravenous (IV) infusion over approximately 30 to 45 minutes on Days 1, 8, and 15, followed by gemcitabine 1000 mg/m2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle were administered as induction therapy.

Once six cycles have been completed, subjects without disease progression or unacceptable toxicity will be eligible for Investigator choice phase, consisting of continuation of nab-paclitaxel and gemcitabine therapy, or chemoradiation therapy, or surgery.

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 21 April 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 45 |
| Country: Number of subjects enrolled | France: 28 |
| Country: Number of subjects enrolled | Spain: 20 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Italy: 6 |
| Worldwide total number of subjects | 107 |
| EEA total number of subjects | 54 |

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) | 44 |
| From 65 to 84 years | 62 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

152 patients were screened and 107 participants enrolled. First subject first visit was 21 April 2015. Last subject last visit was 26 April 2018

### Pre-assignment

Screening details:

Subjects eligible for treatment with nab-paclitaxel and gemcitabine for 6 cycles were to be enrolled, provided all inclusion/exclusion criteria were met within a 14day Screening Period prior to Cycle 1 Day 1.

### Period 1

| | |
|---|---|
| Period 1 title | Induction Period |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | nab-Paclitaxel plus Gemcitabine |

Arm description:

Participants received nab-Paclitaxel 125 mg/m^2 by intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine (Gem) 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle for 6 cycles. For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | nab-Paclitaxel |
| Investigational medicinal product code | |
| Other name | Abraxane |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

nab-Paclitaxel 125 mg/m^2 by intravenous (IV) administration over approximately 30 to 45 minutes on Days 1, 8, and 15.

| | |
|---|---|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | Gemzar |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine 1000 mg/m^2 by IV administration over approximately 30 minutes on Days 1, 8, and 15

| **Number of subjects in period 1** | nab-Paclitaxel plus Gemcitabine |
|---|---|
| Started | 107 |
| Completed | 62 |
| Not completed | 45 |
| Adverse event, serious fatal | 1 |

| | |
|---|---|
| Consent withdrawn by subject | 3 |
| Physician decision | 4 |
| Adverse event, non-fatal | 22 |
| Progressive Disease | 8 |
| Enrolled But Not Treated | 1 |
| Not Specified | 1 |
| Symptomatic Deterioration | 2 |
| Noncompliance With Study Drug | 1 |
| Protocol deviation | 2 |

## Period 2

| | |
|---|---|
| Period 2 title | Investigator's Choice (IC) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| **Arm title** | Investigator Choice (Overall) |

Arm description:

For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period. Investigator Choice includes 3 options: 1. Continued on nab-Paclitaxel and gemcitabine (included 12 subjects) 2. Chemoradiation therapy consisting of capecitabine or gemcitabine with radiation according to institutional practice (included 18 subjects) 3. Surgical Intervention (included 17 subjects)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | nab-Paclitaxel |
| Investigational medicinal product code | |
| Other name | Abraxane |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

nab-Paclitaxel 125 mg/m^2 by intravenous (IV) administration over approximately 30 to 45 minutes on Days 1, 8, and 15 until disease progression or unacceptable toxicity.

| | |
|---|---|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | Gemzar |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine 1000 mg/m^2 by IV administration over approximately 30 minutes on Days 1, 8, and 15 disease progression or unacceptable toxicity.

| **Number of subjects in period 2[1]** | Investigator Choice (Overall) |
|---|---|
| Started | 47 |
| Completed | 37 |
| Not completed | 10 |
| Adverse event, non-fatal | 3 |
| Progressive Disease | 3 |
| Not Specified | 1 |
| Unresectable Surgery | 1 |
| Symptomatic Deterioration | 1 |
| Noncompliance With Study Drug | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all 62 subjects who completed the induction period elected to be treated in the Investigator's Choice period of the study. Only 49 intended to start the Investigator's Choice period. Of these 47 started this period and two subjects who were chosen for surgery did not have surgery because of disease progression and unsuitability based on the assessment by the GI surgeon.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | nab-Paclitaxel plus Gemcitabine |
| Reporting group description: | |
| Participants received nab-Paclitaxel 125 mg/m^2 by intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine (Gem) 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle for 6 cycles. For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period. | |

| Reporting group values | nab-Paclitaxel plus Gemcitabine | Total | |
|---|---|---|---|
| Number of subjects | 107 | 107 | |
| Age, Customized<br>Units: Subjects | | | |
| <65 years | 44 | 44 | |
| >=65 - 75 years | 50 | 50 | |
| >75 years | 13 | 13 | |
| Age Continuous<br>Units: years | | | |
| median | 65.0 | | |
| full range (min-max) | 42 to 85 | - | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 59 | 59 | |
| Male | 48 | 48 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | |
| Not Hispanic or Latino | 78 | 78 | |
| Unknown or Not Reported | 28 | 28 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 3 | 3 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 2 | 2 | |
| White | 72 | 72 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 30 | 30 | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| ECOG performance status assesses how the disease affects the daily living activities of the participant and helps determine appropriate treatment and prognosis. - 0 = Fully Active (Most Favorable Activity); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled. | | | |
| Units: Subjects | | | |
| Grade 0 | 50 | 50 | |
| Grade 1 | 57 | 57 | |

| | | | |
|---|---|---|---|
| Grade 2 | 0 | 0 | |
| Grade 3 | 0 | 0 | |
| Grade 4 | 0 | 0 | |
| Physician Assessment of Peripheral Neuropathy | | | |
| Physician assessment for grading of peripheral neuropathy in participants receiving chemotherapy according to National Cancer Institute Common Toxicity Criteria (NCICTC): Grade 0 = None or no neuromotor or neurosensory loss; Grade 1 = Asymptomatic: loss of deep tendon reflexes or paresthesia; - Grade 2 = Moderate symptoms: limiting instrumental Activities of Daily Living (ADLs); - Grade 3 = Severe symptoms: limiting self-care ADL; assistance device indicated; - Grade 4 = Life-threatening consequences: urgent intervention indicated. | | | |
| Units: Subjects | | | |
| Grade 0 | 101 | 101 | |
| Grade 1 | 6 | 6 | |
| Grade 2 | 0 | 0 | |
| Grade 3 | 0 | 0 | |
| Grade 4 | 0 | 0 | |
| Baseline Neutrophil - to - Lymphocyte Ratio (NLR) | | | |
| Neutrophil to lymphocyte ratio (NLR) is used as a marker of subclinical inflammation. Increased NLR is associated with poor prognosis in advanced pancreatic cancer. | | | |
| Units: Subjects | | | |
| <= 5 | 91 | 91 | |
| > 5 | 14 | 14 | |
| Missing | 2 | 2 | |
| Baseline Albumin | | | |
| Units: g/L | | | |
| median | 39.0 | | |
| full range (min-max) | 28 to 50 | - | |
| Carbohydrate Antigen 19-9 (CA19-9) | | | |
| Serum CA 19-9 concentrations may be elevated in patients with gastrointestinal malignancies such as pancreatic cancer. Measure Analysis Population Description: Baseline CA19-9 measures are missing for six participants. | | | |
| Units: U/mL | | | |
| median | 243.3 | | |
| full range (min-max) | 0 to 20741 | - | |
| Sum of Longest Diameter of Target Lesions | | | |
| Units: mm | | | |
| median | 44.0 | | |
| full range (min-max) | 17 to 130 | - | |
| Number of Target Lesions | | | |
| Units: lesions | | | |
| median | 1.0 | | |
| full range (min-max) | 1 to 3 | - | |
| Time from Primary Diagnosis to First Dose | | | |
| Units: days | | | |
| median | 27.0 | | |
| full range (min-max) | 4 to 95 | - | |

## Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Nab-Paclitaxel Plus Gemcitabine |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

nab-Paclitaxel 125 mg/m^2 intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1,8, and 15 of each 28-day cycle. For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period. - Continuation of nab-paclitaxel and gemcitabine therapy to disease progression or unacceptable toxicity OR - Chemoradiation therapy consisting of the concurrent use of capecitabine or gemcitabine with radiation according to institutional practice (included 18 subjects) OR - Surgical intervention (included 17 subjects)

| **Reporting group values** | Nab-Paclitaxel Plus Gemcitabine | | |
|---|---|---|---|
| Number of subjects | 107 | | |
| Age, Customized<br>Units: Subjects | | | |
| <65 years | 44 | | |
| >=65 - 75 years | 50 | | |
| >75 years | 13 | | |
| Age Continuous<br>Units: years | | | |
| median | 65.0 | | |
| full range (min-max) | 42 to 85 | | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 59 | | |
| Male | 48 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | | |
| Not Hispanic or Latino | 78 | | |
| Unknown or Not Reported | 28 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 3 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 2 | | |
| White | 72 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 30 | | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| ECOG performance status assesses how the disease affects the daily living activities of the participant and helps determine appropriate treatment and prognosis. - 0 = Fully Active (Most Favorable Activity); - 1 = Restricted activity but ambulatory; - 2 = Ambulatory but unable to carry out work activities; - 3 = Limited Self-Care; - 4 = Completely Disabled. | | | |
| Units: Subjects | | | |
| Grade 0 | 50 | | |
| Grade 1 | 57 | | |
| Grade 2 | 0 | | |
| Grade 3 | 0 | | |
| Grade 4 | 0 | | |
| Physician Assessment of Peripheral Neuropathy | | | |
| Physician assessment for grading of peripheral neuropathy in participants receiving chemotherapy | | | |

| | | | |
|---|---|---|---|
| according to National Cancer Institute Common Toxicity Criteria (NCICTC): Grade 0 = None or no neuromotor or neurosensory loss; Grade 1 = Asymptomatic: loss of deep tendon reflexes or paresthesia; - Grade 2 = Moderate symptoms: limiting instrumental Activities of Daily Living (ADLs); - Grade 3 = Severe symptoms: limiting self-care ADL; assistance device indicated; - Grade 4 = Life-threatening consequences: urgent intervention indicated. | | | |
| Units: Subjects | | | |
| Grade 0 | 101 | | |
| Grade 1 | 6 | | |
| Grade 2 | 0 | | |
| Grade 3 | 0 | | |
| Grade 4 | 0 | | |
| Baseline Neutrophil - to - Lymphocyte Ratio (NLR) | | | |
| Neutrophil to lymphocyte ratio (NLR) is used as a marker of subclinical inflammation. Increased NLR is associated with poor prognosis in advanced pancreatic cancer. | | | |
| Units: Subjects | | | |
| <= 5 | 91 | | |
| > 5 | 14 | | |
| Missing | 2 | | |
| Baseline Albumin | | | |
| Units: g/L | | | |
| median | 39.0 | | |
| full range (min-max) | 28 to 50 | | |
| Carbohydrate Antigen 19-9 (CA19-9) | | | |
| Serum CA 19-9 concentrations may be elevated in patients with gastrointestinal malignancies such as pancreatic cancer. Measure Analysis Population Description: Baseline CA19-9 measures are missing for six participants. | | | |
| Units: U/mL | | | |
| median | 243.3 | | |
| full range (min-max) | 0 to 20741 | | |
| Sum of Longest Diameter of Target Lesions | | | |
| Units: mm | | | |
| median | 44.0 | | |
| full range (min-max) | 17 to 130 | | |
| Number of Target Lesions | | | |
| Units: lesions | | | |
| median | 1.0 | | |
| full range (min-max) | 1 to 3 | | |
| Time from Primary Diagnosis to First Dose | | | |
| Units: days | | | |
| median | 27.0 | | |
| full range (min-max) | 4 to 95 | | |

## End points

### End points reporting groups

| Reporting group title | nab-Paclitaxel plus Gemcitabine |
|---|---|

Reporting group description:

Participants received nab-Paclitaxel 125 mg/m^2 by intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine (Gem) 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle for 6 cycles. For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period.

| Reporting group title | Investigator Choice (Overall) |
|---|---|

Reporting group description:

For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period. Investigator Choice includes 3 options: 1. Continued on nab-Paclitaxel and gemcitabine (included 12 subjects) 2. Chemoradiation therapy consisting of capecitabine or gemcitabine with radiation according to institutional practice (included 18 subjects) 3. Surgical Intervention (included 17 subjects)

| Subject analysis set title | Nab-Paclitaxel Plus Gemcitabine |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

nab-Paclitaxel 125 mg/m^2 intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1,8, and 15 of each 28-day cycle. For participants who completed 6 cycles of nab-paclitaxel and gemcitabine without disease progression or unacceptable toxicities, the Investigator then determined the best option for the participant in the Investigator's Choice Period. - Continuation of nab-paclitaxel and gemcitabine therapy to disease progression or unacceptable toxicity OR - Chemoradiation therapy consisting of the concurrent use of capecitabine or gemcitabine with radiation according to institutional practice (included 18 subjects) OR - Surgical intervention (included 17 subjects)

### Primary: Kaplan-Meier Estimates for Time to Treatment Failure (TTF)

| End point title | Kaplan-Meier Estimates for Time to Treatment Failure (TTF)[1] |
|---|---|

End point description:

TTF was defined as the time after the first dose of study therapy to discontinuation of study therapy due to disease progression, death by any cause, or the start of a new non-protocol-defined anticancer therapy/surgery. If a subject does not progress, die or start a new non-protocol-defined anticancer therapy, the subject was censored on the last tumor assessment date.
Tumor evaluations of CT or MRI scans were assessed and response determined according to Response Evaluation Criteria in Solid Tumors (RECIST) guidelines, version 1.1.
The definition for progressive disease (PD) was >= 20% increase in the sum of diameters of target lesions from nadir, and the sum showed an absolute increase of >= 5 mm; the progression of a non-target lesion or the appearance of any new lesions is also considered progression.
Median and its 90% confidence interval (CI) of TTF were estimated using the method of Brookmeyer and Crowley.
Intent to Treat population = all subjects enrolled into the study.

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

End point timeframe:

Day 1 of study treatment up to 28.75 months; (maximum time for the last tumor assessment)

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: The primary goal of this study was to evaluate time to treatment failure (primary endpoint) with nab-paclitaxel plus gemcitabine as induction therapy. Therefore there was no statistical comparison to be made. Treatment choices in period 2 (investigator's choice period) were non-randomized and no comparisons were intended there either.

| End point values | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 107 | | | |
| Units: months | | | | |
| median (confidence interval 90%) | 9.0 (7.26 to 10.05) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Disease Control Rate (DCR): Percentage of Participants With Complete (CR) or Partial Response (PR), or Stable Disease (SD) for ≥ 16 Weeks According to RECIST Version 1.1

| End point title | Disease Control Rate (DCR): Percentage of Participants With Complete (CR) or Partial Response (PR), or Stable Disease (SD) for ≥ 16 Weeks According to RECIST Version 1.1 |
|---|---|

End point description:

DCR was defined as the percentage of participants with a CR or PR or SD from of date of first treatment to 16 weeks. Tumor assessments after start of non-protocol-defined anticancer therapy were excluded. RECIST 1.1 Definition: - CR: disappearance of all target and non-target lesions; any pathological lymph nodes (target or non-target) must have reduction in short axis to < 10 mm and no new lesions diagnosed. - PR: a >= 30% decrease in the sum of diameters of target lesions from baseline; no evidence of progression in any of the non-target lesions diagnosed at baseline; and no new lesions diagnosed. - SD: neither sufficient shrinkage to qualify for PR nor sufficient increase of lesions to qualify for PD. The two-sided 90% binomial confidence intervals (CIs) were estimated by Wilson score method. Intent to treat population was defined as all participants enrolled into the study. Intent to treat population was defined as all participants enrolled into the study.

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

End point timeframe:

Day 1 of study treatment up to the end of investigator choice period plus 28 days; up to 76.9 weeks

| End point values | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 107 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 90%) | 77.6 (70.3 to 83.5) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Response Rate (ORR): Percentage of Participants With Complete (CR) or Partial Response (PR) According to RECIST Version 1.1

| End point title | Overall Response Rate (ORR): Percentage of Participants With Complete (CR) or Partial Response (PR) According to RECIST Version 1.1 |
|---|---|

End point description:

ORR was defined as the percentage of participants that achieved a combined incidence of complete (CR) and partial response (PR) using RECIST 1.1 guidelines as assessed by the investigator at baseline, every 56 (-3/+7 days) and at the 28-day follow-up visit . Assessments after new non-protocol-defined anticancer therapy are excluded. For participants who had resectable surgery in Investigator Choice period, assessments after surgical intervention are excluded. RECIST 1.1 Definition: - CR: disappearance of all target and non-target lesions; any pathological lymph nodes (target or non-target) must have reduction in short axis to < 10 mm and no new lesions diagnosed. - PR: a >= 30% decrease in the sum of diameters of target lesions from baseline; no evidence of progression in any of the non-target lesions diagnosed at baseline; and no new lesions diagnosed. Intent to treat population was defined as all participants enrolled into the study.

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

End point timeframe:

Day 1 of study treatment up to the end of investigator choice period plus 28 days; up to 76.9 weeks

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 107 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 90%) | 39.3 (31.8 to 47.2) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS)

| End point title | Kaplan-Meier Estimate of Progression-Free Survival (PFS) |
|---|---|

End point description:

Progression-free Survival was determined based on RECIST 1.1. criteria and was defined as the time from the date of the first dose to the date of disease progression or death (by any cause), whichever is earlier. The analysis day was calculated from enrollment date for one participant who was not treated. Participants who have no disease progression or have not died were censored to last tumor assessment date with progression-free. The definition for progressive disease (PD) was at least a 20% increase in the sum of diameters of target lesions from nadir; the sum must also demonstrate an absolute increase of >= 5 mm; the progression of a non-target lesion or the appearance of any new lesions is also considered progression. Median and its 90% confidence interval of PFS were estimated using the method of Brookmeyer and Crowley. Intent to treat population was defined as all participants enrolled into the study.

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

End point timeframe:

Day 1 of study treatment up to 28.75 months (maximum time for the last tumor assessment)

| End point values | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 107 | | | |
| Units: months | | | | |
| median (confidence interval 90%) | 10.9 (9.26 to 11.63) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Kaplan-Meier Estimates for Overall Survival (OS)

| End point title | Kaplan-Meier Estimates for Overall Survival (OS) |
|---|---|

End point description:

Overall survival was defined as the time from the date of first dose of study therapy to the date of death (by any cause). Participants who were alive at the end of study or clinical data cut were censored on the last known time that the participant was alive or the clinical cutoff date, whichever was earlier. Median and its 90% confidence interval of OS were estimated using the method of Brookmeyer and Crowley. Intent to treat population was defined as all participants enrolled into the study.

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

End point timeframe:

Day 1 of study treatment up to 31.34 months (maximum time for survival follow-up)

| End point values | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 107 | | | |
| Units: months | | | | |
| median (confidence interval 90%) | 18.8 (14.95 to 24.02) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30): Global Health Status and 5 Functioning Scales

| End point title | Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30): Global Health Status and 5 Functioning Scales |
|---|---|

End point description:

The European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC QLQ-C30) is a validated health-related quality of life (HRQoL) measure. The EORTC QLQ-C30 is composed of both multi-item scales and single-item measures, including 5 functional scales, 3 symptom

scales, 6 single symptom items, and 1 global health status / quality of life scale. All reported measures are transformed to a 0 - 100 scale. In the Global Health Status and 5 functional scales, 0 = worst possible quality of life/health status and 100 = best possible quality of life/health status. The best score on treatment is the best score from all post-baseline visits and is compared to the baseline to get the following responder categories. Responder categories: - Improved: >=10 increase from baseline - Stable: neither increase nor decrease >10 - Worsened: >=10 decrease from baseline. ITT population = all participants enrolled into the study with both baseline and post baseline values.

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

End point timeframe:

Baseline (Day -1), Day 1 of each cycle, for up to 19 cycles each cycle consisting of 28 days and the 28-day follow-up visit

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 95 | | | |
| Units: Participants | | | | |
| Global Health Status: Improved | 43 | | | |
| Global Health Status: Stable | 34 | | | |
| Global Health Status: Worsened | 18 | | | |
| Physical Functioning Scale: Improved | 20 | | | |
| Physical Functioning Scale: Stable | 66 | | | |
| Physical Functioning Scale: Worsened | 9 | | | |
| Role Functioning Scale: Improved | 36 | | | |
| Role Functioning Scale: Stable | 46 | | | |
| Role Functioning Scale: Worsened | 13 | | | |
| Emotional Functioning Scale: Improved | 50 | | | |
| Emotional Functioning Scale: Stable | 40 | | | |
| Emotional Functioning Scale: Worsened | 5 | | | |
| Cognitive Functioning Scale: Improved | 33 | | | |
| Cognitive Functioning Scale: Stable | 51 | | | |
| Cognitive Functioning Scale: Worsened | 11 | | | |
| Social Functioning Scale: Improved | 38 | | | |
| Social Functioning Scale: Stable | 43 | | | |
| Social Functioning Scale: Worsened | 14 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30): Symptom Scales and Single Symptom Items

| End point title | Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30): Symptom Scales and Single Symptom Items |
|---|---|

End point description:

The European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC

QLQ-C30) is a validated health-related quality of life (HRQoL) measure. The EORTC QLQ-C30 is composed of both multi-item scales and single-item measures, including 5 functional scales, 3 symptom scales, 6 single symptom items, and 1 global health status / quality of life scale. All reported measures are transformed to a 0 to 100 scale. In the symptom scales and single symptom items, 0 = optimal health state and 100 = worst possible health state. The best score on treatment is the best score from all post-baseline visits and is compared to the baseline to get the following responder categories. Responder categories: - Improved: >=10 decrease from baseline - Stable: neither increase nor decrease >10 - Worsened: >=10 increase from baseline. ITT population = all participants enrolled into the study with both baseline and post baseline values.

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

End point timeframe:

Baseline (Day -1), Day 1 of each cycle, for up to 19 cycles each cycle consisting of 28 days and the 28-day follow-up visit

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 95 | | | |
| Units: Participants | | | | |
| Symptom Scale-Fatigue: Improved | 46 | | | |
| Symptom Scale-Fatigue: Stable | 24 | | | |
| Symptom Scale-Fatigue: Worsened | 25 | | | |
| Scale-Nausea+Vomiting: Improved | 29 | | | |
| Scale-Nausea+Vomiting: Stable | 64 | | | |
| Scale-Nausea+Vomiting: Worsened | 2 | | | |
| Symptom Scale-Pain: Improved | 62 | | | |
| Symptom Scale-Pain: Stable | 29 | | | |
| Symptom Scale-Pain: Worsened | 4 | | | |
| Symptom - Dyspnoea: Improved | 12 | | | |
| Symptom - Dyspnoea: Stable | 74 | | | |
| Symptom - Dyspnoea: Worsened | 9 | | | |
| Symptom - Insomnia: Improved | 53 | | | |
| Symptom - Insomnia: Stable | 35 | | | |
| Symptom - Insomnia: Worsened | 7 | | | |
| Symptom - Appetite loss: Improved | 48 | | | |
| Symptom - Appetite loss: Stable | 39 | | | |
| Symptom - Appetite loss: Worsened | 8 | | | |
| Symptom - Constipation: Improved | 46 | | | |
| Symptom - Constipation: Stable | 45 | | | |
| Symptom - Constipation: Worsened | 4 | | | |
| Symptom - Diarrhoea: Improved | 18 | | | |
| Symptom - Diarrhoea: Stable | 69 | | | |
| Symptom - Diarrhoea: Worsened | 8 | | | |
| Symptom - Financial difficulties: Improved | 17 | | | |
| Symptom - Financial difficulties: stable: | 74 | | | |
| Symptom - Financial difficulties: Worsened | 4 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): Six Summary Scales

| End point title | Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): Six Summary Scales |
|---|---|

End point description:

The EORTC pancreatic cancer module is a validated tool intended for patients at all disease stages undergoing surgical resection, palliative surgical intervention, endoscopic palliation or palliative chemotherapy. The module includes 26 questions, organized into 7 scales and 10 individual item scores. All reported measures are transformed to a 0 to 100 scale. Six summary scales reported are: - Pancreatic Pain - Digestive Symptoms - Altered Bowel Habits - Hepatic Scale - Body Image - Sexuality Scores of 0 = optimal health state and 100 = worst possible health state. The best score on treatment is the best score from all post-baseline visits and is compared to the baseline. Responder categories: - Improved: >=MID decrease from baseline - Stable: no increase or decrease >MID - Worsened: >=MID increase from baseline MID = half the baseline standard deviation. Intent to treat population was defined as all participants enrolled into the study with both baseline and post baseline values.

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

End point timeframe:

Baseline (Day -1), Day 1 of each cycle, for up to 19 cycles each cycle consisting of 28 days and the 28-day follow-up visit

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 95 | | | |
| Units: Participants | | | | |
| Pancreatic Pain Scale: Improved | 62 | | | |
| Pancreatic Pain Scale: Stable | 33 | | | |
| Pancreatic Pain Scale: Worsened | 0 | | | |
| Digestive Symptom Scale: Improved | 49 | | | |
| Digestive Symptom Scale: Stable | 36 | | | |
| Digestive Symptom Scale: Worsened | 10 | | | |
| Altered Bowel Habits Scale: Improved | 28 | | | |
| Altered Bowel Habits Scale: Stable | 53 | | | |
| Altered Bowel Habits Scale: Worsened | 14 | | | |
| Hepatic Scale: Improved | 25 | | | |
| Hepatic Scale: Stable | 66 | | | |
| Hepatic Scale: Worsened | 4 | | | |
| Body Image Scale: Improved | 22 | | | |
| Body Image Scale: Stable | 50 | | | |
| Body Image Scale: Worsened | 23 | | | |
| Sexuality Scale: Improved | 31 | | | |
| Sexuality Scale: Stable | 51 | | | |
| Sexuality Scale: Worsened | 13 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): Satisfaction with Health Care Scale

| End point title | Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): Satisfaction with Health Care Scale |
|---|---|

End point description:

The EORTC pancreatic cancer module is a validated tool intended for patients at all disease stages undergoing surgical resection, palliative surgical intervention, endoscopic palliation or palliative chemotherapy. The module includes 26 questions, organized into 7 scales and 10 individual item scores. The summary scale for Satisfaction with Health Care is reported. All reported measures are transformed to a 0 to 100 scale. Scores of 0 = not satisfied, worst possible health state and 100 = extremely satisfied, best possible health state. The best score on treatment is the best score from all post-baseline visits and is compared to the baseline to get the following responder categories. Responder categories: - Improved: >=MID increase from baseline - Stable: no increase or decrease >MID - Worsened: >=MID decrease from baseline MID = half the baseline standard deviation. ITT population = all participants enrolled into the study with both baseline and post baseline values.

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

End point timeframe:

Baseline (Day -1), Day 1 of each cycle, for up to 19 cycles each cycle consisting of 28 days and the 28-day follow-up visit

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 95 | | | |
| Units: Participants | | | | |
| Satisfaction with Health Care Scale: Improved | 42 | | | |
| Satisfaction with Health Care Scale: Stable | 40 | | | |
| Satisfaction with Health Care Scale: Worsened | 13 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Participant Counts in Response Categories Using the European

## Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): 10 Individual Item Scores

| End point title | Participant Counts in Response Categories Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire For Pancreatic Cancer (EORTC-QLQ PAN26): 10 Individual Item Scores |
|---|---|

End point description:

The EORTC pancreatic cancer module is a validated tool intended for patients at all disease stages undergoing surgical resection, palliative surgical intervention, endoscopic palliation or palliative chemotherapy. The module includes 26 questions, organized into 7 scales and 10 individual item scores. The 10 individual item scores are reported. All reported measures are transformed to a 0 to 100 scale. Scores of 0 = best possible health state and 100 = worst possible health state. The best score on treatment is the best score from all post-baseline visits and is compared to the baseline to get the following responder categories. Responder categories: - Improved: >=MID decrease from baseline - Stable: no increase or decrease >MID - Worsened: >=MID increase from baseline MID = half the baseline standard deviation. Intent to treat population was defined as all participants enrolled into the study with both baseline and post baseline values.

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

End point timeframe:

Baseline (Day -1), Day 1 of each cycle, for up to 19 cycles each cycle consisting of 28 days and the 28-day follow-up visit

| **End point values** | Nab-Paclitaxel Plus Gemcitabine | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 95 | | | |
| Units: Participants | | | | |
| Abdominal Bloating: Improved | 50 | | | |
| Abdominal Bloating: Stable | 42 | | | |
| Abdominal Bloating: Worsened | 3 | | | |
| Taste Changes: Improved | 20 | | | |
| Taste Changes: Stable | 54 | | | |
| Taste Changes: Worsened | 21 | | | |
| Indigestion: Improved | 41 | | | |
| Indigestion: Stable | 47 | | | |
| Indigestion: Worsened | 7 | | | |
| Flatulence: Improved | 47 | | | |
| Flatulence: Stable | 37 | | | |
| Flatulence: Worsened | 11 | | | |
| Weight Loss: Improved | 36 | | | |
| Weight Loss: Stable | 56 | | | |
| Weight Loss: Worsened | 3 | | | |
| Limb Weakness: Improved | 22 | | | |
| Limb Weakness: Stable | 55 | | | |
| Limb Weakness: Worsened | 18 | | | |
| Dry Mouth: Improved | 37 | | | |
| Dry Mouth: Stable | 45 | | | |
| Dry Mouth: Worsened | 13 | | | |
| Treatment Side-Effects: Improved | 8 | | | |
| Treatment Side-Effects: Stable | 48 | | | |
| Treatment Side-Effects: Worsened | 39 | | | |
| Worry About Future Health: Improved | 42 | | | |

| | | | | |
|---|---|---|---|---|
| Worry About Future Health: Stable | 45 | | | |
| Worry About Future Health: Worsened | 8 | | | |
| Limits on Activity Planning: Improved | 42 | | | |
| Limits on Activity Planning: Stable | 42 | | | |
| Limits on Activity Planning: Worsened | 11 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

| End point title | Number of Participants with Treatment Emergent Adverse Events (TEAEs) |
|---|---|

End point description:

TEAEs are defined as any adverse event (AE) that begin or worsen on or after the start of study drug or procedure of the study period through the maximum duration of the period plus 28 days. The severity of AEs was graded based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0 and the scale: Grade 1 = Mild Grade 2 = Moderate Grade 3 = Severe Grade 4 = Life threatening Grade 5 = Death. Relation to study drug was determined by the investigator. A treatment-related TEAE is defined as TEAE which was considered to be related to one or both of the study drugs and reported as 'Suspected' on the case report form. AEs with a missing relationship were treated as 'treatment-related' in data summaries. IP (investigational product) refers to nab-Paclitaxel and/or Gemcitabine. "Related" TEAE refers to relation to study drug (IP). The Treated population consists of all participants who received at least 1 dose of nab-paclitaxel or gemcitabine.

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

End point timeframe:

Day 1 of study drug up to end of the study; up to 31.3 months

| End point values | nab-Paclitaxel plus Gemcitabine | Nab-Paclitaxel Plus Gemcitabine | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 106[2] | 106[3] | | |
| Units: Participants | | | | |
| >= 1 TEAE | 105 | 105 | | |
| >=1 related TEAE | 102 | 103 | | |
| >=1 TEAE of severity grade 3 or higher | 85 | 90 | | |
| >=1 related TEAE of severity grade 3 or higher | 72 | 75 | | |
| >=1 serious TEAE | 38 | 39 | | |
| >= 1 related serious TEAE | 14 | 14 | | |
| >=1 TEAE leading to discontinuation of IP | 25 | 28 | | |
| >=1 related TEAE leading to discontinuation of IP | 15 | 18 | | |
| >=1 TEAE leading to dose reduction of IP | 69 | 72 | | |
| >=1 related TEAE leading to dose reduction of IP | 68 | 71 | | |
| >=1 TEAE leading to interruption of IP | 66 | 68 | | |

| | | | | |
|---|---|---|---|---|
| >=1 related TEAE leading to interruption of IP | 48 | 50 | | |
| >= TEAE leading to death | 2 | 2 | | |
| >=1 related TEAE leading to death | 0 | 0 | | |

Notes:

[2] - nab-Paclitaxel Plus Gemcitabine in the Induction period

[3] - Overall = nab-pac + Gem in the Induction priod plus a subset who continued regimen in the IC period

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 of study drug up to end of the study; up to 31.3 months

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | nab-Paclitaxel plus Gemcitabine (Induction Period) |

Reporting group description:

nab-Paclitaxel 125 mg/m^2 intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle.

| | |
|---|---|
| Reporting group title | nab-Paclitaxel plus Gemcitabine (Overall) |

Reporting group description:

nab-Paclitaxel 125 mg/m^2 intravenous (IV) infusion administered over approximately 30-45 minutes on Days 1, 8, and 15, followed by gemcitabine 1000 mg/m^2 IV infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle. Overall includes nab-Paclitaxel plus Gemcitabine treatment cycles during the Induction Period, as well as the subset of participants who continued the regimen during the Investigator Choice Period.

| Serious adverse events | nab-Paclitaxel plus Gemcitabine (Induction Period) | nab-Paclitaxel plus Gemcitabine (Overall) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 38 / 106 (35.85%) | 39 / 106 (36.79%) | |
| number of deaths (all causes) | 2 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | 5 / 106 (4.72%) | |
| occurrences causally related to treatment / all | 3 / 6 | 3 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Peripancreatic fluid collection | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Nervous system disorders | | | |
| Presyncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | 3 / 106 (2.83%) | |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstruction gastric | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 106 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Obstructive uropathy | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Escherichia coli | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 106 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreas infection | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 106 (4.72%) | 5 / 106 (4.72%) | |
| occurrences causally related to treatment / all | 2 / 5 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | nab-Paclitaxel plus Gemcitabine (Induction Period) | nab-Paclitaxel plus Gemcitabine (Overall) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 104 / 106 (98.11%) | 104 / 106 (98.11%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 21 / 106 (19.81%) | 23 / 106 (21.70%) | |
| occurrences (all) | 46 | 51 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 16 / 106 (15.09%) | 17 / 106 (16.04%) | |
| occurrences (all) | 43 | 46 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | 16 / 106 (15.09%) | |
| occurrences (all) | 21 | 26 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 6 / 106 (5.66%) | |
| occurrences (all) | 8 | 8 | |
| Neutrophil count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 22 / 106 (20.75%) | 23 / 106 (21.70%) | |
| occurrences (all) | 57 | 67 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 25 / 106 (23.58%) | 27 / 106 (25.47%) | |
| occurrences (all) | 72 | 85 | |
| Weight decreased | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | 12 / 106 (11.32%) | |
| occurrences (all) | 16 | 16 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | 14 / 106 (13.21%) | |
| occurrences (all) | 40 | 45 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | 8 / 106 (7.55%) | |
| occurrences (all) | 10 | 10 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | 12 / 106 (11.32%) | |
| occurrences (all) | 12 | 14 | |
| Dysgeusia | | | |
| subjects affected / exposed | 32 / 106 (30.19%) | 33 / 106 (31.13%) | |
| occurrences (all) | 38 | 40 | |
| Headache | | | |
| subjects affected / exposed | 17 / 106 (16.04%) | 17 / 106 (16.04%) | |
| occurrences (all) | 18 | 19 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 23 / 106 (21.70%) | 25 / 106 (23.58%) | |
| occurrences (all) | 37 | 41 | |
| Paraesthesia | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | 11 / 106 (10.38%) | |
| occurrences (all) | 24 | 24 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 29 / 106 (27.36%) | 30 / 106 (28.30%) | |
| occurrences (all) | 60 | 74 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 49 / 106 (46.23%) | 49 / 106 (46.23%) | |
| occurrences (all) | 155 | 173 | |
| Leukopenia | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | 7 / 106 (6.60%) | |
| occurrences (all) | 20 | 20 | |
| Lymphopenia | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 6 / 106 (5.66%) | |
| occurrences (all) | 14 | 14 | |
| Neutropenia | | | |
| subjects affected / exposed | 44 / 106 (41.51%) | 45 / 106 (42.45%) | |
| occurrences (all) | 92 | 94 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 25 / 106 (23.58%) | 27 / 106 (25.47%) | |
| occurrences (all) | 46 | 49 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 36 / 106 (33.96%) | 36 / 106 (33.96%) | |
| occurrences (all) | 106 | 109 | |
| Chills | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | 18 / 106 (16.98%) | |
| occurrences (all) | 23 | 24 | |
| Fatigue | | | |
| subjects affected / exposed | 53 / 106 (50.00%) | 53 / 106 (50.00%) | |
| occurrences (all) | 127 | 137 | |
| Influenza like illness | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | 8 / 106 (7.55%) | |
| occurrences (all) | 13 | 14 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 45 / 106 (42.45%) | 47 / 106 (44.34%) | |
| occurrences (all) | 75 | 81 | |
| Pain | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | 6 / 106 (5.66%) | |
| occurrences (all) | 5 | 6 | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 39 / 106 (36.79%) | 40 / 106 (37.74%) | |
| occurrences (all) | 75 | 79 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 19 / 106 (17.92%) | 19 / 106 (17.92%) | |
| occurrences (all) | 23 | 25 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | 10 / 106 (9.43%) | |
| occurrences (all) | 13 | 14 | |
| Constipation | | | |
| subjects affected / exposed | 30 / 106 (28.30%) | 32 / 106 (30.19%) | |
| occurrences (all) | 49 | 52 | |
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 106 (45.28%) | 48 / 106 (45.28%) | |
| occurrences (all) | 93 | 95 | |
| Dry mouth | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | 7 / 106 (6.60%) | |
| occurrences (all) | 7 | 7 | |
| Dyspepsia | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | 8 / 106 (7.55%) | |
| occurrences (all) | 8 | 9 | |
| Nausea | | | |
| subjects affected / exposed | 46 / 106 (43.40%) | 47 / 106 (44.34%) | |
| occurrences (all) | 89 | 92 | |
| Stomatitis | | | |
| subjects affected / exposed | 20 / 106 (18.87%) | 20 / 106 (18.87%) | |
| occurrences (all) | 26 | 26 | |
| Vomiting | | | |
| subjects affected / exposed | 30 / 106 (28.30%) | 30 / 106 (28.30%) | |
| occurrences (all) | 44 | 44 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 24 / 106 (22.64%) | 25 / 106 (23.58%) | |
| occurrences (all) | 36 | 38 | |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 14 / 106 (13.21%) | 15 / 106 (14.15%) | |
| occurrences (all) | 16 | 17 | |
| Epistaxis | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | 9 / 106 (8.49%) | |
| occurrences (all) | 12 | 12 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 57 / 106 (53.77%) | 57 / 106 (53.77%) | |
| occurrences (all) | 73 | 74 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | 9 / 106 (8.49%) | |
| occurrences (all) | 11 | 11 | |
| Dry skin | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | 9 / 106 (8.49%) | |
| occurrences (all) | 8 | 9 | |
| Pruritus | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | 12 / 106 (11.32%) | |
| occurrences (all) | 12 | 13 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | 9 / 106 (8.49%) | |
| occurrences (all) | 19 | 19 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | 15 / 106 (14.15%) | |
| occurrences (all) | 19 | 19 | |
| Depression | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 6 / 106 (5.66%) | |
| occurrences (all) | 6 | 6 | |
| Insomnia | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | 11 / 106 (10.38%) | |
| occurrences (all) | 12 | 12 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | 10 / 106 (9.43%) | |
| occurrences (all) | 14 | 15 | |
| Back pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 16 / 106 (15.09%) | 17 / 106 (16.04%) | |
| occurrences (all) | 17 | 18 | |
| Bone pain | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 6 / 106 (5.66%) | |
| occurrences (all) | 9 | 9 | |
| Muscular weakness | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 7 / 106 (6.60%) | |
| occurrences (all) | 9 | 10 | |
| Myalgia | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | 12 / 106 (11.32%) | |
| occurrences (all) | 16 | 17 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 7 / 106 (6.60%) | |
| occurrences (all) | 7 | 8 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 46 / 106 (43.40%) | 46 / 106 (43.40%) | |
| occurrences (all) | 56 | 56 | |
| Dehydration | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | 11 / 106 (10.38%) | |
| occurrences (all) | 13 | 13 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | 12 / 106 (11.32%) | |
| occurrences (all) | 17 | 17 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | 6 / 106 (5.66%) | |
| occurrences (all) | 9 | 9 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | 11 / 106 (10.38%) | |
| occurrences (all) | 18 | 18 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | 14 / 106 (13.21%) | |
| occurrences (all) | 29 | 31 | |
| Hypomagnesaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 106 (6.60%) | 7 / 106 (6.60%) | |
| occurrences (all) | 10 | 11 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | 10 / 106 (9.43%) | |
| occurrences (all) | 16 | 16 | |
| Iron deficiency | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | 7 / 106 (6.60%) | |
| occurrences (all) | 7 | 7 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported