



Clinical trial results:

A Phase III, Randomized, Open-Label, Multi Center, Safety and Efficacy Study to Evaluate Nab Paclitaxel (Abraxane®) as Maintenance Treatment after Induction with Nab-Paclitaxel plus Carboplatin in Subjects with Squamous Cell Non-Small Cell Lung Cancer (NSLSC)

Summary

EudraCT number	2014-003804-66
Trial protocol	DE ES GB IT
Global end of trial date	01 August 2019

Results information

Result version number	v1 (current)
This version publication date	16 August 2020
First version publication date	16 August 2020

Trial information

Trial identification

Sponsor protocol code	ABI-007-NSCL-003
-----------------------	------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02027428
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, 01 908-673-9100, ClinicalTrialDisclosure@celgene.com
Scientific contact	Teng Ong, MD, Celgene Corporation, 01 (908) 3768941, 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	01 August 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate progression free survival (PFS) with nab-paclitaxel as maintenance treatment after response or stable disease (SD) with nab-paclitaxel plus carboplatin in subjects with squamous cell NSCLC.

Protection of trial subjects:

Patient Confidentiality, Informed Consent, Archival of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Italy: 29
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 310
Worldwide total number of subjects	427
EEA total number of subjects	117

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)	162
From 65 to 84 years	262
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 87 sites in Germany, Italy, Spain, the United Kingdom and the United States.

Pre-assignment

Screening details:

Participants with a response or stable disease during Induction were randomized 2:1 into investigative treatment (nab-paclitaxel plus best supportive care [BSC] or BSC only) stratified by disease stage, response during induction and Eastern Cooperative Oncology Group (ECOG) performance status.

Period 1

Period 1 title	Baseline Period: Induction
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All Participants - Induction
-----------	------------------------------

Arm description:

During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² by intravenous (IV) infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL by IV infusion on Day 1 of each 21-day cycle. If the participant had radiological or clinical progressive disease (PD), they were discontinued from the study and not followed. If the participant had a complete response (CR), partial response (PR), or stable disease (SD) without PD at the end of 4 cycles, he/she were eligible to be randomised to the maintenance phase.

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 100 mg/m² by intravenous (IV) infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	Paraplatin,
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle

Number of subjects in period 1	All Participants - Induction
Started	427
Received Study Drug	420
Completed	202
Not completed	225
Adverse event, serious fatal	21
Consent withdrawn by subject	22
Adverse event, non-fatal	51
Symptomatic deterioration	16
Progressive Disease	77
Miscellaneous	14
Study terminated by sponsor	12
Induction - Ongoing	4
Never treated	7
Protocol deviation	1

Period 2

Period 2 title	Maintenance
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nab-Paclitaxel + Best Supportive Care (BSC)

Arm description:

Maintenance Phase: Subjects were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care (BSC) until disease progression.

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 100 mg/m² by intravenous (IV) infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle

Arm title	Best Supportive Care (BSC)
------------------	----------------------------

Arm description:

Participants were administered best supportive care (only) until disease progression.

Arm type	Palliative Care
No investigational medicinal product assigned in this arm	

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The study was not designed for the induction period to be the baseline period. The maintenance period is considered as the baseline period.

Number of subjects in period 2 ^[2]	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)
Started	136	66
Completed	12	6
Not completed	124	60
Adverse event, serious fatal	3	2
Consent withdrawn by subject	6	5
AE	21	1
Symptomatic deterioration	4	1
Not specified	6	3
Progressive Disease	84	-
Lack of efficacy	-	47
Protocol deviation	-	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The maintenance period is considered the baseline period of the trial as the primary objective was to evaluate PFS with nab-paclitaxel as maintenance treatment after response or stable disease with nab-paclitaxel in the induction period.

Baseline characteristics

Reporting groups

Reporting group title	Nab-Paclitaxel + Best Supportive Care (BSC)
Reporting group description:	
Maintenance Phase: Subjects were administered nab-paclitaxel 100 mg/m ² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care (BSC) until disease progression.	
Reporting group title	Best Supportive Care (BSC)
Reporting group description:	
Participants were administered best supportive care (only) until disease progression.	

Reporting group values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)	Total
Number of subjects	136	66	202
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years	48	27	75
≥65 years	88	39	127
Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: years			
arithmetic mean	67.1	66.8	
standard deviation	± 9.02	± 8.06	-
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female	49	23	72
Male	87	43	130
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Hispanic or Latino	3	5	8
Not Hispanic or Latino	132	61	193
Missing	1	0	1
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	1	0	1
Black or African American	9	2	11

White	125	62	187
Other	0	2	2
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Complete response	1	2	3
Partial response	92	42	134
Stable disease	41	21	62
Progressive disease	2	0	2
Not evaluable	0	1	1
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma	136	66	202
Squamous cell carcinoma not confirmed	0	0	0
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.			
Units: Subjects			
Stage IIIB	18	8	26
Stage IV	118	58	176

Subject analysis sets

Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m ² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.	
Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.	
Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.

Subject analysis set title	TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention as determined by the investigator.

Subject analysis set title	TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator.

Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention, as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. Nab-paclitaxel was administered during Induction and Maintenance.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. Carboplatin was administered during Induction.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to BSC
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to best supportive care (BSC) as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. BSC was administered during Maintenance.

Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.

Subject analysis set title	BSC: TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention, as determined by the investigator, for participants randomized to the BSC treatment arm. Nab-paclitaxel was administered during Induction.

Subject analysis set title	BSC: TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator, for participants randomized to the BSC treatment arm. Carboplatin was administered during Induction.

Subject analysis set title	BSC: TEAE Specific to BSC
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to best supportive care (BSC) as determined by the investigator, for participants randomized to the BSC treatment arm. BSC was administered during Maintenance.

Reporting group values	Nab-Paclitaxel + BSC: Induction + Maintenance	BSC: Induction + Maintenance	Nab-Paclitaxel + BSC: Induction + Maintenance
Number of subjects	136	66	136
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years			
≥65 years			
Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: years			
arithmetic mean	69.1	57.6	99.3
standard deviation	±	±	±
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female			
Male			
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			

Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Missing			
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Black or African American			
White			
Other			
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Complete response			
Partial response			
Stable disease			
Progressive disease			
Not evaluable			
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma			
Squamous cell carcinoma not confirmed			
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.			
Units: Subjects			
Stage IIIB			
Stage IV			

Reporting group values	Nab-Paclitaxel + BSC: Induction + Maintenance	BSC: Induction + Maintenance	TEAE Specific to Nab-Paclitaxel
Number of subjects	94	38	420
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years			
≥65 years			

Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: years			
arithmetic mean	1.478	1.413	
standard deviation	±	±	±
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female			
Male			
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Missing			
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Black or African American			
White			
Other			
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Complete response			
Partial response			
Stable disease			
Progressive disease			
Not evaluable			
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma			
Squamous cell carcinoma not confirmed			
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer			

has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.

Units: Subjects			
Stage IIIB			
Stage IV			

Reporting group values	TEAE Specific to Carboplatin	Nab-Paclitaxel + BSC: Induction + Maintenance	Nab-Paclitaxel + BSC: TEAE Specific to Nab-Paclitaxel
Number of subjects	420	130	130
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years			
≥65 years			
Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female			
Male			
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Missing			
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Black or African American			
White			
Other			
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			

Units: Subjects			
Complete response			
Partial response			
Stable disease			
Progressive disease			
Not evaluable			
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma			
Squamous cell carcinoma not confirmed			
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.			
Units: Subjects			
Stage IIIB			
Stage IV			

Reporting group values	Nab-Paclitaxel + BSC: TEAE Specific to Carboplatin	Nab-Paclitaxel + BSC: TEAE Specific to BSC	BSC: Induction + Maintenance
Number of subjects	130	130	62
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years			
≥65 years			
Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female			
Male			
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Hispanic or Latino			

Not Hispanic or Latino Missing			
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native Asian Black or African American White Other			
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Complete response Partial response Stable disease Progressive disease Not evaluable			
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma Squamous cell carcinoma not confirmed			
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.			
Units: Subjects			
Stage IIIB Stage IV			

Reporting group values	BSC: TEAE Specific to Nab-Paclitaxel	BSC: TEAE Specific to Carboplatin	BSC: TEAE Specific to BSC
Number of subjects	62	62	62
Age Categorical			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: participants			
<65 years ≥65 years			
Age Continuous			
Continuous age values in Total column represent the 202 participants in the Maintenance Period. Induction includes participants who were enrolled and treated however, baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the			

maintenance phase.			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units:			
Female			
Male			
Ethnicity (NIH/OMB)			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Missing			
Race/Ethnicity, Customized			
Induction includes participants who were enrolled and treated in the induction phase. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Black or African American			
White			
Other			
Overall Tumor Response at End of Induction			
Tumor response to Induction part chemotherapy for stratification is the response assessed at the last computed tomography (CT) scan before randomization. Baseline characteristics are displayed only for participants randomized in the maintenance phase. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Complete response			
Partial response			
Stable disease			
Progressive disease			
Not evaluable			
Confirmed Histology			
The histology categories included those with a tumor histology of squamous versus non-squamous types. Baseline characteristics for non-randomized participants is not displayed. The total number represents the ITT population in the maintenance phase.			
Units: Subjects			
Squamous cell carcinoma			
Squamous cell carcinoma not confirmed			
Disease Stage at Enrollment			
Disease stage = how big the tumor is and how far it has spread. Disease stages range from 0 (not spread) to IV (spread throughout the body). Stage 0: the cancer has not spread beyond the inner lining of the lung. Stage I: the cancer is small and hasn't spread to the lymph nodes (LN). Stage II: the cancer has spread to some LN near the original tumor. Stage III: the cancer has spread to nearby tissue or spread to far away LN. Stage IV: the cancer has spread to other organs such as lung, brain, or liver. BLC are displayed for participants randomized in the maintenance phase.			
Units: Subjects			

Stage IIIB			
Stage IV			

End points

End points reporting groups

Reporting group title	All Participants - Induction
Reporting group description: During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² by intravenous (IV) infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL by IV infusion on Day 1 of each 21-day cycle. If the participant had radiological or clinical progressive disease (PD), they were discontinued from the study and not followed. If the participant had a complete response (CR), partial response (PR), or stable disease (SD) without PD at the end of 4 cycles, he/she were eligible to be randomised to the maintenance phase.	
Reporting group title	Nab-Paclitaxel + Best Supportive Care (BSC)
Reporting group description: Maintenance Phase: Subjects were administered nab-paclitaxel 100 mg/m ² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care (BSC) until disease progression.	
Reporting group title	Best Supportive Care (BSC)
Reporting group description: Participants were administered best supportive care (only) until disease progression.	
Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m ² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.	
Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.	
Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m ² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.	
Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m ² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete	

response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.

Subject analysis set title	TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention as determined by the investigator.

Subject analysis set title	TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator.

Subject analysis set title	Nab-Paclitaxel + BSC: Induction + Maintenance
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention, as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. Nab-paclitaxel was administered during Induction and Maintenance.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. Carboplatin was administered during Induction.

Subject analysis set title	Nab-Paclitaxel + BSC: TEAE Specific to BSC
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to best supportive care (BSC) as determined by the investigator, for participants randomized to the Nab-Paclitaxel + BSC treatment arm. BSC was administered during Maintenance.

Subject analysis set title	BSC: Induction + Maintenance
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants randomized to this treatment arm for Maintenance, inclusive of their experience during Induction. During induction, participants received nab-paclitaxel plus carboplatin as standard of care. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she continued to the maintenance phase. Maintenance: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.

Subject analysis set title	BSC: TEAE Specific to Nab-Paclitaxel
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to nab-paclitaxel intervention, as determined by the investigator, for participants randomized to the BSC treatment arm. Nab-paclitaxel was administered during Induction.

Subject analysis set title	BSC: TEAE Specific to Carboplatin
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to carboplatin intervention as determined by the investigator, for participants randomized to the BSC treatment arm. Carboplatin was administered during Induction.

Subject analysis set title	BSC: TEAE Specific to BSC
Subject analysis set type	Safety analysis

Subject analysis set description:

TEAE categories specific to best supportive care (BSC) as determined by the investigator, for participants randomized to the BSC treatment arm. BSC was administered during Maintenance.

Primary: Kaplan-Meier Estimate of Progression-Free Survival (PFS) from Randomization into Maintenance

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS) from Randomization into Maintenance
-----------------	--

End point description:

PFS is defined as the time in months from the date of randomization to the date of disease progression based on the investigator's assessment according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 criteria (documented by computerized tomography, not including symptomatic deterioration) or death (any cause) on or prior to 01 Aug 2019. RECIST 1.1 definition: Complete response (CR) disappearance of all target lesions; Partial response (PR) at least a 30% decrease in the sum of diameters of target lesions from baseline; Stable disease (SD) neither sufficient shrinkage to qualify for partial response nor sufficient increase of lesions to qualify for progressive disease (PD); PD = At least a 20% increase in the sum of diameters of target lesions from nadir, and/or the appearance of new lesions. The intent to treat population (ITT) in the maintenance part = all randomized subjects regardless of whether they received study drug or had any efficacy exams collected.

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

End point timeframe:

From the date of randomization to the date of disease progression or death of any cause; up to August 2019; up to 42 months

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: months				
median (confidence interval 95%)	3.12 (2.73 to 4.60)	2.60 (1.64 to 3.45)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
----------------------------	------------------------

Statistical analysis description:

5% level of significance. Hazard ratio is based on stratified Cox proportional hazards regression model. The following stratification factors were evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at the end of Induction.

Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive
-------------------	---

	Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3486 ^[1]
Method	stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.19

Notes:

[1] - Stratification factors evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at end of Induction.

Secondary: Kaplan-Meier Estimate of Overall Survival (OS) From Randomization Into Maintenance

End point title	Kaplan-Meier Estimate of Overall Survival (OS) From Randomization Into Maintenance
-----------------	--

End point description:

Overall survival (OS) was defined as the duration in months between randomization and death from any cause. Participants who were still alive as of the clinical cut-off date had their OS censored at the date of last contact or clinical cut-off (01 August 2019 whichever was earlier. The last contact date was the date of the last record in the database, or if the subject was lost to follow-up, the last known date that the subject was alive. The intent to treat population in the maintenance part included all randomized subjects regardless of whether the subject received any study drug or had any efficacy assessments collected.

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

End point timeframe:

From the date of randomization to death from any cause; up to 01 August 2019; up to 55.89 months

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: months				
median (confidence interval 95%)	17.61 (13.86 to 21.09)	12.16 (7.56 to 18.99)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
----------------------------	------------------------

Statistical analysis description:

5% level of significance. Hazard ratio is based on stratified Cox proportional hazards regression model. The following stratification factors were evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor

response (CR/PR or SD) at the end of Induction.

Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0365 [2]
Method	stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.98

Notes:

[2] - Stratification factors evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at end of Induction.

Secondary: Percentage of Participants Who Achieved a Confirmed Overall Response of Complete Response or Partial Response (Overall Response Rate) Over Entire Study

End point title	Percentage of Participants Who Achieved a Confirmed Overall Response of Complete Response or Partial Response (Overall Response Rate) Over Entire Study
-----------------	---

End point description:

Overall response was defined as the percentage of participants with a confirmed assessment of complete response (CR) or partial response (PR) according to RECIST 1.1 criteria and confirmed in no less than 28 days. The 95% confidence interval (CI) was calculated using Clopper-Pearson method. RECIST 1.1 Definition: - Complete response-disappearance of all target lesions; any pathological lymph nodes (whether target or non target) must have reduction in short axis to < 10 mm. - Partial response-at least a 30% decrease in the sum of diameters of target lesions from baseline. The intent to treat population in the maintenance part included all randomized subjects regardless of whether the subject received any study drug or had any efficacy assessments collected.

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

End point timeframe:

Day 1 of treatment in the induction period and subsequent anticancer therapy, death or discontinuation up to 01 August 2019; maximum treatment duration was 234.1 weeks for entire study.

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: percentage of participants				
number (confidence interval 95%)	69.1 (60.6 to 76.8)	57.6 (44.8 to 69.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: 5% level of significance. The rate ratio and its 95% CI were based on the non-stratified analysis.	
Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.948
upper limit	1.519

Notes:

[3] - Stratification factors evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at the end of Induction, and tumor response (CR/PR or SD) at the end of Induction.

Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS) Over Entire Study

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS) Over Entire Study
-----------------	--

End point description:

PFS was defined as the time in months from Day 1 of treatment for the Induction part to the date of disease progression according to RECIST 1.1 criteria (documented by CT-scan, not including symptomatic deterioration) or death (any cause) on or prior to 01 August 2019, whichever occurred earlier. RECIST 1.1 Definition: - Progressive Disease (PD) - At least a 20% increase in the sum of diameters of target lesions from nadir; the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of new lesions is also considered progression. The intent to treat population in the maintenance part included all randomized subjects regardless of whether the subject received any study drug or had any efficacy assessments collected.

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

End point timeframe:

Between Day 1 of the Induction Part through to the date of disease progression or death; up to 01 August 2019; the maximum treatment duration was 234.1 weeks for the entire study.

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: months				
median (confidence interval 95%)	6.47 (5.65 to 7.79)	5.55 (4.96 to 6.67)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
5% level of significance. Hazard ratio is based on stratified Cox proportional hazards regression model. The following stratification factors were evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at the end of Induction.	
Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4164 ^[4]
Method	stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.22

Notes:

[4] - Stratification factors evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at end of Induction.

Secondary: Kaplan-Meier Estimate of Overall Survival (OS) Over Entire Study

End point title	Kaplan-Meier Estimate of Overall Survival (OS) Over Entire Study
-----------------	--

End point description:

Overall survival was defined as the time in months from Day 1 of treatment for the Induction part to death from any cause. Subjects who were alive at the time of analysis had their OS censored at the date or last contact or clinical cut-off, whichever was earlier. The last contact date was the date of the last record in the database, or if the subject was lost to follow-up, the last known date that the subject was alive. The intent to treat population in the maintenance part included all randomized subjects regardless of whether the subject received any study drug or had any efficacy assessments collected.

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

End point timeframe:

Between Day 1 of treatment in the Induction Part to death from any cause; up to 01 August 2019; survival follow up was 55.89 months.

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: months				
median (confidence interval 95%)	20.57 (17.05 to 24.05)	15.05 (10.81 to 22.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
5% level of significance. Hazard ratio is based on stratified Cox proportional hazards regression model. The following stratification factors were evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at the end of Induction.	
Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0381 ^[5]
Method	stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.98

Notes:

[5] - Stratification factors evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at end of Induction, and tumor response (CR/PR or SD) at end of Induction.

Secondary: Percentage of Participants Who Achieved a Confirmed Overall Response of Complete Response or Partial Response (Overall Response Rate) In Maintenance Beyond the Response in Induction

End point title	Percentage of Participants Who Achieved a Confirmed Overall Response of Complete Response or Partial Response (Overall Response Rate) In Maintenance Beyond the Response in Induction
-----------------	---

End point description:

Overall response in the maintenance period was defined as the percentage of participants who showed an improvement in best overall response from stable disease (SD) or partial response (PR) during Induction to a Complete Response (CR) or PR during Maintenance according to RECIST 1.1 criteria and confirmed in no less than 28 days. Evaluation takes as reference the lesion measurement or status at the last tumor assessment before randomization to maintenance. The 95% CI was calculated using Clopper-Pearson method. RECIST 1.1 Definition: - CR-disappearance of all target lesions; any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. - PR-at least a 30% decrease in the sum of diameters of target lesions from baseline. - SD-neither sufficient shrinkage to qualify for PR nor sufficient increase of lesions to qualify for progressive disease. Included the ITT population of participants randomized to maintenance period.

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

End point timeframe:

For the Induction period the maximum treatment was 19 weeks. For the maintenance period the maximum treatment was 150 weeks.

End point values	Nab-Paclitaxel + Best Supportive Care (BSC)	Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	66		
Units: percentage of participants				

number (confidence interval 95%)	9.6 (5.2 to 15.8)	3.0 (0.4 to 10.5)		
----------------------------------	-------------------	-------------------	--	--

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Nab-Paclitaxel + Best Supportive Care (BSC) v Best Supportive Care (BSC)
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	= 0.0978
Method	Cochran-Mantel-Haenszel
Parameter estimate	Overall Response Rate Ratio
Point estimate	3.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.733
upper limit	13.574

Notes:

[6] - 5% level of significance.

Secondary: Percentage of Participants Who Achieved Disease Control (Disease Control Rate) by Investigator Assessment During Induction and Over the Entire Study

End point title	Percentage of Participants Who Achieved Disease Control (Disease Control Rate) by Investigator Assessment During Induction and Over the Entire Study
-----------------	--

End point description:

Disease control rate was defined as the percentage of subjects who had radiologic CR, PR or SD for ≥ 6 weeks according to RECIST 1.1 criteria (investigator judgement). Only subjects with a confirmed CR/PR are included. Two timeframes are offered: Time to confirmed response within the Induction timeframe and Time to Confirmed Response Over the Entire Study, i.e. the time from Day 1 of treatment in Induction to the first occurrence of CR/PR any time during the study. RECIST 1.1 definition: CR- disappearance of all target lesions; any pathological lymph nodes (whether target or non target) must have reduction in short axis to < 10 mm. PR- at least a 30% decrease in the sum of diameters of target lesions from baseline; SD- neither sufficient shrinkage to qualify for PR nor sufficient increase of lesions to qualify for PD. Induction = the ITT population of subjects treated during Induction. Entire Study = the entire experience of the ITT population of subjects randomized to maintenance.

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

End point timeframe:

Induction is from Day 1 to a maximum treatment time of 19 weeks; entire study from Day 1 Induction through Maintenance up to PD; up to 01 August 2019; maximum treatment duration was 234.1 weeks for entire study.

End point values	All Participants - Induction	Nab-Paclitaxel + BSC: Induction + Maintenance	BSC: Induction + Maintenance	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	420	136	66	
Units: percentage of participants				
number (confidence interval 95%)	47.9 (43.0 to 52.8)	99.3 (96.0 to 100.0)	100.0 (94.6 to 100.0)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: The rate ratio and its 95% confidence interval are based on non-stratified analysis.	
Comparison groups	Nab-Paclitaxel + BSC: Induction + Maintenance v BSC: Induction + Maintenance
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Disease control rate ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.978
upper limit	1.007

Secondary: Time to Confirmed Response During Induction and Over the Entire Study

End point title	Time to Confirmed Response During Induction and Over the Entire Study
End point description: Time to confirmed complete or partial response (CR/PR) is defined as the time from day 1 of treatment in Induction to the first occurrence of confirmed CR/PR. Two timeframes are offered: - Time to confirmed response within the Induction timeframe. - Time to Confirmed Response Over the Entire Study, i.e. the time from Day 1 of treatment in Induction to the first occurrence of confirmed CR/PR any time during the study. Only participants with a confirmed CR or PR are included in this summary. Includes the ITT population of participants who had a response. Induction includes the ITT population of participants treated during Induction who had a response. Induction+Maintenance includes the ITT population of participants randomized to Maintenance who had a response.	
End point type	Secondary
End point timeframe: Induction is from Day 1 to a maximum treatment time of 19 weeks; entire study from Day 1 Induction through Maintenance up to PD; up to 01 August 2019; maximum treatment duration was 234.1 weeks for entire study.	

End point values	All Participants - Induction	Nab-Paclitaxel + BSC: Induction + Maintenance	BSC: Induction + Maintenance	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	126	94	38	
Units: months				
median (full range (min-max))	1.446 (1.15 to 4.60)	1.478 (1.15 to 8.51)	1.413 (1.18 to 4.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate for Duration of Response Over the Entire Study

End point title	Kaplan-Meier Estimate for Duration of Response Over the Entire Study
-----------------	--

End point description:

Duration of overall response was measured from the time criteria were first met for CR/PR until the first date the recurrent or progressive disease (PD) was radiologically documented. Participants who did not have PD after the response were censored on the date of last tumor assessment. If a participant died before PD, the participant was censored on the date of death. The ITT population of participants randomized to the maintenance period and had a confirmed partial or complete response.

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

End point timeframe:

Between Day 1 of the Induction Part through to the date of disease progression or death; up to 01 August 2019; maximum treatment duration was 234.1 weeks for entire study.

End point values	Nab-Paclitaxel + BSC: Induction + Maintenance	BSC: Induction + Maintenance		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	38		
Units: months				
median (confidence interval 95%)	5.95 (4.60 to 7.06)	4.60 (3.68 to 5.49)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
----------------------------	------------------------

Statistical analysis description:

Hazard ratio was based on stratified Cox proportional hazards regression model. The following stratification factors were evaluated in the sparse strata elimination algorithm: stage of disease (IIIB or IV) at diagnosis, ECOG performance status (0 or 1) at the end of Induction, and tumor response (CR/PR or SD) at the end of Induction.

Comparison groups	Nab-Paclitaxel + BSC: Induction + Maintenance v BSC: Induction + Maintenance
-------------------	--

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.47

Secondary: Participants with Treatment-Emergent Adverse Events (TEAEs) in the Induction Part

End point title	Participants with Treatment-Emergent Adverse Events (TEAEs) in the Induction Part
-----------------	---

End point description:

TEAE in the Induction part is defined as any adverse event (AE) with an onset on or after Day 1 of treatment for the Induction part, and on or before the day of randomization for subjects who entered into the Maintenance part, or, for subjects who did not enter into the Maintenance part, before the treatment discontinuation date plus 28 days or any serious AE which occurred thereafter but was determined to be related to any study drug by the investigator. 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. Safety population of participants treated during induction period.

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

End point timeframe:

Day 1 of Induction up Week 23 (maximum treatment in Induction plus 4 weeks if not continuing into Maintenance)

End point values	All Participants - Induction	TEAE Specific to Nab- Paclitaxel	TEAE Specific to Carboplatin	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	420	420 ^[7]	420	
Units: participants				
TEAE	419	99999	99999	
Serious TEAE	177	99999	99999	
Severity Grade 3/4 TEAE	337	99999	99999	
Severity Grade 3 or higher TEAE	340	99999	99999	
Treatment-related (trt-related) TEAE	408	407	394	
Trt-related serious TEAE	82	80	73	
TEAE-study drug dose reduced or interrupted	341	340	291	
Trt-related TEAE-dose reduced or interrupted	301	292	236	
TEAE-study drug withdrawn	55	55	53	
Trt-related TEAE-study drug withdrawn	35	34	29	
TEAE-outcome of death	32	99999	99999	
Trt-related TEAE-outcome of death	7	7	6	

Notes:

[7] - 99999 = Category not specific to study intervention

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Treatment-Emergent Adverse Events (TEAEs) Over the Entire Study

End point title	Participants with Treatment-Emergent Adverse Events (TEAEs) Over the Entire Study
-----------------	---

End point description:

TEAE over entire study is defined as any adverse event (AE) with an onset on or after Day 1 of treatment for the Induction part, and before the treatment discontinuation date plus 28 days, or any serious AE which occurred thereafter but was determined to be related to any study drug by the investigator. 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. Safety population of participants randomized into maintenance, inclusive of both the induction and maintenance periods.

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

End point timeframe:

From Day 1 of study drug treatment up to 01 August 2019; maximum treatment duration was 234.1 weeks, plus 28 days (4 weeks)

End point values	Nab-Paclitaxel + BSC: Induction + Maintenance	Nab-Paclitaxel + BSC: TEAE Specific to Nab-Paclitaxel	Nab-Paclitaxel + BSC: TEAE Specific to Carboplatin	Nab-Paclitaxel + BSC: TEAE Specific to BSC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130	130	130	130
Units: participants				
TEAE	130	99999	99999	99999
Serious TEAE	54	99999	99999	99999
Severity Grade 3/4 TEAE	108	99999	99999	99999
Severity Grade 3 or higher TEAE	109	99999	99999	99999
Treatment-related (trt-related) TEAE	129	129	123	18
Trt-related serious TEAE	22	22	16	1
TEAE-study drug dose reduced or interrupted	115	113	95	17
Trt-related TEAE-dose reduced or interrupted	107	104	85	0
TEAE-study drug withdrawn	22	22	1	20
Trt-related TEAE- study drug withdrawn	18	18	1	2
TEAE-outcome of death	4	99999	99999	99999
Trt-related TEAE-outcome of death	0	0	0	0

End point values	BSC: Induction + Maintenance	BSC: TEAE Specific to Nab-Paclitaxel	BSC: TEAE Specific to Carboplatin	BSC: TEAE Specific to BSC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	62	62	62
Units: participants				
TEAE	62	99999	99999	99999
Serious TEAE	21	99999	99999	99999
Severity Grade 3/4 TEAE	48	99999	99999	99999
Severity Grade 3 or higher TEAE	48	99999	99999	99999
Treatment-related (trt-related) TEAE	61	61	58	1
Trt-related serious TEAE	8	8	7	0
TEAE-study drug dose reduced or interrupted	52	52	45	1
Trt-related TEAE-dose reduced or interrupted	45	45	37	0
TEAE-study drug withdrawn	0	1	1	0
Trt-related TEAE- study drug withdrawn	1	0	0	0
TEAE-outcome of death	2	99999	99999	99999
Trt-related TEAE-outcome of death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1. Induction: Day 1 up to 23 weeks (maximum treatment in induction plus (+) 4 weeks if not continuing into maintenance) 2. Nab-Paclitaxel + Best Supportive Care Randomization into maintenance up to 154 weeks (maximum treatment in maintenance + 4 weeks)

Adverse event reporting additional description:

3. BSC: Randomization into Maintenance up to 120 weeks (maximum treatment in Maintenance + 4 weeks); TEAEs are reported up to the data cut off date of 01 August 2019.

All-Cause Mortality is reported for the ITT population (received at least 1 dose of study treatment regardless of whether any efficacy exams were collected) up to 01 August 2019.

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	V21.0
--------------------	-------

Reporting groups

Reporting group title	All Participants - Induction
-----------------------	------------------------------

Reporting group description:

During induction, participants received nab-paclitaxel plus carboplatin as standard of care: nab-paclitaxel 100 mg/m² IV infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle and carboplatin AUC = 6 mg*min/mL IV on Day 1 of each 21-day cycle. If the participant had radiological or clinical progressive disease (PD), they were discontinued from the study and not followed. If the participant had a complete response, partial response, or stable disease without PD at the end of 4 cycles, he/she were eligible to be randomised to the maintenance phase.

Reporting group title	Nab-Paclitaxel + Best Supportive Care (Maintenance)
-----------------------	---

Reporting group description:

Maintenance Phase: Following randomization, participants in this treatment arm were administered nab-paclitaxel 100 mg/m² by IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle, plus best supportive care until disease progression.

Reporting group title	Best Supportive Care (Maintenance)
-----------------------	------------------------------------

Reporting group description:

Maintenance Phase: Following randomization, participants in this treatment arm were administered best supportive care (only) until disease progression.

Serious adverse events	All Participants - Induction	Nab-Paclitaxel + Best Supportive Care (Maintenance)	Best Supportive Care (Maintenance)
Total subjects affected by serious adverse events			
subjects affected / exposed	177 / 420 (42.14%)	32 / 130 (24.62%)	13 / 62 (20.97%)
number of deaths (all causes)	32	3	2
number of deaths resulting from adverse events	7	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	11 / 420 (2.62%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	4 / 12	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	6 / 420 (1.43%)	3 / 130 (2.31%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 6	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site pain			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	5 / 420 (1.19%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 1	0 / 0
Fatigue			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	4 / 420 (0.95%)	0 / 130 (0.00%)	2 / 62 (3.23%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	6 / 420 (1.43%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	4 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial haemorrhage			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease				
subjects affected / exposed	7 / 420 (1.67%)	0 / 130 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1	
Cough				
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Dyspnoea				
subjects affected / exposed	15 / 420 (3.57%)	0 / 130 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 16	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Epistaxis				
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Haemoptysis				
subjects affected / exposed	5 / 420 (1.19%)	0 / 130 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0	
Hypoxia				
subjects affected / exposed	7 / 420 (1.67%)	0 / 130 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Laryngospasm				
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pleural effusion				
subjects affected / exposed	6 / 420 (1.43%)	0 / 130 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0	
Pneumonia aspiration				

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	9 / 420 (2.14%)	2 / 130 (1.54%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 10	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	7 / 420 (1.67%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	3 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			

subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspiration bronchial			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	8 / 420 (1.90%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	1 / 11	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			

subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial haemorrhage			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	2 / 420 (0.48%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 420 (0.48%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Syncope			
subjects affected / exposed	4 / 420 (0.95%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 420 (4.05%)	3 / 130 (2.31%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	21 / 23	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	8 / 420 (1.90%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	8 / 8	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	4 / 420 (0.95%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	12 / 420 (2.86%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	12 / 12	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	4 / 420 (0.95%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	5 / 420 (1.19%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	3 / 420 (0.71%)	1 / 130 (0.77%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	1 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	11 / 420 (2.62%)	1 / 130 (0.77%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	6 / 11	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	2 / 420 (0.48%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nausea			

subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis relapsing			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 420 (0.48%)	2 / 130 (1.54%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	7 / 420 (1.67%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	5 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 420 (0.00%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 420 (0.48%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			

subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	4 / 420 (0.95%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraspinal abscess			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	24 / 420 (5.71%)	4 / 130 (3.08%)	3 / 62 (4.84%)
occurrences causally related to treatment / all	6 / 28	0 / 4	0 / 4
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 1
Sepsis			

subjects affected / exposed	9 / 420 (2.14%)	3 / 130 (2.31%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	5 / 11	0 / 4	0 / 0
deaths causally related to treatment / all	2 / 3	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 420 (0.24%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	5 / 420 (1.19%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 420 (0.00%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	14 / 420 (3.33%)	1 / 130 (0.77%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	8 / 14	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	3 / 420 (0.71%)	0 / 130 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 420 (0.48%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	1 / 420 (0.24%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	All Participants - Induction	Nab-Paclitaxel + Best Supportive Care (Maintenance)	Best Supportive Care (Maintenance)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	417 / 420 (99.29%)	122 / 130 (93.85%)	45 / 62 (72.58%)
Vascular disorders			
Hypotension			
subjects affected / exposed	50 / 420 (11.90%)	9 / 130 (6.92%)	1 / 62 (1.61%)
occurrences (all)	63	12	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	73 / 420 (17.38%)	12 / 130 (9.23%)	1 / 62 (1.61%)
occurrences (all)	121	16	1
Chills			
subjects affected / exposed	22 / 420 (5.24%)	3 / 130 (2.31%)	1 / 62 (1.61%)
occurrences (all)	23	3	1
Fatigue			
subjects affected / exposed	175 / 420 (41.67%)	24 / 130 (18.46%)	0 / 62 (0.00%)
occurrences (all)	267	40	0
Oedema peripheral			
subjects affected / exposed	48 / 420 (11.43%)	23 / 130 (17.69%)	3 / 62 (4.84%)
occurrences (all)	59	35	3
Pyrexia			
subjects affected / exposed	29 / 420 (6.90%)	10 / 130 (7.69%)	2 / 62 (3.23%)
occurrences (all)	35	11	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	72 / 420 (17.14%)	15 / 130 (11.54%)	9 / 62 (14.52%)
occurrences (all)	83	22	10
Dyspnoea			
subjects affected / exposed	76 / 420 (18.10%)	13 / 130 (10.00%)	3 / 62 (4.84%)
occurrences (all)	94	16	3
Epistaxis			
subjects affected / exposed	79 / 420 (18.81%)	4 / 130 (3.08%)	1 / 62 (1.61%)
occurrences (all)	97	4	1

Haemoptysis			
subjects affected / exposed	28 / 420 (6.67%)	5 / 130 (3.85%)	2 / 62 (3.23%)
occurrences (all)	32	5	2
Productive cough			
subjects affected / exposed	19 / 420 (4.52%)	10 / 130 (7.69%)	3 / 62 (4.84%)
occurrences (all)	20	13	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	30 / 420 (7.14%)	4 / 130 (3.08%)	0 / 62 (0.00%)
occurrences (all)	31	5	0
Insomnia			
subjects affected / exposed	53 / 420 (12.62%)	5 / 130 (3.85%)	2 / 62 (3.23%)
occurrences (all)	57	5	2
Investigations			
Blood creatinine increased			
subjects affected / exposed	22 / 420 (5.24%)	5 / 130 (3.85%)	0 / 62 (0.00%)
occurrences (all)	33	8	0
Neutrophil count decreased			
subjects affected / exposed	29 / 420 (6.90%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences (all)	40	0	0
Platelet count decreased			
subjects affected / exposed	26 / 420 (6.19%)	0 / 130 (0.00%)	0 / 62 (0.00%)
occurrences (all)	47	0	0
Weight decreased			
subjects affected / exposed	42 / 420 (10.00%)	9 / 130 (6.92%)	2 / 62 (3.23%)
occurrences (all)	52	13	2
Weight increased			
subjects affected / exposed	6 / 420 (1.43%)	8 / 130 (6.15%)	0 / 62 (0.00%)
occurrences (all)	8	11	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	39 / 420 (9.29%)	7 / 130 (5.38%)	0 / 62 (0.00%)
occurrences (all)	61	8	0
Nervous system disorders			
Dizziness			

subjects affected / exposed	57 / 420 (13.57%)	12 / 130 (9.23%)	1 / 62 (1.61%)
occurrences (all)	66	17	1
Dysgeusia			
subjects affected / exposed	56 / 420 (13.33%)	2 / 130 (1.54%)	0 / 62 (0.00%)
occurrences (all)	58	2	0
Headache			
subjects affected / exposed	23 / 420 (5.48%)	4 / 130 (3.08%)	5 / 62 (8.06%)
occurrences (all)	26	5	5
Peripheral sensory neuropathy			
subjects affected / exposed	152 / 420 (36.19%)	56 / 130 (43.08%)	6 / 62 (9.68%)
occurrences (all)	233	107	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	256 / 420 (60.95%)	24 / 130 (18.46%)	6 / 62 (9.68%)
occurrences (all)	587	36	8
Leukopenia			
subjects affected / exposed	80 / 420 (19.05%)	1 / 130 (0.77%)	1 / 62 (1.61%)
occurrences (all)	187	1	1
Neutropenia			
subjects affected / exposed	225 / 420 (53.57%)	14 / 130 (10.77%)	0 / 62 (0.00%)
occurrences (all)	566	23	0
Thrombocytopenia			
subjects affected / exposed	163 / 420 (38.81%)	9 / 130 (6.92%)	2 / 62 (3.23%)
occurrences (all)	348	11	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	27 / 420 (6.43%)	4 / 130 (3.08%)	2 / 62 (3.23%)
occurrences (all)	32	4	2
Constipation			
subjects affected / exposed	130 / 420 (30.95%)	14 / 130 (10.77%)	0 / 62 (0.00%)
occurrences (all)	170	18	0
Diarrhoea			
subjects affected / exposed	158 / 420 (37.62%)	18 / 130 (13.85%)	4 / 62 (6.45%)
occurrences (all)	239	27	7
Dyspepsia			

subjects affected / exposed	37 / 420 (8.81%)	3 / 130 (2.31%)	1 / 62 (1.61%)
occurrences (all)	39	3	1
Nausea			
subjects affected / exposed	191 / 420 (45.48%)	16 / 130 (12.31%)	2 / 62 (3.23%)
occurrences (all)	284	22	2
Stomatitis			
subjects affected / exposed	44 / 420 (10.48%)	2 / 130 (1.54%)	1 / 62 (1.61%)
occurrences (all)	56	2	1
Vomiting			
subjects affected / exposed	93 / 420 (22.14%)	12 / 130 (9.23%)	2 / 62 (3.23%)
occurrences (all)	131	14	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	105 / 420 (25.00%)	6 / 130 (4.62%)	2 / 62 (3.23%)
occurrences (all)	123	6	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 420 (6.19%)	12 / 130 (9.23%)	2 / 62 (3.23%)
occurrences (all)	27	16	2
Back pain			
subjects affected / exposed	23 / 420 (5.48%)	12 / 130 (9.23%)	6 / 62 (9.68%)
occurrences (all)	31	13	8
Muscular weakness			
subjects affected / exposed	30 / 420 (7.14%)	4 / 130 (3.08%)	3 / 62 (4.84%)
occurrences (all)	38	5	4
Myalgia			
subjects affected / exposed	26 / 420 (6.19%)	2 / 130 (1.54%)	1 / 62 (1.61%)
occurrences (all)	31	2	1
Pain in extremity			
subjects affected / exposed	24 / 420 (5.71%)	10 / 130 (7.69%)	1 / 62 (1.61%)
occurrences (all)	29	15	3
Infections and infestations			
Pneumonia			
subjects affected / exposed	11 / 420 (2.62%)	9 / 130 (6.92%)	1 / 62 (1.61%)
occurrences (all)	11	12	1
Upper respiratory tract infection			

subjects affected / exposed	18 / 420 (4.29%)	11 / 130 (8.46%)	2 / 62 (3.23%)
occurrences (all)	18	12	3
Urinary tract infection			
subjects affected / exposed	28 / 420 (6.67%)	7 / 130 (5.38%)	4 / 62 (6.45%)
occurrences (all)	30	7	6
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	101 / 420 (24.05%)	17 / 130 (13.08%)	3 / 62 (4.84%)
occurrences (all)	123	18	3
Dehydration			
subjects affected / exposed	57 / 420 (13.57%)	4 / 130 (3.08%)	1 / 62 (1.61%)
occurrences (all)	75	4	1
Hypocalcaemia			
subjects affected / exposed	23 / 420 (5.48%)	3 / 130 (2.31%)	0 / 62 (0.00%)
occurrences (all)	35	3	0
Hypokalaemia			
subjects affected / exposed	61 / 420 (14.52%)	6 / 130 (4.62%)	2 / 62 (3.23%)
occurrences (all)	92	10	2
Hypomagnesaemia			
subjects affected / exposed	58 / 420 (13.81%)	9 / 130 (6.92%)	2 / 62 (3.23%)
occurrences (all)	97	11	2
Hyponatraemia			
subjects affected / exposed	29 / 420 (6.90%)	3 / 130 (2.31%)	0 / 62 (0.00%)
occurrences (all)	49	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2014	1. Incorporated the recommendation received from the US FDA to remove the cross-over part of the trial 2. Enabled potential participation of centers outside of the US.
07 May 2015	1. Incorporated the intention to produce and review summaries of the QoL and biomarker data (Induction part only, pre-randomization) while the study was ongoing. 2. Clarified the secondary objectives (DCR over entire study was added) and the definitions of the analysis populations for the Induction and Maintenance parts.
18 April 2016	1. Addendum A clarified protocol details following requests from the United Kingdom regulatory health authority. Addendum A was implemented only in the United Kingdom. 2. Added text regarding true abstinence and periodic abstinence for Inclusion Criterion 17. 3. Added text to Table of Events regarding investigator discussion of possible side effects, peripheral neuropathy assessment, and AE evaluation. 4. Added text to concomitant medications and procedures regarding concurrent carboplatin therapy with nephrotoxic drugs, ototoxic drugs, and warfarin. Added text regarding concomitant administration of paclitaxel with medications known to inhibit or induce either Cytochrome P450 (CYP) 2C8 or CYP3A4. 5. Added text regarding events considered sufficient reasons for discontinuing a subject from IP.
13 March 2017	1. Incorporated changes to the study sample size (reduction of subject population and targeted number of PFS events).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported