Clinical trial results:
A randomized phase II study evaluating different schedules of nab-Paclitaxelin metastatic breast cancer.

Summary

EudraCT number	2012-003058-10
Trial protocol	BE SI IE IT ES
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	28 March 2021
First version publication date	28 March 2021

Trial information

Trial identification

Sponsor protocol code	IBCSG 42-12/BIG 2-12 SNAP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01746225
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IBCSG
Sponsor organisation address	Effingerstrasse 40, Bern, Switzerland, 3008
Public contact	IBCSG Coordinating Center, International Breast Cancer Study Group (IBCSG), +41 31389 93 91, regulatoryoffice@ibcsg.org
Scientific contact	IBCSG Coordinating Center, International Breast Cancer Study Group (IBCSG), +41 31389 93 91, regulatoryoffice@ibcsg.org

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	Interim
Date of interim/final analysis	02 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of three different schedules of nab-Paclitaxel administration, as measured by progression-free survival (PFS), using the historical reference of PFS of docetaxel for first-line treatment of metastatic breast cancer.

Protection of trial subjects:

The IBCSG has an Office for Human Research Protection (OHRP) Federal Wide Assurance (FWA00009439) and follows all of the policies and procedures that are part of that assurance. All potential subjects for this trial received a full explanation of the trial, its purpose, treatments, risks, benefits, and of other items.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovenia: 7
Country: Number of subjects enrolled	Spain: 42
Country: Number of subjects enrolled	Belgium: 33
Country: Number of subjects enrolled	Ireland: 61
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	Switzerland: 75
Worldwide total number of subjects	258
EEA total number of subjects	183

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)	160
From 65 to 84 years	98
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was activated on 30 October 2012, and the first patient was enrolled on 16 April 2013. The study was closed to enrolment on 7 August 2015. 258 patients had been accrued in 35 centers in 5 countries.

Pre-assignment

Screening details:

No screening details available.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

nab-Paclitaxel 150 mg/m2 days 1, 8, 15 every 28 days for 3 cycles, and nab-Paclitaxel 150 mg/m2 days 1, 15 every 28 days during the fourth and subsequent cycles

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:

During the induction phase, patients receive for 3 cycles:
nab-Paclitaxel 125 mg/m2 IV infusion over 30 minutes on days 1, 8, 15 every 28 days

In the absence of progressive disease, patients continue to the maintenance phase and receive:
nab-Paclitaxel 150 mg/m2 IV infusion over 30 minutes on days 1 and 15 every 28 days

Arm title	Arm B

Arm description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

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:

During the induction phase, patients receive for 3 cycles:
nab-Paclitaxel 125 mg/m2 IV infusion over 30 minutes on days 1, 8, 15 every 28 days

In the absence of progressive disease, patients continue to the maintenance phase and receive:
nab-Paclitaxel 100 mg/m2 IV infusion over 30 minutes on days 1, 8 and 15 every 28 days

Arm title	Arm C

Arm description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

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:

During the induction phase, patients receive for 3 cycles:
nab-Paclitaxel 125 mg/m2 IV infusion over 30 minutes on days 1, 8, 15 every 28 days

In the absence of progressive disease, patients continue to the maintenance phase and receive:
nab-Paclitaxel 75 mg/m2 IV infusion over 30 minutes on days 1, 8, 15 and 22 every 28 days

Number of subjects in period 1[1]	Arm A	Arm B	Arm C
Started	83	86	86
Completed	43	40	43
Not completed	40	46	43
Consent withdrawn by subject	5	15	19
Physician decision	14	11	3
Adverse Event	15	12	17
Death	1	-	1
Continuing Treatment	5	8	3

Notes:

[1] - 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: Intention-to-treat population. Arm A had randomized 86 patient, but only 83 were analyzed. 3 patients excluded from analysis, who immediately withdrew consent or cancelled treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
nab-Paclitaxel 150 mg/m2 days 1, 8, 15 every 28 days for 3 cycles, and nab-Paclitaxel 150 mg/m2 days 1, 15 every 28 days during the fourth and subsequent cycles	

Reporting group title	Arm B
Reporting group description:	
Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)	

Reporting group title	Arm C
Reporting group description:	
Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	83	86	86
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	58	56	60
inter-quartile range (Q1-Q3)	49 to 67	45 to 65	52 to 68
Gender categorical Units: Subjects			
Female	83	86	86
Male	0	0	0

Reporting group values	Total		
Number of subjects	255		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)	-		
Gender categorical			
Units: Subjects			
Female	255		
Male	0		

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

nab-Paclitaxel 150 mg/m2 days 1, 8, 15 every 28 days for 3 cycles, and nab-Paclitaxel 150 mg/m2 days 1, 15 every 28 days during the fourth and subsequent cycles

Reporting group title	Arm B

Reporting group description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

Reporting group title	Arm C

Reporting group description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)[1]

End point description:

Disease response and progression will be evaluated according to the revised Response Evaluation Criteria in Solid Tumors (RECIST V 1.1) Patients may have measurable or non-measurable disease. CT can is the method to measure lesion.

End point type	Primary

End point timeframe:

At the end of the third induction cycle and during maintenance nab-Paclitaxel every three months until PD

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: For each arm separately, PFS was compared to the historic PFS of first-line docetaxel using a one-sample one-sided log-rank test, of the null hypothesis, H0: median PFS≤7 months vs. H1: median PFS>7 months.

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[2]	86	86	
Units: months				
median (confidence interval 90%)	7.9 (6.8 to 8.4)	9.0 (8.1 to 10.9)	8.5 (6.7 to 9.5)	

Notes:

[2] - Three patients (either untreated or cancelled) were excluded from this final analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Feasibility

End point title	Feasibility

End point description:

Whether or not the patient completed treatment according to the protocol for at least 24 weeks. Patients

who progressed within 24 weeks were considered as not completing.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks follow-up

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	86	86	
Units: Participants	40	43	44	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control: Overall Response of Stable Disease for a Duration of ≥24 Weeks

End point title	Disease Control: Overall Response of Stable Disease for a Duration of ≥24 Weeks

End point description:

Overall response of stable disease (or non-CR/non-PD for patients with non-measurable disease) for a duration of ≥24 weeks, or better (i.e., partial or complete response) according to RECIST criteria [Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR.]

End point type	Secondary

End point timeframe:

From date of randomization until the date of first documented progression or date of death from any cause, whichever came first, assessed up to 18 months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	86	86	
Units: Participants	54	59	52	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

Best response according to RECIST 1.1 criteria [assessed by MRI] recorded from the start of treatment

across all time points until end of study treatment. Confirmation of partial or complete response by an additional scan was not requested in this trial.

End point type	Secondary

End point timeframe:

From date of randomization until the date of first documented progression or date of death from any cause, whichever came first, assessed up to 18 months.

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	86	86	
Units: Participants				
Complete Response (CR)	5	6	4	
Partial Response (PR)	34	41	35	
Stable Disease (SD)/Non-CR/Non-PD	39	33	31	
Progressive Disease (PD)	3	5	11	
Not Evaluable (NE)	2	1	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Time from randomization until death from any cause, or censored at date last known alive.

No upper limit for the confidence interval was reported, as insufficient number of participants with events. For the sake of completeness a fictive value of 30 was entered.

End point type	Secondary

End point timeframe:

Reported after 18.2 months median follow-up since randomization.

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	86	86	
Units: Months				
median (confidence interval 90%)	25.8 (16.9 to 30)	26.2 (21.0 to 30)	25.5 (22.7 to 30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Physical Well-being (Change From Day 1 of Cycle 4 to Day 1 of Cycle 6)

End point title	Changes in Physical Well-being (Change From Day 1 of Cycle 4 to Day 1 of Cycle 6)

End point description:

Changes in Physical Well-being (Change From Day 1 of Cycle 4 to Day 1 of Cycle 6). Key domains will be assessed by global linear analogue self-assessment (LASA) indicator. The LASAindicators range from 0 to 100. For all QL measures higher scores reflect a better condition (e.g.,better physical well-being).

End point type	Secondary

End point timeframe:

Assessed from day 1 of cycle 4 through day 1 of cycle 12.

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	72	61	
Units: Units on a scale				
arithmetic mean (confidence interval 95%)	-2 (-9 to 5)	1 (-6 to 7)	4 (-4 to 11)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

An adverse event is defined as any untoward medical occurrence that occurs from the first dose of study medication until 30 days after the final dose, regardless of whether it is considered related to a medication.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Arm A

Reporting group description:

nab-Paclitaxel 150 mg/m2 days 1, 8, 15 every 28 days for 3 cycles, and nab-Paclitaxel 150 mg/m2 days 1, 15 every 28 days during the fourth and subsequent cycles

Reporting group title	Arm B

Reporting group description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

Reporting group title	Arm C

Reporting group description:

Induction phase: 3 cycles of nab-Paclitaxel days 1, 8, 15. Maintenance phase with three maintenance schedules of nab-Paclitaxel (same total dose per cycle, different number of administrations)

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 83 (61.45%)	43 / 86 (50.00%)	57 / 86 (66.28%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid Cancer			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Fibroids			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
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			
Thromboembolic event			

subjects affected / exposed	2 / 83 (2.41%)	0 / 86 (0.00%)	3 / 86 (3.49%)
occurrences causally related to treatment / all	0 / 2	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 83 (1.20%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	1 / 83 (1.20%)	1 / 86 (1.16%)	0 / 86 (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
Pain			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Immune system disorders			
Anaphylaxis			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Dyspnea			
subjects affected / exposed	1 / 83 (1.20%)	2 / 86 (2.33%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pleural effusion			

subjects affected / exposed	1 / 83 (1.20%)	1 / 86 (1.16%)	0 / 86 (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
COPD Exacerbation			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic Chest Pain			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Creatinine increased			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
White blood cell decreased			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	2 / 83 (2.41%)	1 / 86 (1.16%)	0 / 86 (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
Supraventricular Tachycardia			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 83 (2.41%)	1 / 86 (1.16%)	0 / 86 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Diarrhea			
subjects affected / exposed	1 / 83 (1.20%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	2 / 83 (2.41%)	0 / 86 (0.00%)	0 / 86 (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
Pancreatitis			

subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation +/- gastritis			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Diverticulitis			
subjects affected / exposed	0 / 83 (0.00%)	3 / 86 (3.49%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea and Vomiting			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Calculi			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Urinary tract obstruction			

subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Renal Failure			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone Fracture (Rib)			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Spinal fracture			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Back pain			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Bone pain			
subjects affected / exposed	3 / 83 (3.61%)	0 / 86 (0.00%)	0 / 86 (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
Osteonecrosis of jaw			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
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			
Appendicitis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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

Bronchial infection			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	2 / 83 (2.41%)	0 / 86 (0.00%)	4 / 86 (4.65%)
occurrences causally related to treatment / all	2 / 2	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 83 (1.20%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory infection			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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 Infection			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Port-a-Cath Infection			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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
Metabolism and nutrition disorders			

Hypokalemia			
subjects affected / exposed	1 / 83 (1.20%)	0 / 86 (0.00%)	0 / 86 (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
Hypophosphatemia			
subjects affected / exposed	0 / 83 (0.00%)	1 / 86 (1.16%)	0 / 86 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 83 (93.98%)	83 / 86 (96.51%)	80 / 86 (93.02%)
Investigations			
Neutrophil count decreased			
subjects affected / exposed	28 / 83 (33.73%)	35 / 86 (40.70%)	42 / 86 (48.84%)
occurrences (all)	28	35	42
Platelet count decreased			
subjects affected / exposed	8 / 83 (9.64%)	8 / 86 (9.30%)	4 / 86 (4.65%)
occurrences (all)	8	8	4
Cardiac disorders			
Heart Failure			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	3
Sinus Tachycardia			
subjects affected / exposed	2 / 83 (2.41%)	4 / 86 (4.65%)	3 / 86 (3.49%)
occurrences (all)	2	4	3
Nervous system disorders			
Peripheral Sensory Neuropathy			
subjects affected / exposed	51 / 83 (61.45%)	58 / 86 (67.44%)	55 / 86 (63.95%)
occurrences (all)	51	58	55
Recurrent Laryngeal nerve Palsy			
subjects affected / exposed	0 / 83 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			

Anemia			
subjects affected / exposed	46 / 83 (55.42%)	55 / 86 (63.95%)	55 / 86 (63.95%)
occurrences (all)	46	55	55
Immune system disorders			
Allergic Reaction			
subjects affected / exposed	8 / 83 (9.64%)	4 / 86 (4.65%)	4 / 86 (4.65%)
occurrences (all)	8	4	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	32 / 83 (38.55%)	31 / 86 (36.05%)	40 / 86 (46.51%)
occurrences (all)	32	31	40
Vomiting			
subjects affected / exposed	10 / 83 (12.05%)	11 / 86 (12.79%)	17 / 86 (19.77%)
occurrences (all)	10	11	17
Diarrhea			
subjects affected / exposed	21 / 83 (25.30%)	28 / 86 (32.56%)	27 / 86 (31.40%)
occurrences (all)	21	28	27
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	2 / 83 (2.41%)	2 / 86 (2.33%)	4 / 86 (4.65%)
occurrences (all)	2	2	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2014	In the original design of this phase II trial, the induction phase planned three cycles of nab-Paclitaxel 150 mg/m2 days 1, 8, 15 every 28 days. Following the first safety review of 48 treated patients, it was decided to modify the dose in the induction phase to 125 mg/m2. The change was included in Amendment 1 (dated 11 August 2014) and this amendment was activated on 5 September 2014.
23 January 2015	Based on recommendations from the IBCSG DSMC, IBCSG decided to increase the total sample size from 240 to 258 patients. The statistical considerations (power calculations) in the protocol were adapted accordingly. Amendment 2 (dated 06 January 2015) was activated on 23 January 2015.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported