Clinical trial results:
ICE II: An investigational randomized phase II-(III) study on epirubicin plus cyclophospamide (or CMF) vs nab-paclitaxel plus capecitabine as adjuvant chemotherapy for elderly non frail patients with an increased risk for relapse of a primary carcinoma of the breast

Summary

EudraCT number	2008-003995-23
Trial protocol	DE
Global end of trial date	24 January 2014

Results information

Result version number	v1 (current)
This version publication date	24 November 2021
First version publication date	24 November 2021
Summary attachment (see zip file)	ICE II CSR Synopsis (CSR ICE 2 Synopse Version 2 10.01.2020 signed.pdf)

Trial information

Trial identification

Sponsor protocol code	GBG52

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204437
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GBG Forschungs GmbH
Sponsor organisation address	Martin Behaim Str. 12, Neu-Isenburg, Germany, 63263
Public contact	Medicine and Research, GBG Forschungs GmbH, +49 610274800, publications@gbg.de
Scientific contact	Medicine and Research, GBG Forschungs GmbH, +49 610274800, publications@gbg.de

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	11 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2013
Global end of trial reached?	Yes
Global end of trial date	24 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the compliance and safety of epirubicin plus cyclophosphamide or CMF (EC/CMF) and nab-paclitaxel in combination with capecitabine (nPX)

Protection of trial subjects:

The trial protocol including amendments, the patient information and the informed consent were reviewed and approved from a properly constituted IRB/IEC for each site prior to the study start. The trial was in compliance with the International Conference on Harmonization (ICH) - Harmonized Tripartite Guideline for Good Clinical Practice (GCP) (E6), and the Commission Directives in the European Community as well as with the applicable German national laws and regulations, and with Declaration of Helsinki and its revisions in all aspects of preparation, monitoring, reporting, auditing, and archiving.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 391
Worldwide total number of subjects	391
EEA total number of subjects	391

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)	0
From 65 to 84 years	391
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 4 years (Q-II 2009 –Q-II 2013) in 63 sites in Germany. 400 patients were randomized and 391 started Treatment: 198 in EC/CMF arm (EC: 182; CMF: 16) and 193 in nPX arm).

Pre-assignment

Screening details:

Female or male >=65yrs, Charlson comorbidity index<=2, ECOG<=2, life expect. >=5yrs, completely resected uni-/bilateral, nonmetastatic primary invasive BC . Patients with pT1/2 pN0/1 and either HER2-positive, HR-negative, grade 3, high uPA or PAI-1 BC or any pT3/4 pN2/3 BC irresp. of additional risk factors and time since axillary surgery of <=3mth

Pre-assignment period milestones

Number of subjects started	391
Number of subjects completed	391

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EC/CMF

Arm description:

Standard treatment with either 4 cycles EC (epirubicin 90mg/m² and cyclophosphamide 600mg/m² IV on day 1 every 3 weeks) (N=182 patients) or 6 cycles CMF (cyclophosphamide 500 mg/m², methotrexate 40mg/m², 5-fluorouracil 600 mg/m² IV on days 1+8 every 4 weeks) (N=16 patients) based on investigators decision

Arm type	Active comparator
Investigational medicinal product name	Epirubicin plus cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: Epirubicin 90 mg/m2, Cyclophosphamide 600 mg/m2
Route: i.v.
Schedule: days 1q22
Duration: 4 cycles or unacceptable toxicity, patient’s request or withdrawal from study

Investigational medicinal product name	CMF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: Cyclophosphamide 500 mg/m2; Methotrexate 40mg/m2, 5-FU 600 mg/m2
Route: i.v.
Schedule: days 1+8 q29
Duration: 6 cycles or unacceptable toxicity, patient’s request or withdrawal from study

Arm title	nP-X

Arm description:

Experimental treatment with 6 cycles nab-paclitaxel (100 mg/m² IV over 30 min, on days weekly in five out of 6 weeks) plus capecitabine (1000 mg/m² PO bid on days 1-14 every 3 weeks).

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m² IV over 30 min, on days weekly in five out of 6 weeks

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1000 mg/m² PO bid on days 1-14 every 3 weeks

Number of subjects in period 1	EC/CMF	nP-X
Started	198	193
Completed	185	124
Not completed	13	69
Adverse event, serious fatal	1	5
Physician decision	2	9
Consent withdrawn by subject	3	18
Adverse event, non-fatal	7	32
other	-	5

Baseline characteristics

Reporting groups	
Reporting group title	EC/CMF
Reporting group description:	
Standard treatment with either 4 cycles EC (epirubicin 90mg/m² and cyclophosphamide 600mg/m² IV on day 1 every 3 weeks) (N=182 patients) or 6 cycles CMF (cyclophosphamide 500 mg/m², methotrexate 40mg/m², 5-fluorouracil 600 mg/m² IV on days 1+8 every 4 weeks) (N=16 patients) based on investigators decision	
Reporting group title	nP-X
Reporting group description:	
Experimental treatment with 6 cycles nab-paclitaxel (100 mg/m² IV over 30 min, on days weekly in five out of 6 weeks) plus capecitabine (1000 mg/m² PO bid on days 1-14 every 3 weeks).	

Reporting group values	EC/CMF	nP-X	Total
Number of subjects	198	193	391
Age categorical Units: Subjects			
64-69	52	49	101
70-80	144	143	287
>80	2	1	3
Gender categorical Units: Subjects			
Female	196	191	387
Male	2	2	4

End points

End points reporting groups

Reporting group title	EC/CMF
Reporting group description:	
Standard treatment with either 4 cycles EC (epirubicin 90mg/m² and cyclophosphamide 600mg/m² IV on day 1 every 3 weeks) (N=182 patients) or 6 cycles CMF (cyclophosphamide 500 mg/m², methotrexate 40mg/m², 5-fluorouracil 600 mg/m² IV on days 1+8 every 4 weeks) (N=16 patients) based on investigators decision	
Reporting group title	nP-X
Reporting group description:	
Experimental treatment with 6 cycles nab-paclitaxel (100 mg/m² IV over 30 min, on days weekly in five out of 6 weeks) plus capecitabine (1000 mg/m² PO bid on days 1-14 every 3 weeks).	

Primary: Compliance

End point title	Compliance
End point description:	
Discontinuations of study treatment	
End point type	Primary
End point timeframe:	
during active study treatment	

End point values	EC/CMF	nP-X		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	193		
Units: percent				
number (not applicable)	13	69		

Statistical analyses

Statistical analysis title	Discontinuations between arms
Statistical analysis description:	
Treatment groups were compared using Fisher's exact test (for binary Parameters).	
Comparison groups	EC/CMF v nP-X
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Primary: Compliance

End point title	Compliance
End point description: Chemotherapy dose reduction	
End point type	Primary
End point timeframe: during active study treatment	

End point values	EC/CMF	nP-X		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	193		
Units: percent				
number (not applicable)	9	112		

Statistical analyses

Statistical analysis title	Chemotherapy dose reduction between arms
Statistical analysis description: Treatment groups were compared using Fisher's exact test (for binary Parameters).	
Comparison groups	nP-X v EC/CMF
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Primary: Compliance

End point title	Compliance
End point description: Cycle delays	
End point type	Primary
End point timeframe: during active study treatment	

End point values	EC/CMF	nP-X		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	193		
Units: percent				
number (not applicable)	35	125		

Statistical analyses

Statistical analysis title	Cycle delays between arms
Statistical analysis description: Treatment groups were compared using Fisher`s exact test (for binary Parameters).	
Comparison groups	EC/CMF v nP-X
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Primary: Compliance

End point title	Compliance
End point description: RTDI in %	
End point type	Primary
End point timeframe: during active study treatment	

End point values	EC/CMF	nP-X		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198[1]	193		
Units: percent				
number (not applicable)	97.5	85.4		

Notes:
[1] - RTDI EC 100.0%, RTDI CMF 94.9%

Statistical analyses

Statistical analysis title	RTDI between arms
Statistical analysis description: Treatment groups were compared using Fisher`s exact test (for binary Parameters).	
Comparison groups	nP-X v EC/CMF

Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.001
Method	Fisher exact

Notes:

[2] - Median RTDI for EC was 100% (25-103.7), for CMF 94.9 (8.3-100.0)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring during the study treatment period were reported

Adverse event reporting additional description:

Non-serious AEs are reported per patient; any grade (1-4) during the complete treatment duration for the overall safety population.
Free-text AEs are listed if occurring in >20%
For SAEs relatedness was not tabulated, therefore here we conservatively record all SAEs as related to treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	n.a.

Reporting groups

Reporting group title	EC/CMF

Reporting group description:

Standard treatment with either 4 cycles EC (epirubicin 90mg/m² and cyclophosphamide 600mg/m² IV on day 1 every 3 weeks) or 6 cycles CMF (cyclophosphamide 500 mg/m², methotrexate 40mg/m², 5-fluorouracil 600 mg/m² IV on days 1+8 every 4 weeks) based on investigators decision

Reporting group title	nP-X

Reporting group description:

Experimental treatment with 6 cycles nab-paclitaxel (100 mg/m² IV over 30 min, on days weekly in five out of 6 weeks) plus capecitabine (1000 mg/m² PO bid on days 1-14 every 3 weeks).

Serious adverse events	EC/CMF	nP-X	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 198 (19.19%)	62 / 193 (32.12%)	
number of deaths (all causes)	1	5	
number of deaths resulting from adverse events	1	5	
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	5 / 198 (2.53%)	14 / 193 (7.25%)	
occurrences causally related to treatment / all	5 / 5	14 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other vascular disorders			
subjects affected / exposed	1 / 198 (0.51%)	3 / 193 (1.55%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	4 / 198 (2.02%)	8 / 193 (4.15%)	
occurrences causally related to treatment / all	4 / 4	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever	Additional description: Fever without neutropenia		
subjects affected / exposed	0 / 198 (0.00%)	3 / 193 (1.55%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other general diorders			
subjects affected / exposed	0 / 198 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pain			
subjects affected / exposed	0 / 198 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reactions			
subjects affected / exposed	0 / 198 (0.00%)	2 / 193 (1.04%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Other reproductive system disorders			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 198 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 198 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning, procedural complications			
subjects affected / exposed	3 / 198 (1.52%)	3 / 193 (1.55%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Other cardiac disease			
subjects affected / exposed	0 / 198 (0.00%)	4 / 193 (2.07%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	3 / 3	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 198 (0.00%)	2 / 193 (1.04%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other neurological disorders			

subjects affected / exposed	1 / 198 (0.51%)	5 / 193 (2.59%)	
occurrences causally related to treatment / all	1 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	8 / 198 (4.04%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	8 / 8	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 198 (1.52%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 198 (0.00%)	2 / 193 (1.04%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	5 / 198 (2.53%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other hematological disorders			
subjects affected / exposed	4 / 198 (2.02%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 198 (0.51%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 198 (1.01%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 198 (1.01%)	11 / 193 (5.70%)	
occurrences causally related to treatment / all	2 / 2	11 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis	Additional description: Mucositis, Stomatitis, esophagitis		
subjects affected / exposed	0 / 198 (0.00%)	2 / 193 (1.04%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other gastrointestinal disorders			
subjects affected / exposed	2 / 198 (1.01%)	2 / 193 (1.04%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Other hepatobiliary disorders			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hand-foot syndrome			
subjects affected / exposed	0 / 198 (0.00%)	3 / 193 (1.55%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail changes			
subjects affected / exposed	0 / 198 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Other musculo-skeletal disorders			
subjects affected / exposed	1 / 198 (0.51%)	0 / 193 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			

subjects affected / exposed	3 / 198 (1.52%)	10 / 193 (5.18%)	
occurrences causally related to treatment / all	3 / 3	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Other metabolic disorders			
subjects affected / exposed	0 / 198 (0.00%)	3 / 193 (1.55%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EC/CMF	nP-X	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	198 / 198 (100.00%)	193 / 193 (100.00%)	
Investigations			
Bilirubin			
subjects affected / exposed	0 / 198 (0.00%)	11 / 193 (5.70%)	
occurrences (all)	0	11	
ASAT			
subjects affected / exposed	30 / 198 (15.15%)	60 / 193 (31.09%)	
occurrences (all)	30	60	
ALAT			
subjects affected / exposed	36 / 198 (18.18%)	66 / 193 (34.20%)	
occurrences (all)	36	66	
Alkaline phosphatase			
subjects affected / exposed	30 / 198 (15.15%)	43 / 193 (22.28%)	
occurrences (all)	30	43	
Serum creatinine			
subjects affected / exposed	17 / 198 (8.59%)	31 / 193 (16.06%)	
occurrences (all)	17	31	
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	12 / 198 (6.06%)	25 / 193 (12.95%)	
occurrences (all)	12	25	
Cardiac disorders			

Congestive heart failure NYHA			
subjects affected / exposed	1 / 198 (0.51%)	6 / 193 (3.11%)	
occurrences (all)	1	6	
Cardiac except congestive heart failure			
subjects affected / exposed	13 / 198 (6.57%)	14 / 193 (7.25%)	
occurrences (all)	13	14	
Cardiac ischemia			
subjects affected / exposed	0 / 198 (0.00%)	19 / 193 (9.84%)	
occurrences (all)	0	1	
Nervous system disorders			
Hand-foot syndrome			
subjects affected / exposed	13 / 198 (6.57%)	152 / 193 (78.76%)	
occurrences (all)	13	152	
Dizziness			
subjects affected / exposed	41 / 198 (20.71%)	53 / 193 (27.46%)	
occurrences (all)	41	53	
Sensory neuropathy			
subjects affected / exposed	22 / 198 (11.11%)	115 / 193 (59.59%)	
occurrences (all)	22	115	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	191 / 198 (96.46%)	163 / 193 (84.46%)	
occurrences (all)	191	163	
Neutropenia			
subjects affected / exposed	164 / 198 (82.83%)	120 / 193 (62.18%)	
occurrences (all)	164	120	
Febrile neutropenia			
subjects affected / exposed	8 / 198 (4.04%)	2 / 193 (1.04%)	
occurrences (all)	8	2	
Anaemia			
subjects affected / exposed	170 / 198 (85.86%)	169 / 193 (87.56%)	
occurrences (all)	170	169	
Thrombopenia			
subjects affected / exposed	98 / 198 (49.49%)	33 / 193 (17.10%)	
occurrences (all)	98	33	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	139 / 198 (70.20%)	142 / 193 (73.58%)	
occurrences (all)	139	142	
Oedema			
subjects affected / exposed	21 / 198 (10.61%)	50 / 193 (25.91%)	
occurrences (all)	21	50	
Fever without neutropenia			
subjects affected / exposed	7 / 198 (3.54%)	12 / 193 (6.22%)	
occurrences (all)	7	12	
Immune system disorders			
Allergic reactions			
subjects affected / exposed	8 / 198 (4.04%)	28 / 193 (14.51%)	
occurrences (all)	8	28	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	119 / 198 (60.10%)	101 / 193 (52.33%)	
occurrences (all)	119	101	
Vomiting			
subjects affected / exposed	33 / 198 (16.67%)	41 / 193 (21.24%)	
occurrences (all)	33	41	
Diarrhoea			
subjects affected / exposed	45 / 198 (22.73%)	117 / 193 (60.62%)	
occurrences (all)	45	117	
Mucositis, stomatitis, oesophagitis			
subjects affected / exposed	93 / 198 (46.97%)	107 / 193 (55.44%)	
occurrences (all)	93	107	
Constipation			
subjects affected / exposed	49 / 198 (24.75%)	41 / 193 (21.24%)	
occurrences (all)	49	41	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	23 / 198 (11.62%)	36 / 193 (18.65%)	
occurrences (all)	23	36	
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	176 / 198 (88.89%)	166 / 193 (86.01%)	
occurrences (all)	176	166	
Musculoskeletal and connective tissue disorders			
Joint/muscle pain			
subjects affected / exposed	45 / 198 (22.73%)	53 / 193 (27.46%)	
occurrences (all)	45	53	
Infections and infestations			
Infection without neutropenia			
subjects affected / exposed	11 / 198 (5.56%)	18 / 193 (9.33%)	
occurrences (all)	11	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2010	The trial protocol was amended once: After 78 patients had been recruited supply of nab-paclitaxel was stopped because of impurities in the drug vials in one German center. At 1st of April 2010 the BfArM issued a temporary suspension of the clinical trial authorization and requested corrective actions from the sponsor and the working supply with nab-Paclitaxel as inevitable for re-initiation of the trial. There was a period of nine months without nab-paclitaxel and patients under treatment received paclitaxel instead. Recruitment was stopped for this period. In its meeting on June 30, 2010 the IDMC recommended that analysis should be performed with and without complete nab-paclitaxel. The provision of the complete nab-Paclitaxel medication required for the entire treatment duration was made mandatory for the start of any new patient via Amendment 1, which also included the introduction of two additional geriatric scores (IADL and G8 score), resulting from a request of the IDMC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26111104