Clinical trial results:
A randomized phase III trial comparing two dose-dense, dose-intensified approaches (iddEPC and PM(Cb)) for neoadjuvant treatment of patients with high-risk early breast cancer (GeparOcto)

Summary

EudraCT number	2014-000619-14
Trial protocol	DE
Global end of trial date	30 January 2017

Results information

Result version number	v1 (current)
This version publication date	09 March 2022
First version publication date	09 March 2022
Summary attachment (see zip file)	GeparOcto CSR Synopsis (GBG 84 - GeparOcto CSR Synopsis (19.07.2019) incl. Annex 1.pdf)

Trial information

Trial identification

Sponsor protocol code	GBG84

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02125344
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 , publications@gbg.de
Scientific contact	Medicine and Research, GBG Forschungs GmbH , 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	15 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2016
Global end of trial reached?	Yes
Global end of trial date	30 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the pathological complete response (pCR= ypT0/is ypN0) rates of neoadjuvant treatment with sequential, dose-dense, dose-intensified epirubicin, paclitaxel, and cyclophosphamide (iddETC) vs weekly paclitaxel plus non-pegylated liposomal doxorubicin (plus additional carboplatin in triple-negative breast cancer, PM[Cb]) in patients with high-risk operable or locally advanced breast cancer.

Only for those patients randomized for the supportive anemia treatment:
To compare the frequency of patients reaching hemoglobin (Hb) levels ≥ 11g/dl 6 weeks after treatment start of a first episode of anemia grade ≥2 (Hb < 10g/dl) between patients receiving supportive treatment for iron deficiency with parental ferric carboxymaltose versus physician's choice (no supportive treatment, oral iron substitution, erythropoiesis-stimulating agent (ESA), or both).

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:

Carboplatin for triple-negative breast cancer and trastuzumab for HER2-positive disease

Evidence for comparator:

Standard of Care (SoC)

Actual start date of recruitment	01 December 2014
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: 945
Worldwide total number of subjects	945
EEA total number of subjects	945

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)	886
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 12/2014 and 06/2016, 1204 patients were screened, 961 patients were randomised, and 945 started treatment. Treatment was completed by 393/470 (83.6%) patients in the iddEPC and 313/475 (65.9%) in the PM(Cb) arm.

Pre-assignment

Screening details:

Patients of at least 18 years of age with previously untreated, unilateral or bilateral, non-metastatic invasive breast cancer (BC); with cT1c-cT4a-d and centrally assessed human epidermal growth factor receptor (HER)2-positive BC or TNBC were eligible, irrespective of nodal status, luminal B-like tumours only if pN-positive.

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	iddEPC

Arm description:

A total of 480 patients were randomised to receive sequential treatment with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide (iddEPC), 470 started treatment, 393 completed treatment, and 467 received surgery.
Note, the number of patients started treatment is given for "started"

Arm type	Experimental
Investigational medicinal product name	epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

150 mg/m², given on day 1 every 2 weeks for 3 cycles

Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

2000 mg/m², given on day 1 every 2 weeks for 3 cycles

Investigational medicinal product name	paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

225 mg/m² given every two weeks for 3 cycles

Arm title	PM(Cb)

Arm description:

A total of 481 patients with breast cancer (BC) were randomised to receive weekly treatment with paclitaxel plus non-pegylated liposomal doxorubicin (M, Myocet) with additional carboplatin (PM(Cb) in triple-negative BC (TNBC), 475 started treatment, 313 patients completed treatment regularly, and 471 received surgery.
Note, the number of patients started treatment is given for "started".

Arm type	Active comparator
Investigational medicinal product name	paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m², given weekly for 18 weeks

Investigational medicinal product name	non-pegylated liposomal doxorubicin
Investigational medicinal product code	
Other name	NPLD (Myocet)
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/m², given weekly for 18 weeks

Investigational medicinal product name	carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

AUC 1.5, given weekly for 18 weeks

Number of subjects in period 1	iddEPC	PM(Cb)
Started	470	475
Completed	393	313
Not completed	77	162
Adverse event, serious fatal	-	1
Physician decision	10	13
Adverse event, non-fatal	47	114
local progress	3	8
distant metastases	-	1
patient decision	17	25

Baseline characteristics

Reporting groups	
Reporting group title	iddEPC

Reporting group description:

A total of 480 patients were randomised to receive sequential treatment with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide (iddEPC), 470 started treatment, 393 completed treatment, and 467 received surgery.
Note, the number of patients started treatment is given for "started"

Reporting group title	PM(Cb)

Reporting group description:

A total of 481 patients with breast cancer (BC) were randomised to receive weekly treatment with paclitaxel plus non-pegylated liposomal doxorubicin (M, Myocet) with additional carboplatin (PM(Cb) in triple-negative BC (TNBC), 475 started treatment, 313 patients completed treatment regularly, and 471 received surgery.
Note, the number of patients started treatment is given for "started".

Reporting group values	iddEPC	PM(Cb)	Total
Number of subjects	470	475	945
Age categorical Units: Subjects			
Adults (18-64 years)	439	447	886
From 65-84 years	31	28	59
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	470	475	945
Male	0	0	0

End points

End points reporting groups

Reporting group title	iddEPC

Reporting group description:

A total of 480 patients were randomised to receive sequential treatment with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide (iddEPC), 470 started treatment, 393 completed treatment, and 467 received surgery.
Note, the number of patients started treatment is given for "started"

Reporting group title	PM(Cb)

Reporting group description:

A total of 481 patients with breast cancer (BC) were randomised to receive weekly treatment with paclitaxel plus non-pegylated liposomal doxorubicin (M, Myocet) with additional carboplatin (PM(Cb) in triple-negative BC (TNBC), 475 started treatment, 313 patients completed treatment regularly, and 471 received surgery.
Note, the number of patients started treatment is given for "started".

Primary: pCR (ypT0/is ypN0)

End point title	pCR (ypT0/is ypN0)

End point description:

The primary efficacy endpoint of this study was pathological complete response (pCR=ypT0/is ypN0), defined as no microscopic evidence of residual invasive viable tumor cells in all resected specimens of the breast and axilla.

End point type	Primary

End point timeframe:

The entire treatment period was 18 weeks.

End point values	iddEPC	PM(Cb)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	470	475		
Units: percent				
number (confidence interval 95%)				
pCR (ypT0/is ypN0)	48.3 (43.7 to 52.9)	48.0 (43.4 to 52.6)		

Statistical analyses

Statistical analysis title	pCR (ypT0/is ypN0) - absolute diffrences

Statistical analysis description:

Analysis of the primary endpoint was based on the modified intent-to-treat (mITT) set including all patients who were randomised and received at least one dose of study medication. The primary endpoint was summarized as pCR rate for each treatment group. Two-sided 95% confidence intervals (CI) were calculated. The difference in the rates of pCR between groups was evaluated as an absolute difference and its 95% CI.

Comparison groups	iddEPC v PM(Cb)

Number of subjects included in analysis	945
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.979
Method	Chi-squared corrected

Notes:

[1] - Significance was tested with the two-sided continuity corrected χ2-test with significance level of alpha = 0.05. It was pre-planned in the study protocol that, if the superiority test failed to detect a significant difference, the non-inferiority was to be tested.

Statistical analysis title	pCR (ypT0/is ypN0) - absolute diffrences
Comparison groups	iddEPC v PM(Cb)
Number of subjects included in analysis	945
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.979
Method	Chi-squared corrected
Parameter estimate	absolute difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	6.1

Notes:

[2] - The non-inferiority margin for the pCR rate difference was set to 5%, non-inferiority was to be claimed, if the lower limit of the two-sided 95% CI for the pCR rate difference (PM(Cb) arm minus iddEPC arm) was greater than -5%.

Statistical analysis title	pCR (ypT0/is ypN0) - odds ratio

Statistical analysis description:

A multivariate logistic regression analysis was performed for the primary efficacy endpoint pCR to report odds ratios with 95% CI, adjusted for the factors biological subtype, Ki-67, LPBC, age, cT, cN, tumor grading, histological tumor type

Comparison groups	iddEPC v PM(Cb)
Number of subjects included in analysis	945
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.931
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.988
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.31

Notes:

[3] - Multivariate logistic regression analysis

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:

AEs are reported per patient during the complete treatment duration for the overall safety population. Non-serious AEs any grade per patient occurring more frequently (> 20%) are presented. Of note, overall number of single AE occurrences per term was not assessed, only per patient; SAEs are reported regardless of causality.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	iddEPC

Reporting group description:

sequential treatment with intense dose-dense epirubicin, paclitaxel, and cyclophosphamide (iddEPC)

Reporting group title	PM(Cb)

Reporting group description:

weekly treatment with paclitaxel (P) plus non-pegylated liposomal doxorubicin (M) with additional carboplatin (Cb) in TNBC (PM(Cb))

Serious adverse events	iddEPC	PM(Cb)	
Total subjects affected by serious adverse events			
subjects affected / exposed	174 / 470 (37.02%)	171 / 475 (36.00%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	1	
Vascular disorders			
Embolism			
subjects affected / exposed	2 / 470 (0.43%)	5 / 475 (1.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 470 (0.43%)	4 / 475 (0.84%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 470 (0.00%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	0 / 470 (0.00%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	40 / 470 (8.51%)	43 / 475 (9.05%)	
occurrences causally related to treatment / all	0 / 40	0 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	13 / 470 (2.77%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 13	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 470 (0.21%)	4 / 475 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	3 / 470 (0.64%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immune system disorders			
subjects affected / exposed	3 / 470 (0.64%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	2 / 470 (0.43%)	0 / 475 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	2 / 470 (0.43%)	15 / 475 (3.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	4 / 470 (0.85%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 470 (0.21%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigations			
subjects affected / exposed	1 / 470 (0.21%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 470 (0.00%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ejection fraction decreased			
subjects affected / exposed	2 / 470 (0.43%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	9 / 470 (1.91%)	7 / 475 (1.47%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	43 / 470 (9.15%)	10 / 475 (2.11%)	
occurrences causally related to treatment / all	0 / 43	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	40 / 470 (8.51%)	0 / 475 (0.00%)	
occurrences causally related to treatment / all	0 / 40	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	26 / 470 (5.53%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 26	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	9 / 470 (1.91%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 470 (0.21%)	6 / 475 (1.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	0 / 470 (0.00%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 470 (0.64%)	21 / 475 (4.42%)	
occurrences causally related to treatment / all	0 / 3	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	5 / 470 (1.06%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			

subjects affected / exposed	4 / 470 (0.85%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	6 / 470 (1.28%)	0 / 475 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	4 / 470 (0.85%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	1 / 470 (0.21%)	4 / 475 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 470 (0.00%)	5 / 475 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	1 / 470 (0.21%)	0 / 475 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 470 (0.43%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	3 / 470 (0.64%)	31 / 475 (6.53%)	
occurrences causally related to treatment / all	0 / 3	1 / 31	
deaths causally related to treatment / all	0 / 0	1 / 1	
Urinary tract infection			
subjects affected / exposed	3 / 470 (0.64%)	6 / 475 (1.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	3 / 470 (0.64%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 470 (0.21%)	4 / 475 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 470 (0.21%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 470 (0.00%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 470 (0.21%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 470 (0.43%)	1 / 475 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			

subjects affected / exposed	0 / 470 (0.00%)	3 / 475 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 470 (0.21%)	2 / 475 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	iddEPC	PM(Cb)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	470 / 470 (100.00%)	475 / 475 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	346 / 470 (73.62%)	234 / 475 (49.26%)	
occurrences (all)	346	234	
Alkaline phosphatase increased			
subjects affected / exposed	300 / 470 (63.83%)	182 / 475 (38.32%)	
occurrences (all)	300	182	
Aspartate aminotransferase increased			
subjects affected / exposed	208 / 470 (44.26%)	134 / 475 (28.21%)	
occurrences (all)	208	134	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	392 / 470 (83.40%)	345 / 475 (72.63%)	
occurrences (all)	392	345	
Headache			
subjects affected / exposed	152 / 470 (32.34%)	117 / 475 (24.63%)	
occurrences (all)	152	117	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	466 / 470 (99.15%)	437 / 475 (92.00%)	
occurrences (all)	466	437	

Leukopenia			
subjects affected / exposed	450 / 470 (95.74%)	401 / 475 (84.42%)	
occurrences (all)	450	401	
Neutropenia			
subjects affected / exposed	422 / 470 (89.79%)	305 / 475 (64.21%)	
occurrences (all)	422	305	
Thrombopenia			
subjects affected / exposed	367 / 470 (78.09%)	145 / 475 (30.53%)	
occurrences (all)	367	145	
General disorders and administration site conditions			
Fatigue	Additional description: Fatigue and asthenia		
subjects affected / exposed	372 / 470 (79.15%)	342 / 475 (72.00%)	
occurrences (all)	372	342	
Fever	Additional description: Fever without neutropenia		
subjects affected / exposed	107 / 470 (22.77%)	146 / 475 (30.74%)	
occurrences (all)	107	146	
Gastrointestinal disorders			
Mucositis			
subjects affected / exposed	270 / 470 (57.45%)	312 / 475 (65.68%)	
occurrences (all)	270	312	
Nausea			
subjects affected / exposed	316 / 470 (67.23%)	236 / 475 (49.68%)	
occurrences (all)	316	236	
Diarrhoea			
subjects affected / exposed	191 / 470 (40.64%)	262 / 475 (55.16%)	
occurrences (all)	191	262	
Stomatitis			
subjects affected / exposed	156 / 470 (33.19%)	174 / 475 (36.63%)	
occurrences (all)	156	174	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	59 / 470 (12.55%)	132 / 475 (27.79%)	
occurrences (all)	59	132	
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	412 / 470 (87.66%)	421 / 475 (88.63%)	
occurrences (all)	412	421	
Skin reactions			
subjects affected / exposed	252 / 470 (53.62%)	364 / 475 (76.63%)	
occurrences (all)	252	364	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	207 / 470 (44.04%)	103 / 475 (21.68%)	
occurrences (all)	207	103	
Myalgia			
subjects affected / exposed	175 / 470 (37.23%)	97 / 475 (20.42%)	
occurrences (all)	175	97	
Infections and infestations			
Infection other than pneumonia			
subjects affected / exposed	205 / 470 (43.62%)	252 / 475 (53.05%)	
occurrences (all)	205	252	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	117 / 470 (24.89%)	88 / 475 (18.53%)	
occurrences (all)	117	88	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2015	There was one substantial amendment to the protocol of GeparOcto pertaining to the supportive anemia treatment. As the number of patients requiring supportive treatment for iron deficiency was too low meeting the original threshold of serum ferritin of <300ng/ml during the initial phase of the study, this threshold was changed to <600ng/ml by the amendment.

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/30528802

http://www.ncbi.nlm.nih.gov/pubmed/34801353

http://www.ncbi.nlm.nih.gov/pubmed/33191846

http://www.ncbi.nlm.nih.gov/pubmed/32163106

http://www.ncbi.nlm.nih.gov/pubmed/35158789