Clinical trial results:
A prospective, Belgian multi-center, single-arm, phase II study of neoadjuvant weekly paclitaxel and carboplatin followed by dose dense epirubicin and cyclophosphamide in stage II and III triple negative breast cancer.

Summary

EudraCT number	2014-003723-21
Trial protocol	BE
Global end of trial date	30 September 2020

Results information

Result version number	v1 (current)
This version publication date	14 May 2021
First version publication date	14 May 2021
Summary attachment (see zip file)	Abstract ESMO 2017 (abstract ESMO 2017.jdg.docx)

Trial information

Trial identification

Sponsor protocol code	BSMO-2014-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	BSMO
Sponsor organisation address	C. Heymanslaan 10, Ghent, Belgium, 9000
Public contact	Dr. Fontaine, UZ Brussel, +32 2477.64.15, christel.fontaine@uzbrussel.be
Scientific contact	Dr. Fontaine, UZ Brussel, +32 2477.64.15, christel.fontaine@uzbrussel.be

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	30 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the rate of pCR in the breast and axilla (ypT0/is, ypN0). Pathological complete response is defined as no presence of invasive residuals in the breast and resected axillary lymph nodes.

Protection of trial subjects:

Signed Informed consent, in this consent is explained that the patient data is anonymized.
Safety data will be collected on a continuous basis and will be reviewed by the Sponsor in order to ensure that it is appropriate to continue the study

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	09 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	53
From 65 to 84 years	10

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Stage II and III triple negative breast cancer patients suitable for preoperative chemotherapy

Pre-assignment

Screening details:

The patient should provide a signed Informed Consent Form prior to any study screening evaluations. Once the patient Informed Consent Form has been signed and eligibility is confirmed, the patient can be enrolled. All screening evaluations will be performed according to local standards within 28 days prior to treatment Day 1.

Pre-assignment period milestones

Number of subjects started	63
Number of subjects completed	63

Period 1

Period 1 title	Treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Treatment Phase
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Carboplatinum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

In the first part of the adjuvant chemotherapy all patients should receive weekly paclitaxel at a dose of 80mg/m² in a 1-h infusion followed by carboplatin at an area under the curve(AUC of 2mg*min/ml) in 30-min infusion given weekly for 12 weeks

Investigational medicinal product name	AUC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

(AUC of 2mg*min/ml) in 30-min infusion given weekly for 12 weeks

Investigational medicinal product name	Epirubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

2 weekly epirubicin at a dose of 90mg/m² in 1-h infusion

Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

cyclophosphamide at a dose of 600mg/m² in a 30 to 60 min infusion

Number of subjects in period 1	Treatment Phase
Started	63
Completed	63

Baseline characteristics

Reporting groups

Reporting group title	Treatment phase

Reporting group description: -

Reporting group values	Treatment phase	Total	
Number of subjects	63	63	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	63	63	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	55		
full range (min-max)	29 to 74	-	
Gender categorical Units: Subjects			
Female	63	63	
Male	0	0	

End points

End points reporting groups

Reporting group title	Treatment Phase
Reporting group description: -	
Subject analysis set title	Single arm study
Subject analysis set type	Per protocol
Subject analysis set description: Single arm study	
Subject analysis set title	Single arm study
Subject analysis set type	Per protocol
Subject analysis set description: Single arm study, fantom arm to resolve the query	

Primary: pCR rate in the breast and axilla (ypT0/is, ypN0).

End point title	pCR rate in the breast and axilla (ypT0/is, ypN0).

End point description:

After breast surgery pathologic complete response will be assessed by the pathologist as no invasive residual tumor in the breast and axilla (ypT0/is, ypN0 (f+or f-). ypN0f+ means that no metastatic disease is detected in the lymph node but there is evidence of response or downstaging due to fibrosis in the lymph node; ypN0f- means that there is no metastatic disease nor evidence of response or downstaging detected in the lymph node.
In case of metastatic disease in the lymph node we refer to the TNM classification.
In case there was no clinical lymph node involvement baseline, and the sentinel procedure was negative, no further axillary lymph node dissection is required after neoadjuvant chemotherapy, and only the ypT stage will be assessed pathologically. The yPN status will be considered as yPN0 in that case.
Partial response to therapy will be considered as minimal residual disease if< 10% of the invasive residual tumor is remaining after surgery or considered as evidence of r

End point type	Primary

End point timeframe:

To determine the pCR rate in the breast and axilla (ypT0/is, ypN0). Pathological complete response is defined as no presence of invasive residuals in the breast and resected axillary lymph nodes. After 3 months therapy

End point values	Treatment Phase	Single arm study	Single arm study	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	63	63	63	
Units: %				
number (not applicable)	63	63	63	

Attachments (see zip file)	powerpointChristel Fontaine poster SABCS 2018 (002).ppt

Statistical analyses

Statistical analysis title	Optimal Simon Two-stage

Statistical analysis description:

The study size sample has been calculated according to the optimal Simon’s two-stage design method.

The target sample size is 63patients with a 80% power to detect a pCR rate of > or=47% (alfa=0.05).The optimal Simon two-stage design is used to test the null hypothesis (H0) that the weekly regimen of paclitaxel and carboplatin followed by dose dense cyclophosphamide and epirubicin elicite a pCR(ypT0/is, ypN0) rate in a cohort of triple negative patients of < or =30% versus the alternative

Comparison groups	Treatment Phase v Single arm study v Single arm study
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Simon two-stage
Parameter estimate	Hypothesis
Point estimate	0.05
Confidence interval	
level	Other: 80 %
sides	1-sided
upper limit	80
Variability estimate	Standard deviation
Dispersion value	0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events that begin or worsen after start of treatment should be recorded in the CRF. Conditions that were already present at the time of informed consent should be recorded in the CRF. Throughout the duration of the study according NCICTC AE v4.0

Adverse event reporting additional description:

An adverse event is defined as the appearance of undesirable sign(s), symptom(s), or medical condition(s) that occur after patient's signed informed consent has been obtained. Abnormal laboratory values or test results occurring after informed consent constitute adverse events only if they induce clinical signs or symptoms, are considered clinic

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	all patients

Reporting group description: -

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 63 (47.62%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Nervous Breakdown			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	17 / 63 (26.98%)		
occurrences causally related to treatment / all	17 / 17		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anemia			

subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 63 (3.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General deterioration			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
shingles			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			

subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PAC infection			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urine infection			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 63 (36.51%)		
Nervous system disorders			
Polyneuropathy			
subjects affected / exposed	23 / 63 (36.51%)		
occurrences (all)	23		
Blood and lymphatic system disorders			
WBC count decreased			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 63 (36.51%)		
occurrences (all)	23		
Ear and labyrinth disorders			

epistaxis subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 5		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhea subjects affected / exposed occurrences (all) Pyrosis subjects affected / exposed occurrences (all)	 11 / 63 (17.46%) 11 7 / 63 (11.11%) 7 5 / 63 (7.94%) 5		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 20 / 63 (31.75%) 20		
Musculoskeletal and connective tissue disorders arthralgia subjects affected / exposed occurrences (all)	 3 / 63 (4.76%) 3		
Infections and infestations Abdominal infection subjects affected / exposed occurrences (all)	 1 / 63 (1.59%) 1		
Metabolism and nutrition disorders anorexia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all)	 15 / 63 (23.81%) 15 23 / 63 (36.51%) 23 15 / 63 (23.81%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2015	Addition of a site

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: