

**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 |

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: | |
| <p>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.</p> <p>In case of metastatic disease in the lymph node we refer to the TNM classification.</p> <p>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.</p> <p>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</p> | |
| 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 63 patients with a 80% power to detect a pCR rate of $\geq 47\%$ ($\alpha=0.05$). The optimal Simon two-stage design is used to test the null hypothesis (H_0) that the weekly regimen of paclitaxel and carboplatin followed by dose dense cyclophosphamide and epirubicin elicit a pCR (ypT0/is, ypN0) rate in a cohort of triple negative patients of $\leq 30\%$ 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

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|-----------------|-------|
| 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.

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| None reported |
|---------------|

Notes: