



## Clinical trial results:

**Randomized, open-label, phase II study comparing the efficacy and safety of cabazitaxel versus weekly paclitaxel given as neo-adjuvant treatment in patients with operable triple-negative or luminal B/HER2-negative breast cancer.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-003330-16 |
| Trial protocol           | DE             |
| Global end of trial date | 27 August 2015 |

### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)                                    |
| This version publication date     | 26 June 2022                                    |
| First version publication date    | 26 June 2022                                    |
| Summary attachment (see zip file) | CSR Synopsis (CSR Synopsis Genevieve V 1.0.pdf) |

### Trial information

#### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | GBG74 |
|-----------------------|-------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01779479 |
| 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                       | 30 April 2016  |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 27 August 2015 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To compare the pathologic complete response (pCR) rate in the breast (ypT0/is ypN0/+) in patients with operable Triple Negative or luminal B/HER2 normal breast cancer treated with either cabazitaxel or weekly paclitaxel.

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:

Cabazitaxel is compared against weekly paclitaxel which is currently most widely used treatment of breast cancer patients. A head-to-head comparison in the neoadjuvant setting will allow a rapid and precise comparison of efficacy and tolerability of cabazitaxel versus paclitaxel to decide in how far further development of this taxoid in breast cancer is reasonable.

|   |                     |
|---|---------------------|
| Actual start date of recruitment                          | 01 October 2012     |
| Long term follow-up planned                               | Yes                 |
| Long term follow-up rationale                             | Scientific research |
| Long term follow-up duration                              | 5 Years             |
| Independent data monitoring committee (IDMC) involvement? | Yes                 |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 333 |
| Worldwide total number of subjects   | 333          |
| EEA total number of subjects         | 333          |

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)                     | 281 |
| From 65 to 84 years                      | 52  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

#### Recruitment details:

Between April 2013 and June 2015, 407 patients were screened, 333 were randomised (166 in cabazitaxel arm and 167 in paclitaxel arm) and started treatment of whom 263 (74.7% in cabazitaxel arm and 83.2% in paclitaxel arm) completed treatment.

### Pre-assignment

#### Screening details:

Eligibility criteria were primary invasive BC, clinical stage cT2-3 any cN or cT1c cN+/pN(SLN+) and centrally confirmed prior to enrolment TNBC or luminal B/HER2-negative BC.

### 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         |
| <b>Arm title</b>             | Cabazitaxel |

#### Arm description:

A total of 166 patients were randomised to receive cabazitaxel and started treatment, 124 patients completed treatment regularly. After amendment 2, 78 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 83 patients received surgery after cabazitaxel treatment and 78 underwent surgery after additional anthracycline-containing chemotherapy. Note, the number of patients started treatment is given for "started".

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Cabazitaxel                     |
| Investigational medicinal product code |                                 |
| Other name                             | Jevtana, EU/1/11/676/001        |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Infusion                        |

#### Dosage and administration details:

Cabazitaxel 25 mg/m<sup>2</sup> i.v. (Day 1) every 3 weeks (cycle) as 1-hour i.v infusion for a total of up to 4 cycles over a maximum total treatment period of 15 weeks before surgery.

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Paclitaxel |
|------------------|------------|

#### Arm description:

A total of 167 patients were randomised to receive paclitaxel and started treatment, 139 patients completed treatment regularly. After amendment 2, 77 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 88 patients received surgery after paclitaxel treatment and 75 underwent surgery after additional anthracycline-containing chemotherapy. 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                             | 77226.00.00                     |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Infusion                        |

#### Dosage and administration details:

Paclitaxel 80 mg/m<sup>2</sup> as 1-hour i.v infusion. Patients will receive weekly (Day 1, 8, 15) paclitaxel administrations for a maximum of 12 infusions for a maximum of 4 cycles over a maximum total treatment period of 15 weeks before surgery (1 cycle = 3 weeks).  
Paclitaxel is used according to the recommendations of the manufacturers via normal procedures at

each site.

| <b>Number of subjects in period 1</b> | Cabazitaxel | Paclitaxel |
|---------------------------------------|-------------|------------|
| Started                               | 166         | 167        |
| Completed                             | 124         | 139        |
| Not completed                         | 42          | 28         |
| Adverse event, serious fatal          | 2           | -          |
| Physician decision                    | 6           | 6          |
| progression                           | 20          | 11         |
| Adverse event, non-fatal              | 13          | 7          |
| patient's decision                    | 1           | 4          |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Cabazitaxel |
|-----------------------|-------------|

Reporting group description:

A total of 166 patients were randomised to receive cabazitaxel and started treatment, 124 patients completed treatment regularly. After amendment 2, 78 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 83 patients received surgery after cabazitaxel treatment and 78 underwent surgery after additional anthracycline-containing chemotherapy. Note, the number of patients started treatment is given for "started".

|                       |            |
|-----------------------|------------|
| Reporting group title | Paclitaxel |
|-----------------------|------------|

Reporting group description:

A total of 167 patients were randomised to receive paclitaxel and started treatment, 139 patients completed treatment regularly. After amendment 2, 77 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 88 patients received surgery after paclitaxel treatment and 75 underwent surgery after additional anthracycline-containing chemotherapy . Note, the number of patients started treatment is given for "started".

| Reporting group values | Cabazitaxel | Paclitaxel | Total |
|------------------------|-------------|------------|-------|
| Number of subjects     | 166         | 167        | 333   |
| Age categorical        |             |            |       |
| Units: Subjects        |             |            |       |
| Adults (18-64 years)   | 145         | 136        | 281   |
| From 65-84 years       | 21          | 31         | 52    |
| Gender categorical     |             |            |       |
| Units: Subjects        |             |            |       |
| Female                 | 166         | 167        | 333   |
| Male                   | 0           | 0          | 0     |

## End points

### End points reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Cabazitaxel |
|-----------------------|-------------|

Reporting group description:

A total of 166 patients were randomised to receive cabazitaxel and started treatment, 124 patients completed treatment regularly. After amendment 2, 78 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 83 patients received surgery after cabazitaxel treatment and 78 underwent surgery after additional anthracycline-containing chemotherapy. Note, the number of patients started treatment is given for "started".

|                       |            |
|-----------------------|------------|
| Reporting group title | Paclitaxel |
|-----------------------|------------|

Reporting group description:

A total of 167 patients were randomised to receive paclitaxel and started treatment, 139 patients completed treatment regularly. After amendment 2, 77 patients without pCR received additional anthracycline-containing chemotherapy prior surgery. Overall, 88 patients received surgery after paclitaxel treatment and 75 underwent surgery after additional anthracycline-containing chemotherapy. 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 endpoint pCR (ypT0/is ypN0/+) was analysed in the mITT analysis set. The pCR rate was defined as the complete absence of invasive carcinoma on histological examination in the breast irrespective of lymph node involvement (ypT0/Tis, ypN0/+) at the time of definitive surgery and confirmed by independent blinded centralized histology report review. With Amendment 2 patients with invasive tumor residuals after end of study treatment had the option to receive anthracycline-containing chemotherapy prior to surgery. This change resulted in a modification of the definition of treatment failures for the primary endpoint: patients in whom pCR could not be determined (e.g. patients in whom histology was not evaluable) or who have invasive tumor residuals in the core biopsy taken after end of study treatment was included in the denominator, i.e. these patients was considered as treatment failures.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

from treatment start until surgery after study treatment; the entire treatment period was 12 weeks

| End point values                 | Cabazitaxel      | Paclitaxel         |  |  |
|----------------------------------|------------------|--------------------|--|--|
| Subject group type               | Reporting group  | Reporting group    |  |  |
| Number of subjects analysed      | 166              | 167                |  |  |
| Units: percent                   |                  |                    |  |  |
| number (confidence interval 95%) |                  |                    |  |  |
| pCR (ypT0/is ypN0/+)             | 1.2 (0.0 to 2.9) | 10.8 (6.1 to 15.5) |  |  |

### Statistical analyses

|                            |                              |
|----------------------------|------------------------------|
| Statistical analysis title | pCR (ypT0/is ypN0/+) - rates |
|----------------------------|------------------------------|

---

**Statistical analysis description:**

In the primary efficacy analysis the difference of the pCR rates was tested using a one-sided Fisher's exact test with a type I error of 10%.

|   |                            |
|---|----------------------------|
| Comparison groups                       | Cabazitaxel v Paclitaxel   |
| Number of subjects included in analysis | 333                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority <sup>[1]</sup> |
| P-value                                 | = 0.001                    |
| Method                                  | Fisher exact               |

**Notes:**

[1] - The pCR rates for each treatment group and the difference in pCR rates between treatment arms with their 95% CIs were calculated according to Pearson and Clopper



## 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:

Predefined AEs are reported per patient during the complete treatment duration for the safety population (N=133). 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 | n.a. |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Cabazitaxel |
|-----------------------|-------------|

Reporting group description:

Cabazitaxel given as neo-adjuvant treatment in patients with operable triple-negative or luminal B/HER2-negative breast cancer

|                       |            |
|-----------------------|------------|
| Reporting group title | Paclitaxel |
|-----------------------|------------|

Reporting group description:

Paclitaxel was given as neo-adjuvant treatment in patients with operable triple-negative or luminal B/HER2-negative breast cancer.

| Serious adverse events  | Cabazitaxel       | Paclitaxel        |  |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                   |                   |  |
| subjects affected / exposed   | 42 / 166 (25.30%) | 17 / 167 (10.18%) |  |
| number of deaths (all causes)                                       | 2                 | 1                 |  |
| number of deaths resulting from adverse events                      | 0                 | 0                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |  |
| Neoplasms   |                   |                   |  |
| subjects affected / exposed   | 0 / 166 (0.00%)   | 1 / 167 (0.60%)   |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| Injury, poisoning and procedural complications                      |                   |                   |  |
| Injury, poisoning and procedural complications                      |                   |                   |  |
| subjects affected / exposed   | 0 / 166 (0.00%)   | 1 / 167 (0.60%)   |  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             |  |
| Vascular disorders  |                   |                   |  |

|  |                   |                 |  |
|--|-------------------|-----------------|--|
| Other vascular disorders                             |                   |                 |  |
| subjects affected / exposed                          | 1 / 166 (0.60%)   | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1             | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Nervous system disorders                             |                   |                 |  |
| Other neurological disorders                         |                   |                 |  |
| subjects affected / exposed                          | 2 / 166 (1.20%)   | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2             | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Blood and lymphatic system disorders                 |                   |                 |  |
| Anemia   |                   |                 |  |
| subjects affected / exposed                          | 2 / 166 (1.20%)   | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2             | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Leukopenia   |                   |                 |  |
| subjects affected / exposed                          | 2 / 166 (1.20%)   | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2             | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Neutropenia  |                   |                 |  |
| subjects affected / exposed                          | 23 / 166 (13.86%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all      | 0 / 23            | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Febrile neutropenia                                  |                   |                 |  |
| subjects affected / exposed                          | 17 / 166 (10.24%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all      | 0 / 17            | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| General disorders and administration site conditions |                   |                 |  |
| Fatigue  |                   |                 |  |
| subjects affected / exposed                          | 0 / 166 (0.00%)   | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all      | 0 / 0             | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0           |  |
| Fever without neutropenia                            |                   |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                                | 2 / 166 (1.20%) | 2 / 167 (1.20%) |  |
| occurrences causally related to treatment / all            | 0 / 2           | 0 / 2           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Pain NOS   |                 |                 |  |
| subjects affected / exposed                                | 0 / 166 (0.00%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all            | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Other general disorders and administration site conditions |                 |                 |  |
| subjects affected / exposed                                | 2 / 166 (1.20%) | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all            | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all                 | 0 / 2           | 0 / 0           |  |
| Immune system disorders                                    |                 |                 |  |
| Allergic reactions   |                 |                 |  |
| subjects affected / exposed                                | 1 / 166 (0.60%) | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                                 |                 |                 |  |
| Vomiting   |                 |                 |  |
| subjects affected / exposed                                | 1 / 166 (0.60%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all            | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Diarrhea   |                 |                 |  |
| subjects affected / exposed                                | 5 / 166 (3.01%) | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all            | 0 / 5           | 0 / 0           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Mucositis/esophagitis                                      |                 |                 |  |
| subjects affected / exposed                                | 0 / 166 (0.00%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all            | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |
| Constipation   |                 |                 |  |
| subjects affected / exposed                                | 0 / 166 (0.00%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all            | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all                 | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Other gastrointestinal disorders                |                 |                 |  |
| subjects affected / exposed                     | 2 / 166 (1.20%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Dyspnea   |                 |                 |  |
| subjects affected / exposed                     | 1 / 166 (0.60%) | 1 / 167 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Other renal and urinary disorders               |                 |                 |  |
| subjects affected / exposed                     | 6 / 166 (3.61%) | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Arthralgia                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 166 (0.60%) | 0 / 167 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Infection                                       |                 |                 |  |
| subjects affected / exposed                     | 6 / 166 (3.61%) | 8 / 167 (4.79%) |  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 8           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Cabazitaxel         | Paclitaxel          |  |
|---|---------------------|---------------------|--|
| Total subjects affected by non-serious adverse events |                     |                     |  |
| subjects affected / exposed                           | 166 / 166 (100.00%) | 167 / 167 (100.00%) |  |
| Investigations  |                     |                     |  |
| Alkaline phosphatase increased                        |                     |                     |  |
| subjects affected / exposed                           | 34 / 166 (20.48%)   | 14 / 167 (8.38%)    |  |
| occurrences (all)                                     | 34                  | 14                  |  |
| Aspartate aminotransferase                            |                     |                     |  |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| increased<br>subjects affected / exposed<br>occurrences (all)                          | 38 / 166 (22.89%)<br>38   | 43 / 167 (25.75%)<br>43   |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 66 / 166 (39.76%)<br>66   | 75 / 167 (44.91%)<br>75   |  |
| Nervous system disorders   |                           |                           |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                           | 30 / 166 (18.07%)<br>30   | 38 / 167 (22.75%)<br>38   |  |
| Peripheral sensory neuropathy<br>subjects affected / exposed<br>occurrences (all)      | 35 / 166 (21.08%)<br>35   | 105 / 167 (62.87%)<br>105 |  |
| Blood and lymphatic system disorders   |                           |                           |  |
| Anemia<br>subjects affected / exposed<br>occurrences (all)                             | 135 / 166 (81.33%)<br>135 | 122 / 167 (73.05%)<br>122 |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                         | 133 / 166 (80.12%)<br>133 | 97 / 167 (58.08%)<br>97   |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                        | 121 / 166 (72.89%)<br>121 | 62 / 167 (37.13%)<br>62   |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                        | 84 / 166 (50.60%)<br>84   | 54 / 167 (32.34%)<br>54   |  |
| Thrombopenia<br>subjects affected / exposed<br>occurrences (all)                       | 60 / 166 (36.14%)<br>60   | 13 / 167 (7.78%)<br>13    |  |
| General disorders and administration<br>site conditions                                |                           |                           |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                            | 112 / 166 (67.47%)<br>112 | 118 / 167 (70.66%)<br>118 |  |
| Gastrointestinal disorders   |                           |                           |  |
| Nausea   |                           |                           |  |

|   |                         |                           |  |
|---|-------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)                          | 77 / 166 (46.39%)<br>77 | 48 / 167 (28.74%)<br>48   |  |
| Diarrhea<br>subjects affected / exposed<br>occurrences (all)              | 73 / 166 (43.98%)<br>73 | 40 / 167 (23.95%)<br>40   |  |
| Mucositis/esophagitis<br>subjects affected / exposed<br>occurrences (all) | 38 / 166 (22.89%)<br>38 | 60 / 167 (35.93%)<br>60   |  |
| Respiratory, thoracic and mediastinal disorders                           |                         |                           |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)             | 5 / 166 (3.01%)<br>5    | 42 / 167 (25.15%)<br>42   |  |
| Dyspnea<br>subjects affected / exposed<br>occurrences (all)               | 25 / 166 (15.06%)<br>25 | 37 / 167 (22.16%)<br>37   |  |
| Skin and subcutaneous tissue disorders                                    |                         |                           |  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)              | 96 / 166 (57.83%)<br>96 | 150 / 167 (89.82%)<br>150 |  |
| Musculoskeletal and connective tissue disorders                           |                         |                           |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)            | 53 / 166 (31.93%)<br>53 | 50 / 167 (29.94%)<br>50   |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)               | 28 / 166 (16.87%)<br>28 | 35 / 167 (20.96%)<br>35   |  |
| Infections and infestations   |                         |                           |  |
| Infection<br>subjects affected / exposed<br>occurrences (all)             | 50 / 166 (30.12%)<br>50 | 42 / 167 (25.15%)<br>42   |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 18 October 2013  | Additional precaution regarding application of IMP cabazitaxel with OATP1B1 substrates  |
| 20 December 2013 | With Amendment 2 the study design was changed to give patients with invasive tumor residuals after end of study treatment detected in core biopsy the option to receive anthracycline-containing chemotherapy prior to surgery. This change resulted in a modification of the definition of treatment failures for the primary endpoint: patients in whom success cannot be determined (e.g. patients in whom histology is not evaluable) or who have invasive tumor residuals in the core biopsy taken after end of study treatment will be included in the denominator, i.e. these patients will be considered as treatment failures. |
| 28 November 2014 | Prolongation of enrolment period.   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28768217>