



Clinical trial results:

A Randomized, Placebo-Controlled, Double-Blind, Phase 3 Study Evaluating Safety and Efficacy of the Addition of Veliparib Plus Carboplatin Versus the Addition of Carboplatin to Standard Neoadjuvant Chemotherapy Versus Standard Neoadjuvant Chemotherapy in Subjects With Early Stage Triple Negative Breast Cancer (TNBC)

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2013-002377-21 |
| Trial protocol | BE DE CZ HU GB ES IT PL FR |
| Global end of trial date | 12 November 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 29 October 2021 |
| First version publication date | 29 October 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M14-011 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02032277 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | AbbVie |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB |
| Public contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |

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 | 12 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the rate of pathologic complete response (pCR) in breast and any resected lymph node tissue after treatment with neoadjuvant veliparib in combination with carboplatin and paclitaxel followed by doxorubicin + cyclophosphamide compared to two neoadjuvant chemotherapy regimens (carboplatin + paclitaxel followed by doxorubicin + cyclophosphamide or paclitaxel alone followed by doxorubicin + cyclophosphamide) in participants with early stage TNBC.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment | 02 April 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 19 |
| Country: Number of subjects enrolled | Belgium: 25 |
| Country: Number of subjects enrolled | Canada: 10 |
| Country: Number of subjects enrolled | Czechia: 20 |
| Country: Number of subjects enrolled | France: 36 |
| Country: Number of subjects enrolled | Germany: 55 |
| Country: Number of subjects enrolled | Hungary: 20 |
| Country: Number of subjects enrolled | Italy: 13 |
| Country: Number of subjects enrolled | Korea, Republic of: 73 |
| Country: Number of subjects enrolled | Netherlands: 3 |
| Country: Number of subjects enrolled | Russian Federation: 23 |
| Country: Number of subjects enrolled | Spain: 39 |
| Country: Number of subjects enrolled | Taiwan: 8 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | United States: 282 |
| Worldwide total number of subjects | 634 |
| EEA total number of subjects | 211 |

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) | 555 |
| From 65 to 84 years | 79 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures and baseline tumor assessments were performed within 28 days prior to the first dose of study drug (except the baseline mammogram, which could be up to 56 days prior to the start of study treatment).

Period 1

| | |
|------------------------------|--------------------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Data analyst, Carer |

Blinding implementation details:

AbbVie, the Investigator, the study site personnel, and subject remained blinded to each subject's treatment with veliparib/placebo. AbbVie, the Investigator, the study site personnel other than pharmacy personnel, and the subject remained blinded to each subject's treatment with carboplatin/placebo throughout the course of the study.

Arms

| | |
|------------------------------|-------------------------------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |

Arm description:

veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m²) followed by doxorubicin/cyclophosphamide (AC)

| | |
|----------------------------------------|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1

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

Dosage and administration details:

carboplatin (AUC 6 mg/mL/min) on Day 1 of four 21-day cycles via infusion during Chemotherapy Segment 1

| | |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

paclitaxel (80 mg/m²) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: doxorubicin (60 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: cyclophosphamide (600 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |
| Arm title | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Arm description: placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m ²) followed by AC | |
| Arm type | Placebo |
| Investigational medicinal product name | placebo for veliparib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: placebo for veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1 | |
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: carboplatin (AUC 6 mg/mL/min) on Day 1 of four 21-day cycles via infusion during Chemotherapy Segment 1 | |
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: paclitaxel (80 mg/m ²) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1 | |
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: doxorubicin (60 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: cyclophosphamide (600 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |
| Arm title | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Arm description: placebo + placebo + paclitaxel (80 mg/m ²) followed by AC | |
| Arm type | Placebo |
| Investigational medicinal product name | placebo for veliparib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: placebo for veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1 | |
| Investigational medicinal product name | placebo for carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: placebo for carboplatin via infusion during Chemotherapy Segment 1 | |
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: paclitaxel (80 mg/m ²) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1 | |
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: doxorubicin (60 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: cyclophosphamide (600 mg/m ²) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2 | |

| Number of subjects in period 1 | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
|---------------------------------------|--------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------|
| Started | 316 | 160 | 158 |
| Completed | 248 | 123 | 115 |
| Not completed | 68 | 37 | 43 |
| Consent withdrawn by subject | 13 | 8 | 10 |
| Death | 38 | 16 | 24 |
| Lost to follow-up | 16 | 10 | 8 |
| Other, Not Specified | 1 | 3 | 1 |

Baseline characteristics

Reporting groups

| | |
|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reporting group title | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |
| Reporting group description: | veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m ²) followed by doxorubicin/cyclophosphamide (AC) |
| Reporting group title | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Reporting group description: | placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m ²) followed by AC |
| Reporting group title | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Reporting group description: | placebo + placebo + paclitaxel (80 mg/m ²) followed by AC |

| Reporting group values | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
|-------------------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|
| Number of subjects | 316 | 160 | 158 |
| Age categorical | | | |
| Units: Subjects | | | |
| <= 50 years | 151 | 87 | 81 |
| > 50 years | 165 | 73 | 77 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 316 | 160 | 158 |
| Male | 0 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 48 | 19 | 21 |
| Not Hispanic or Latino | 268 | 140 | 136 |
| Unknown or Not Reported | 0 | 1 | 1 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 51 | 23 | 18 |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | 0 |
| Black or African American | 33 | 7 | 15 |
| White | 232 | 127 | 124 |
| More than one race | 0 | 0 | 1 |
| Unknown or Not Reported | 0 | 1 | 0 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 634 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| <= 50 years | 319 | | |
| > 50 years | 315 | | |

| | | | |
|-------------------------------------------|-----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 634 | | |
| Male | 0 | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 88 | | |
| Not Hispanic or Latino | 544 | | |
| Unknown or Not Reported | 2 | | |
| Race | | | |
| Units: Subjects | | | |
| Asian | 92 | | |
| Native Hawaiian or Other Pacific Islander | 2 | | |
| Black or African American | 55 | | |
| White | 483 | | |
| More than one race | 1 | | |
| Unknown or Not Reported | 1 | | |

End points

End points reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Reporting group title | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |
| Reporting group description: veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m ²) followed by doxorubicin/cyclophosphamide (AC) | |
| Reporting group title | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Reporting group description: placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m ²) followed by AC | |
| Reporting group title | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Reporting group description: placebo + placebo + paclitaxel (80 mg/m ²) followed by AC | |

Primary: Percentage of Participants With Pathological Complete Response (pCR)

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| End point title | Percentage of Participants With Pathological Complete Response (pCR) |
| End point description: pCR in the breast tissue and the lymph node tissue was assessed upon completion of pre-operative systemic therapy and definitive surgery. pCR was defined by the absence of any residual invasive cancer on hematoxylin and eosin evaluation of the resected breast specimen and any resected lymph node tissue following completion of neoadjuvant systemic therapy. | |
| End point type | Primary |
| End point timeframe: At the time of definitive surgery (approximately 24-36 weeks from first dose of study drug) | |

| End point values | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo | |
|-----------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 316 | 160 | 158 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 53.2 (47.7 to 58.7) | 57.5 (49.8 to 65.2) | 31.0 (23.8 to 38.2) | |

Statistical analyses

| | |
|------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |

| | |
|-----------------------------------------|-----------------|
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.2 |

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | -4.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.8 |
| upper limit | 5.1 |

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.357 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.2 |

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC v Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | -4.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.8 |
| upper limit | 4.9 |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 3.8 |

| | |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |

| | |
|-----------------------------------------|---------------|
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 22.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 13.1 |
| upper limit | 31.2 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 3.9 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 22.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 13.2 |
| upper limit | 31.2 |

Secondary: Percentage of Participants With Events of Disease Progression or Death

| | |
|-----------------|------------------------------------------------------------------------|
| End point title | Percentage of Participants With Events of Disease Progression or Death |
|-----------------|------------------------------------------------------------------------|

End point description:

Event free survival (EFS) was secondary endpoint, defined as the time from random assignment to documentation of the first of the following events: discontinuation of study therapy due to protocol-defined progression prior to surgery; local, regional, or distant invasive recurrence of breast cancer following curative surgery; a new breast cancer; a new onset malignancy; or death as a result of any cause.

Due to low event rates, the median EFS could not be estimated for any of the treatment arms. Therefore, the data table presents the percentage of participants with any of the above events within the given time frame. If a participant had not experienced any of the above events, that participant was censored at date of last available disease assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4 years from the date of definitive surgery (i.e., approximately 24-36 weeks from first dose of study drug)

| End point values | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo | |
|-----------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 316 | 160 | 158 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 20.6 | 18.8 | 29.7 | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Unstratified analysis

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.69 |
| Method | Logrank |

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|

Statistical analysis description:

Unstratified analysis

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.778 |
| Method | Wilcoxon p-value |

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.69 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.092 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.709 |
| upper limit | 1.683 |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.62 |
| Method | Logrank |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |

| | |
|-----------------------------------------|------------------|
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.627 |
| Method | Wilcoxon p-value |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.62 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.116 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.724 |
| upper limit | 1.721 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Unstratified analysis

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo v Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 |
| Method | Wilcoxon p-value |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

Unstratified analysis

| | |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------|

| | |
|-----------------------------------------|-------------------------------|
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.021 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.643 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.442 |
| upper limit | 0.935 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 10 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.015 |
| Method | Logrank |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 11 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.04 |
| Method | Wilcoxon p-value |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 12 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.

| | |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------|

| | |
|-----------------------------------------|-------------------------------|
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.016 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.432 |
| upper limit | 0.917 |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.02 |
| Method | Logrank |

Secondary: Percentage of Participants With an Event of Death

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title | Percentage of Participants With an Event of Death |
| End point description: | |
| <p>Overall survival (OS) was secondary endpoint, defined as the number of days from the day the participant was randomized to the date of the participant's death. All events of death were included, regardless of whether the event occurred while the participant was still taking study drug, or after the participant discontinued study drug.</p> <p>Due to low event rates, the median EFS could not be estimated for any of the treatment arms. Therefore, the data table presents the percentage of participants with any of the above events within the given time frame. If a participant had not died, then the data was censored at the date when the participant was last known to be alive.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 4 years from the date of definitive surgery (i.e., approximately 24-36 weeks from first dose of study drug) | |

| End point values | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo | |
|-----------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 316 | 160 | 158 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 12.0 | 10.0 | 13.9 | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description: Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.536 |
| Method | Logrank |

| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.642 |
| Method | Wilcoxon p-value |

| Statistical analysis title | Statistical Analysis 3 |
|------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description: Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.536 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.202 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 2.156 |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.454 |
| Method | Logrank |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.404 |
| Method | Wilcoxon p-value |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.455 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.25 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.696 |
| upper limit | 2.242 |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.431 |
| Method | Logrank |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 8 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.426 |
| Method | Wilcoxon p-value |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 9 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.432 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.479 |
| upper limit | 1.37 |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 10 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.454 |
| Method | Logrank |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 11 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.837 |
| Method | Wilcoxon p-value |

| | |
|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 12 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 474 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.452 |
| Method | Cox proportional hazard model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.817 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.483 |
| upper limit | 1.383 |

Secondary: Percentage of Participants Eligible for Breast Conservation After Therapy

| | |
|-----------------|---------------------------------------------------------------------------|
| End point title | Percentage of Participants Eligible for Breast Conservation After Therapy |
|-----------------|---------------------------------------------------------------------------|

End point description:

Whether a participant was eligible for breast conserving surgery for whom mastectomy was planned at diagnosis was determined by the participant's surgeon prior to chemotherapy and after completion of chemotherapy. The breast conservation rate (BCR) was defined as the rate at which participants are eligible for breast conservation after neoadjuvant therapy among participants for whom mastectomy was planned at diagnosis, and is presented as the percentage of participants eligible for breast conservation after therapy among participants who were deemed ineligible for breast conservation surgery at screening.

Randomized participants who were deemed ineligible for breast conservation surgery at screening. Only participants with evaluations at both screening and pre-op visits were included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At the time of definitive surgery (approximately 24-36 weeks from first dose of study drug)

| End point values | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo | |
|-----------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 34 | 34 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 61.6 (50.5 to 72.8) | 44.1 (27.4 to 60.8) | 44.1 (27.4 to 60.8) | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Unstratified analysis

| | |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 4.6 |

| | |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 17.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 37.6 |

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 4.5 |

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |

| | |
|-----------------------------------------|-------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.132 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference |
| Point estimate | 15.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.3 |
| upper limit | 35.9 |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 4.6 |

| | |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Unstratified analysis | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 17.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 37.6 |

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 4.5 |

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical Analysis 8 |
| Statistical analysis description: | |
| Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation. | |
| Comparison groups | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.139 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference |
| Point estimate | 15.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6 |
| upper limit | 36.3 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 30 days following discontinuation of study drug administration; up to a maximum of 150 days.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------------------------------------|
| Reporting group title | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC |
|-----------------------|-------------------------------------------------------------|

Reporting group description:

veliparib (50 mg PO BID) + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m²) followed by AC

| | |
|-----------------------|-----------------------------------------------------------|
| Reporting group title | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC |
|-----------------------|-----------------------------------------------------------|

Reporting group description:

placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m²) followed by AC

| | |
|-----------------------|-------------------------------------------------------|
| Reporting group title | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC |
|-----------------------|-------------------------------------------------------|

Reporting group description:

placebo + placebo + paclitaxel (80 mg/m²) followed by AC

| Serious adverse events | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC |
|---------------------------------------------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 95 / 313 (30.35%) | 22 / 157 (14.01%) | 42 / 158 (26.58%) |
| number of deaths (all causes) | 38 | 22 | 16 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| METASTASES TO MENINGES | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 1 / 157 (0.64%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMBOLISM | | | |

| | | | |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| DEATH | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| FATIGUE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MALAISE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYREXIA | | | |
| subjects affected / exposed | 4 / 313 (1.28%) | 1 / 157 (0.64%) | 2 / 158 (1.27%) |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 1 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 2 / 157 (1.27%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| HYPOXIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAINFUL RESPIRATION | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 6 / 313 (1.92%) | 3 / 157 (1.91%) | 2 / 158 (1.27%) |
| occurrences causally related to treatment / all | 2 / 6 | 2 / 3 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| ADJUSTMENT DISORDER WITH DEPRESSED MOOD | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENTAL STATUS CHANGES | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PSYCHOGENIC SEIZURE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|----------------------------------------------------|-----------------|-----------------|-----------------|
| Investigations | | | |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| ANKLE FRACTURE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMORAL NECK FRACTURE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RIB FRACTURE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND SECRETION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WRIST FRACTURE | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIAL FLUTTER | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYOCARDIAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUS TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUPRAVENTRICULAR EXTRASYSTOLES | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUPRAVENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VENTRICULAR EXTRASYSTOLES | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| CEREBROVASCULAR ACCIDENT | | | |

| | | | |
|-------------------------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MIGRAINE WITH AURA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PARTIAL SEIZURES | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEIZURE | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 3 / 313 (0.96%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 11 / 313 (3.51%) | 3 / 157 (1.91%) | 6 / 158 (3.80%) |
| occurrences causally related to treatment / all | 3 / 14 | 0 / 3 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEBRILE NEUTROPENIA | | | |

| | | | |
|-------------------------------------------------|-------------------|-----------------|-------------------|
| subjects affected / exposed | 51 / 313 (16.29%) | 6 / 157 (3.82%) | 23 / 158 (14.56%) |
| occurrences causally related to treatment / all | 5 / 55 | 0 / 6 | 1 / 26 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 2 / 157 (1.27%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 4 / 313 (1.28%) | 1 / 157 (0.64%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 4 / 313 (1.28%) | 0 / 157 (0.00%) | 2 / 158 (1.27%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROCOLITIS | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHOIDAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MALLORY-WEISS SYNDROME | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |
| subjects affected / exposed | 6 / 313 (1.92%) | 2 / 157 (1.27%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIC COLITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCTALGIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STOMATITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 313 (0.96%) | 2 / 157 (1.27%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| HEPATITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| HIDRADENITIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| ATYPICAL PNEUMONIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERAEemia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 2 / 158 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRONCHITIS | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED SEPSIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROCOLITIS INFECTIOUS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 2 / 158 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROCOLITIS VIRAL | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HERPES SIMPLEX MENINGITIS | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGEAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOCYSTIS JIROVECI PNEUMONIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 4 / 313 (1.28%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPSIS | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TONSILLITIS | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 3 / 158 (1.90%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR DEVICE INFECTION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VULVAL ABSCESS | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND INFECTION | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 157 (0.64%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 0 / 157 (0.00%) | 1 / 158 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 157 (0.00%) | 0 / 158 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC | Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC | Arm C: Placebo + Placebo + Paclitaxel, Followed by AC |
|----------------------------------------------------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 312 / 313 (99.68%) | 157 / 157 (100.00%) | 158 / 158 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 3 / 313 (0.96%) | 8 / 157 (5.10%) | 0 / 158 (0.00%) |
| occurrences (all) | 3 | 8 | 0 |
| Vascular disorders | | | |

| | | | |
|------------------------------------------------------|--------------------|-------------------|-------------------|
| FLUSHING | | | |
| subjects affected / exposed | 11 / 313 (3.51%) | 9 / 157 (5.73%) | 7 / 158 (4.43%) |
| occurrences (all) | 14 | 10 | 7 |
| HOT FLUSH | | | |
| subjects affected / exposed | 51 / 313 (16.29%) | 22 / 157 (14.01%) | 28 / 158 (17.72%) |
| occurrences (all) | 63 | 27 | 34 |
| HYPERTENSION | | | |
| subjects affected / exposed | 17 / 313 (5.43%) | 6 / 157 (3.82%) | 3 / 158 (1.90%) |
| occurrences (all) | 27 | 7 | 3 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 51 / 313 (16.29%) | 20 / 157 (12.74%) | 25 / 158 (15.82%) |
| occurrences (all) | 134 | 43 | 64 |
| FATIGUE | | | |
| subjects affected / exposed | 183 / 313 (58.47%) | 89 / 157 (56.69%) | 92 / 158 (58.23%) |
| occurrences (all) | 339 | 158 | 169 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 17 / 313 (5.43%) | 4 / 157 (2.55%) | 2 / 158 (1.27%) |
| occurrences (all) | 18 | 8 | 2 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 29 / 313 (9.27%) | 16 / 157 (10.19%) | 15 / 158 (9.49%) |
| occurrences (all) | 32 | 19 | 18 |
| PAIN | | | |
| subjects affected / exposed | 17 / 313 (5.43%) | 8 / 157 (5.10%) | 9 / 158 (5.70%) |
| occurrences (all) | 22 | 9 | 10 |
| PYREXIA | | | |
| subjects affected / exposed | 39 / 313 (12.46%) | 16 / 157 (10.19%) | 15 / 158 (9.49%) |
| occurrences (all) | 49 | 22 | 17 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 12 / 313 (3.83%) | 2 / 157 (1.27%) | 9 / 158 (5.70%) |
| occurrences (all) | 14 | 2 | 10 |
| Reproductive system and breast disorders | | | |
| BREAST PAIN | | | |
| subjects affected / exposed | 7 / 313 (2.24%) | 13 / 157 (8.28%) | 3 / 158 (1.90%) |
| occurrences (all) | 7 | 14 | 6 |

| | | | |
|-------------------------------------------------|-------------------|-------------------|-------------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 64 / 313 (20.45%) | 24 / 157 (15.29%) | 25 / 158 (15.82%) |
| occurrences (all) | 77 | 31 | 30 |
| DYSпноEA | | | |
| subjects affected / exposed | 55 / 313 (17.57%) | 21 / 157 (13.38%) | 31 / 158 (19.62%) |
| occurrences (all) | 73 | 26 | 44 |
| EPISTAXIS | | | |
| subjects affected / exposed | 46 / 313 (14.70%) | 27 / 157 (17.20%) | 21 / 158 (13.29%) |
| occurrences (all) | 52 | 31 | 22 |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 13 / 313 (4.15%) | 11 / 157 (7.01%) | 6 / 158 (3.80%) |
| occurrences (all) | 15 | 13 | 6 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 26 / 313 (8.31%) | 8 / 157 (5.10%) | 16 / 158 (10.13%) |
| occurrences (all) | 28 | 9 | 16 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 24 / 313 (7.67%) | 18 / 157 (11.46%) | 15 / 158 (9.49%) |
| occurrences (all) | 27 | 18 | 17 |
| INSOMNIA | | | |
| subjects affected / exposed | 71 / 313 (22.68%) | 31 / 157 (19.75%) | 37 / 158 (23.42%) |
| occurrences (all) | 75 | 36 | 43 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 32 / 313 (10.22%) | 10 / 157 (6.37%) | 18 / 158 (11.39%) |
| occurrences (all) | 51 | 15 | 27 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 26 / 313 (8.31%) | 6 / 157 (3.82%) | 16 / 158 (10.13%) |
| occurrences (all) | 40 | 6 | 24 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 9 / 313 (2.88%) | 3 / 157 (1.91%) | 8 / 158 (5.06%) |
| occurrences (all) | 11 | 4 | 10 |
| Nervous system disorders | | | |

| | | | |
|-------------------------------------------------------------------------------------------------------------------|---------------------------|--------------------------|---------------------------|
| DIZZINESS subjects affected / exposed occurrences (all) | 55 / 313 (17.57%) 64 | 20 / 157 (12.74%) 22 | 24 / 158 (15.19%) 34 |
| DYSGEUSIA subjects affected / exposed occurrences (all) | 75 / 313 (23.96%) 82 | 29 / 157 (18.47%) 32 | 39 / 158 (24.68%) 40 |
| HEADACHE subjects affected / exposed occurrences (all) | 88 / 313 (28.12%) 109 | 46 / 157 (29.30%) 63 | 40 / 158 (25.32%) 53 |
| PARAESTHESIA subjects affected / exposed occurrences (all) | 31 / 313 (9.90%) 41 | 12 / 157 (7.64%) 21 | 17 / 158 (10.76%) 19 |
| PERIPHERAL SENSORY NEUROPATHY subjects affected / exposed occurrences (all) | 135 / 313 (43.13%) 190 | 77 / 157 (49.04%) 121 | 70 / 158 (44.30%) 93 |
| Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all) | 212 / 313 (67.73%) 632 | 37 / 157 (23.57%) 59 | 105 / 158 (66.46%) 281 |
| LEUKOPENIA subjects affected / exposed occurrences (all) | 62 / 313 (19.81%) 138 | 21 / 157 (13.38%) 33 | 43 / 158 (27.22%) 102 |
| NEUTROPENIA subjects affected / exposed occurrences (all) | 237 / 313 (75.72%) 836 | 45 / 157 (28.66%) 96 | 115 / 158 (72.78%) 406 |
| THROMBOCYTOPENIA subjects affected / exposed occurrences (all) | 169 / 313 (53.99%) 460 | 4 / 157 (2.55%) 6 | 67 / 158 (42.41%) 147 |
| Eye disorders DRY EYE subjects affected / exposed occurrences (all) | 14 / 313 (4.47%) 14 | 9 / 157 (5.73%) 10 | 5 / 158 (3.16%) 5 |
| VISION BLURRED subjects affected / exposed occurrences (all) | 11 / 313 (3.51%) 11 | 8 / 157 (5.10%) 9 | 4 / 158 (2.53%) 4 |
| Gastrointestinal disorders | | | |

| | | | |
|----------------------------------------|--------------------|--------------------|--------------------|
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 37 / 313 (11.82%) | 13 / 157 (8.28%) | 21 / 158 (13.29%) |
| occurrences (all) | 45 | 19 | 27 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 25 / 313 (7.99%) | 9 / 157 (5.73%) | 6 / 158 (3.80%) |
| occurrences (all) | 37 | 11 | 9 |
| CONSTIPATION | | | |
| subjects affected / exposed | 135 / 313 (43.13%) | 71 / 157 (45.22%) | 62 / 158 (39.24%) |
| occurrences (all) | 168 | 102 | 77 |
| DIARRHOEA | | | |
| subjects affected / exposed | 120 / 313 (38.34%) | 58 / 157 (36.94%) | 50 / 158 (31.65%) |
| occurrences (all) | 184 | 78 | 68 |
| DRY MOUTH | | | |
| subjects affected / exposed | 24 / 313 (7.67%) | 9 / 157 (5.73%) | 3 / 158 (1.90%) |
| occurrences (all) | 26 | 9 | 3 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 46 / 313 (14.70%) | 29 / 157 (18.47%) | 32 / 158 (20.25%) |
| occurrences (all) | 60 | 43 | 38 |
| GASTROESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 30 / 313 (9.58%) | 13 / 157 (8.28%) | 9 / 158 (5.70%) |
| occurrences (all) | 36 | 18 | 9 |
| NAUSEA | | | |
| subjects affected / exposed | 225 / 313 (71.88%) | 98 / 157 (62.42%) | 119 / 158 (75.32%) |
| occurrences (all) | 450 | 169 | 256 |
| STOMATITIS | | | |
| subjects affected / exposed | 121 / 313 (38.66%) | 41 / 157 (26.11%) | 48 / 158 (30.38%) |
| occurrences (all) | 162 | 49 | 67 |
| VOMITING | | | |
| subjects affected / exposed | 90 / 313 (28.75%) | 26 / 157 (16.56%) | 58 / 158 (36.71%) |
| occurrences (all) | 130 | 38 | 93 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 190 / 313 (60.70%) | 102 / 157 (64.97%) | 95 / 158 (60.13%) |
| occurrences (all) | 231 | 120 | 119 |
| DERMATITIS ACNEIFORM | | | |

| | | | |
|-------------------------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 25 / 313 (7.99%) | 16 / 157 (10.19%) | 10 / 158 (6.33%) |
| occurrences (all) | 29 | 18 | 13 |
| DRY SKIN | | | |
| subjects affected / exposed | 9 / 313 (2.88%) | 8 / 157 (5.10%) | 5 / 158 (3.16%) |
| occurrences (all) | 9 | 8 | 5 |
| ERYTHEMA | | | |
| subjects affected / exposed | 4 / 313 (1.28%) | 10 / 157 (6.37%) | 4 / 158 (2.53%) |
| occurrences (all) | 5 | 10 | 5 |
| NAIL DISCOLOURATION | | | |
| subjects affected / exposed | 20 / 313 (6.39%) | 10 / 157 (6.37%) | 7 / 158 (4.43%) |
| occurrences (all) | 20 | 10 | 7 |
| NAIL DISORDER | | | |
| subjects affected / exposed | 12 / 313 (3.83%) | 9 / 157 (5.73%) | 7 / 158 (4.43%) |
| occurrences (all) | 12 | 10 | 7 |
| ONYCHOLYSIS | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 8 / 157 (5.10%) | 7 / 158 (4.43%) |
| occurrences (all) | 2 | 9 | 8 |
| PRURITUS | | | |
| subjects affected / exposed | 21 / 313 (6.71%) | 12 / 157 (7.64%) | 14 / 158 (8.86%) |
| occurrences (all) | 25 | 15 | 14 |
| RASH | | | |
| subjects affected / exposed | 25 / 313 (7.99%) | 9 / 157 (5.73%) | 13 / 158 (8.23%) |
| occurrences (all) | 26 | 10 | 16 |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 17 / 313 (5.43%) | 8 / 157 (5.10%) | 4 / 158 (2.53%) |
| occurrences (all) | 27 | 13 | 5 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 37 / 313 (11.82%) | 37 / 157 (23.57%) | 25 / 158 (15.82%) |
| occurrences (all) | 52 | 41 | 35 |
| BACK PAIN | | | |
| subjects affected / exposed | 34 / 313 (10.86%) | 13 / 157 (8.28%) | 14 / 158 (8.86%) |
| occurrences (all) | 40 | 13 | 14 |
| BONE PAIN | | | |

| | | | |
|------------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 43 / 313 (13.74%) | 11 / 157 (7.01%) | 18 / 158 (11.39%) |
| occurrences (all) | 49 | 12 | 23 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 16 / 313 (5.11%) | 3 / 157 (1.91%) | 6 / 158 (3.80%) |
| occurrences (all) | 19 | 3 | 6 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 16 / 313 (5.11%) | 4 / 157 (2.55%) | 3 / 158 (1.90%) |
| occurrences (all) | 18 | 4 | 4 |
| MYALGIA | | | |
| subjects affected / exposed | 67 / 313 (21.41%) | 37 / 157 (23.57%) | 31 / 158 (19.62%) |
| occurrences (all) | 96 | 48 | 45 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 20 / 313 (6.39%) | 8 / 157 (5.10%) | 15 / 158 (9.49%) |
| occurrences (all) | 23 | 8 | 18 |
| Infections and infestations | | | |
| FOLLICULITIS | | | |
| subjects affected / exposed | 7 / 313 (2.24%) | 10 / 157 (6.37%) | 7 / 158 (4.43%) |
| occurrences (all) | 9 | 12 | 7 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 23 / 313 (7.35%) | 10 / 157 (6.37%) | 10 / 158 (6.33%) |
| occurrences (all) | 28 | 12 | 12 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 27 / 313 (8.63%) | 13 / 157 (8.28%) | 10 / 158 (6.33%) |
| occurrences (all) | 35 | 14 | 13 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 22 / 313 (7.03%) | 12 / 157 (7.64%) | 12 / 158 (7.59%) |
| occurrences (all) | 27 | 14 | 14 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 74 / 313 (23.64%) | 28 / 157 (17.83%) | 39 / 158 (24.68%) |
| occurrences (all) | 96 | 44 | 57 |
| DEHYDRATION | | | |
| subjects affected / exposed | 25 / 313 (7.99%) | 8 / 157 (5.10%) | 15 / 158 (9.49%) |
| occurrences (all) | 52 | 19 | 27 |
| HYPERGLYCAEMIA | | | |

| | | | |
|-----------------------------|-------------------|------------------|-------------------|
| subjects affected / exposed | 12 / 313 (3.83%) | 5 / 157 (3.18%) | 10 / 158 (6.33%) |
| occurrences (all) | 16 | 8 | 16 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 36 / 313 (11.50%) | 11 / 157 (7.01%) | 16 / 158 (10.13%) |
| occurrences (all) | 56 | 14 | 29 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 23 / 313 (7.35%) | 2 / 157 (1.27%) | 10 / 158 (6.33%) |
| occurrences (all) | 34 | 2 | 12 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 24 November 2013 | <ul style="list-style-type: none">• Update Residual Cancer Burden (RCB) to a tertiary endpoint and clarify that RCB information will not be collected from all sites.• Revise pregnancy testing requirements; Remove 3 hour PK sample at paclitaxel (P)1 visit and request PK samples at P1 visit only if feasible.• Updated the blood samples for Pharmacogenetic analysis to include the collection of an additional (optional) 4mL whole blood sample (for a total of 2 samples) at P1.• Clarify plan for tumor biopsy collection and remove biopsy collection at AC1; Add Quality of Life Questionnaire (QLQ)-C30 questionnaire in the study procedures, remove Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy (QLQ CIPN20) questionnaire and revise the frequency and duration of collection.• Update survival data collection frequency to every 6 months and clarify which data points will be collected in the survival portion of the study. |
| 01 April 2014 | <ul style="list-style-type: none">• Update Inclusion Criterion 7 to require the use of contraception for 6 months following completion of therapy.• Add Inclusion Criterion 9 to ensure subjects are capable of taking oral medication.• Add requirement for pregnancy testing at P4, P7, P10 and AC1 visits.• Add requirement for urine testing at AC2 and AC4 visits. |
| 22 July 2014 | <ul style="list-style-type: none">• Increase approximate number of participating sites to 250.• Update clinical stage in Inclusion Criterion 2 to T2-3 N0-2 or T1 N1-2.• Allow for subjects with Stage III disease to undergo alternate imaging per local standards. |
| 25 November 2014 | <ul style="list-style-type: none">• Update Study Procedures, Medical History and Oncology History to collect menses history and family history of breast and ovarian cancer to evaluate (post-study analysis) for chemotherapy induced amenorrhea and to generate hypotheses around benefits of investigational therapy in subjects with or without a family history of breast and/or ovarian cancer.• Update PK methods to include additional timepoints to collect a sample for analysis to coincide with the time of relapse; increase the sample volume for plasma markers to ensure sufficient plasma is available for testing using the current methods; include circulating nucleic acid sample collection for additional sequencing studies.• Correct the duration for avoiding pregnancy from 90 days to 6 months to align with Inclusion Criterion. |
| 31 August 2016 | <ul style="list-style-type: none">• Update appropriate sections to move Event Free Survival (EFS) and Overall Survival (OS) from Tertiary Efficacy Endpoints to Secondary Efficacy Endpoints• Change primary contact for protocol deviations. |
| 25 October 2018 | <ul style="list-style-type: none">• Revise the duration subjects will be evaluated for disease recurrent during the Post-Surgery Follow-Up period for the secondary endpoint of event-free survival (EFS).• Update primary study contacts for protocol deviations. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported