



Clinical trial results:

A Randomized, Phase 2 Study of the Efficacy and Tolerability of Veliparib in Combination with Temozolomide or Veliparib in Combination with Carboplatin and Paclitaxel Versus Placebo Plus Carboplatin and Paclitaxel in Subjects with BRCA1 or BRCA2 Mutation and Metastatic Breast Cancer

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2011-002913-12 |
| Trial protocol | CZ HU DK SK FI SE BE NL ES |
| Global end of trial date | 02 September 2020 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 27 August 2021 |
| First version publication date | 27 August 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M12-895 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01506609 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AbbVie |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United States, SL6 4UB |
| Public contact | Global Medical Services, AbbVie, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, 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 | 02 September 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 September 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the progression-free survival (PFS) of oral veliparib in combination with TMZ or in combination with carboplatin and paclitaxel compared to placebo plus carboplatin and paclitaxel in subjects with Breast Cancer Gene (BRCA)1 or BRCA2 mutation and locally recurrent or metastatic breast cancer.

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 | 23 January 2012 |
| 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 | Argentina: 6 |
| Country: Number of subjects enrolled | Australia: 14 |
| Country: Number of subjects enrolled | Belgium: 12 |
| Country: Number of subjects enrolled | Brazil: 4 |
| Country: Number of subjects enrolled | Canada: 17 |
| Country: Number of subjects enrolled | Czechia: 12 |
| Country: Number of subjects enrolled | Denmark: 9 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | France: 36 |
| Country: Number of subjects enrolled | Hungary: 7 |
| Country: Number of subjects enrolled | Israel: 9 |
| Country: Number of subjects enrolled | Netherlands: 8 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Poland: 7 |
| Country: Number of subjects enrolled | Romania: 1 |
| Country: Number of subjects enrolled | Russian Federation: 5 |
| Country: Number of subjects enrolled | Spain: 9 |
| Country: Number of subjects enrolled | Sweden: 5 |
| Country: Number of subjects enrolled | Ukraine: 20 |

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 110 |
| Worldwide total number of subjects | 294 |
| EEA total number of subjects | 109 |

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) | 283 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Under the original protocol, approximately 4 participants were randomized in a 1:1:1 ratio (Group 1) to 1 of the 3 treatment arms at approximately 3 research sites. Participants randomized under the original protocol were in Group 1, and were not included in the primary efficacy analyses.

Pre-assignment

Screening details:

Following approval of Amendment 1, the veliparib dose in combination with carboplatin + paclitaxel was increased to 120 mg BID. Participants were randomized 1:1:1 ratio (Group 2) to 1 of the 3 treatment arms at approximately 120 sites. Participants randomized following Amendment 1 approval were in Group 2 and included in primary efficacy analyses.

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 |

Blinding implementation details:

This is a partially blinded study. AbbVie, the investigator, the study site personnel, and the subject remained blinded to each subject's treatment with veliparib or placebo in the carboplatin + paclitaxel arms throughout the course of the study. All subjects randomized to the veliparib + TMZ treatment arm were treated in an open-label fashion.

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 Placebo + Carboplatin/ Paclitaxel |

Arm description:

Placebo BID Days 1 through 7 plus carboplatin target area under the curve (mg•min/mL) (AUC) 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects self-administer the morning dose of placebo and the evening dose placebo approximately 12 hours after the morning dose with or without food in the same calendar day for Days 1 through 7 of the 21-day cycle.

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

Dosage and administration details:

Carboplatin will be administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion.

| | |
|--|---------------------------------------|
| 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 will be administered intravenously over approximately 3 hours at a dose of 175 mg/m².

| | |
|------------------|---|
| Arm title | Group 1 Veliparib + Carboplatin/ Paclitaxel |
|------------------|---|

Arm description:

Veliparib 80 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|--|--------------|
| 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:

Subjects will self-administer the morning dose of veliparib and the evening dose of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day for Days 1 through 7 of the 21-day cycle.

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

Dosage and administration details:

Carboplatin will be administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion.

| | |
|--|---------------------------------------|
| 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 will be administered intravenously over approximately 3 hours at a dose of 175 mg/m².

| | |
|------------------|-------------------------|
| Arm title | Group 1 Veliparib + TMZ |
|------------------|-------------------------|

Arm description:

Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m² QD Days 1 through 5 in each 28-day cycle.

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

Dosage and administration details:

Subjects will self-administer the morning dose of veliparib and TMZ at the same time under fasting conditions (to reduce the chance of nausea and vomiting per the TMZ label recommendation) and the evening doses of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day.

| | |
|--|-----------|
| 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: Subjects will self-administer the morning dose of veliparib and TMZ at the same time under fasting conditions (to reduce the chance of nausea and vomiting per the TMZ label recommendation) and the evening doses of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day. | |
| Arm title | Group 2 Placebo + Carboplatin/ Paclitaxel |
| Arm description: Placebo BID Days 1 through 7 plus carboplatin carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: Subjects self-administer the morning dose of placebo and the evening dose placebo approximately 12 hours after the morning dose with or without food in the same calendar day for Days 1 through 7 of the 21-day cycle. | |
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: Carboplatin will be administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion. | |
| 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 will be administered intravenously over approximately 3 hours at a dose of 175 mg/m ² . | |
| Arm title | Group 2 Veliparib + Carboplatin/ Paclitaxel |
| Arm description: Veliparib 120 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| 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: Subjects will self-administer the morning dose of veliparib and the evening dose of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day for Days 1 through 7 of the 21-day cycle. | |
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin will be administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion.

| | |
|--|---------------------------------------|
| 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 will be administered intravenously over approximately 3 hours at a dose of 175 mg/m².

| | |
|------------------|-------------------------|
| Arm title | Group 2 Veliparib + TMZ |
|------------------|-------------------------|

Arm description:

Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m² QD Days 1 through 5 in each 28-day cycle.

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

Dosage and administration details:

Subjects will self-administer the morning dose of veliparib and TMZ at the same time under fasting conditions (to reduce the chance of nausea and vomiting per the TMZ label recommendation) and the evening doses of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day.

| | |
|--|-----------|
| 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:

Subjects will self-administer the morning dose of veliparib and TMZ at the same time under fasting conditions (to reduce the chance of nausea and vomiting per the TMZ label recommendation) and the evening doses of veliparib approximately 12 hours after the morning dose with or without food in the same calendar day.

| Number of subjects in period 1 | Group 1 Placebo + Carboplatin/ Paclitaxel | Group 1 Veliparib + Carboplatin/ Paclitaxel | Group 1 Veliparib + TMZ |
|--|--|--|-------------------------|
| Started | 2 | 1 | 1 |
| Completed | 0 | 0 | 0 |
| Not completed | 2 | 1 | 1 |
| Adverse Event Related to Progression | - | - | - |
| Consent withdrawn by subject | - | - | - |
| Missing / Unknown Reason | 1 | - | 1 |
| Progressive Disease per Protocol | 1 | - | - |
| Sponsor Discontinued Study | - | - | - |
| Adverse Event Not Related to Progression | - | 1 | - |

| | | | |
|----------------------|---|---|---|
| Lost to follow-up | - | - | - |
| Other, Not Specified | - | - | - |

| Number of subjects in period 1 | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ |
|--|--|--|-------------------------|
| | | | |
| Started | 99 | 97 | 94 |
| Completed | 0 | 1 | 0 |
| Not completed | 99 | 96 | 94 |
| Adverse Event Related to Progression | 3 | 7 | 3 |
| Consent withdrawn by subject | 9 | 7 | 7 |
| Missing / Unknown Reason | 4 | 4 | 2 |
| Progressive Disease per Protocol | 64 | 57 | 74 |
| Sponsor Discontinued Study | 2 | 2 | - |
| Adverse Event Not Related to Progression | 6 | 10 | 5 |
| Lost to follow-up | 1 | 2 | - |
| Other, Not Specified | 10 | 7 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Group 1 Placebo + Carboplatin/ Paclitaxel |
| Reporting group description: Placebo BID Days 1 through 7 plus carboplatin target area under the curve (mg•min/mL) (AUC) 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 1 Veliparib + Carboplatin/ Paclitaxel |
| Reporting group description: Veliparib 80 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 1 Veliparib + TMZ |
| Reporting group description: Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m ² QD Days 1 through 5 in each 28-day cycle. | |
| Reporting group title | Group 2 Placebo + Carboplatin/ Paclitaxel |
| Reporting group description: Placebo BID Days 1 through 7 plus carboplatin carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 2 Veliparib + Carboplatin/ Paclitaxel |
| Reporting group description: Veliparib 120 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 2 Veliparib + TMZ |
| Reporting group description: Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m ² QD Days 1 through 5 in each 28-day cycle. | |

| Reporting group values | Group 1 Placebo + Carboplatin/ Paclitaxel | Group 1 Veliparib + Carboplatin/ Paclitaxel | Group 1 Veliparib + TMZ |
|------------------------|---|---|-------------------------|
| Number of subjects | 2 | 1 | 1 |
| Age categorical | | | |
| Units: Subjects | | | |
| < 45 years | 2 | 1 | 0 |
| 45 to 64 years | 0 | 0 | 1 |
| >= 65 years | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 1 | 1 |
| Male | 0 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| No Ethnicity | 2 | 1 | 1 |
| Race | | | |
| Units: Subjects | | | |
| White | 2 | 1 | 1 |
| Black | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Other, Not Specified | 0 | 0 | 0 |

| Reporting group values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ |
|---|--|--|----------------------------|
| Number of subjects | 99 | 97 | 94 |
| Age categorical Units: Subjects | | | |
| < 45 years | 47 | 49 | 41 |
| 45 to 64 years | 49 | 47 | 46 |
| >= 65 years | 3 | 1 | 7 |
| Gender categorical Units: Subjects | | | |
| Female | 97 | 95 | 92 |
| Male | 2 | 2 | 2 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 6 | 7 | 5 |
| No Ethnicity | 93 | 90 | 89 |
| Race Units: Subjects | | | |
| White | 93 | 92 | 83 |
| Black | 4 | 3 | 10 |
| Asian | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 0 |
| Other, Not Specified | 2 | 0 | 0 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 294 | | |
| Age categorical Units: Subjects | | | |
| < 45 years | 140 | | |
| 45 to 64 years | 143 | | |
| >= 65 years | 11 | | |
| Gender categorical Units: Subjects | | | |
| Female | 288 | | |
| Male | 6 | | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 18 | | |
| No Ethnicity | 276 | | |
| Race Units: Subjects | | | |
| White | 272 | | |
| Black | 17 | | |
| Asian | 2 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |

| | | | |
|----------------------|---|--|--|
| Other, Not Specified | 2 | | |
|----------------------|---|--|--|

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Group 1 Placebo + Carboplatin/ Paclitaxel |
| Reporting group description: Placebo BID Days 1 through 7 plus carboplatin target area under the curve (mg•min/mL) (AUC) 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 1 Veliparib + Carboplatin/ Paclitaxel |
| Reporting group description: Veliparib 80 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 1 Veliparib + TMZ |
| Reporting group description: Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m ² QD Days 1 through 5 in each 28-day cycle. | |
| Reporting group title | Group 2 Placebo + Carboplatin/ Paclitaxel |
| Reporting group description: Placebo BID Days 1 through 7 plus carboplatin carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 2 Veliparib + Carboplatin/ Paclitaxel |
| Reporting group description: Veliparib 120 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m ² administered on Day 3 of each 21-day cycle. | |
| Reporting group title | Group 2 Veliparib + TMZ |
| Reporting group description: Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m ² QD Days 1 through 5 in each 28-day cycle. | |

Primary: Progression-Free Survival (PFS)

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|---|--|
| End point title | Progression-Free Survival (PFS) ^[1] |
| End point description: PFS is defined as the number of months from the date the participant was randomized to the date of radiographic progression as determined by the central imaging center, or to the date of all cause deaths within 63 days of last tumor assessment if disease progression was not reached. Group 2: All randomized participants with suspected deleterious or deleterious BRCA1 or BRCA2 mutation determined by sponsor core lab. | |
| End point type | Primary |
| End point timeframe: Radiographic evaluation every 9 weeks, clinical evaluation every cycle (data cutoff date: 04 March 2016); maximum duration of follow up for PFS was 34 months. | |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Group 2 was used for all efficacy analyses per protocol.

| End point values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ | |
|----------------------------------|--|--|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 98 | 95 | 91 | |
| Units: months | | | | |
| median (confidence interval 95%) | 12.3 (9.3 to 14.5) | 14.1 (11.5 to 16.2) | 7.4 (5.9 to 8.5) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + Carboplatin/ Paclitaxel |
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.227 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.789 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.536 |
| upper limit | 1.162 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + TMZ |
| Number of subjects included in analysis | 189 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.858 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.278 |
| upper limit | 2.702 |

Secondary: Overall Survival (OS)

| | |
|-----------------|--------------------------------------|
| End point title | Overall Survival (OS) ^[2] |
|-----------------|--------------------------------------|

End point description:

Time to death for a given participant was defined as the number of months from the day the participant is randomized to the date of the participant's death. All events of death were included, regardless of whether the event occurs while the participant was still taking study drug, or after the participant discontinued study drug. If a participant had not died, then the data will be censored at the date when the participant was last known to be alive.

Group 2: All randomized participants with suspected deleterious or deleterious BRCA1 or BRCA2 mutation determined by sponsor core lab.

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

End point timeframe:

From Cycle 1 Day 1 until participant's death or 3 years post discontinuation (data cutoff date: 04 March 2016); maximum duration of follow up for OS was 72 months.

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Group 2 was used for all efficacy analyses per protocol.

| End point values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ | |
|----------------------------------|--|--|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 98 | 95 | 91 | |
| Units: months | | | | |
| median (confidence interval 95%) | 25.4 (18.3 to 32.1) | 28.3 (24.9 to 33.4) | 19.1 (14.3 to 21.3) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + Carboplatin/ Paclitaxel |
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.368 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.848 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.218 |

| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|---|
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + TMZ |

| | |
|---|-------------------|
| Number of subjects included in analysis | 189 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.512 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.074 |
| upper limit | 2.127 |

Secondary: Clinical Benefit Rate (CBR) at Week 18

| | |
|-----------------|---|
| End point title | Clinical Benefit Rate (CBR) at Week 18 ^[3] |
|-----------------|---|

End point description:

CBR: percentage of participants who were progression-free at 18 weeks, defined as complete response (CR), partial response (PR), stable disease (SD) or non-CR/non-disease progression (PD) per Response Evaluation Criteria in Solid Tumors [RECIST] 1.1.

CR: The disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 0 mm. PR: \geq 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters (SOD). PD: \geq 20% increase in the SOD of target lesions, taking as reference the smallest SOD recorded since the treatment started (baseline or after) or the appearance of \geq 1 new lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SOD since the treatment started (baseline or after).

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

End point timeframe:

Week 18

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Group 2 was used for all efficacy analyses per protocol.

| End point values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ | |
|-----------------------------------|--|--|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 98 | 95 | 91 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 87.0 (78.3 to 92.4) | 90.7 (82.2 to 95.2) | 73.0 (62.2 to 81.2) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + Carboplatin/ Paclitaxel |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.434 ^[4] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[4] - P-value is from Cochran-Mantel-Haenszel test stratified by estrogen receptor/progesterone receptor status and prior cytotoxic therapy use.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + TMZ |
| Number of subjects included in analysis | 189 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.019 ^[5] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[5] - P-value is from Cochran-Mantel-Haenszel test stratified by estrogen receptor/progesterone receptor status and prior cytotoxic therapy use.

Secondary: Objective Response Rate (ORR)

| | |
|-----------------|--|
| End point title | Objective Response Rate (ORR) ^[6] |
|-----------------|--|

End point description:

The objective response rate, defined as percentage of participants with a confirmed CR or PR based on RECIST 1.1 criteria. CR: The disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 0 mm. PR: ≥ 30% decrease in the sum of diameters of target lesions, taking as reference the baseline SODs.

Group 2: All randomized participants with suspected deleterious or deleterious BRCA1 or BRCA2 mutation determined by sponsor core lab. Participants with at least 1 measurable lesion at baseline.

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

End point timeframe:

Radiographic evaluation every 9 weeks, clinical evaluation every cycle (data cutoff date: 04 March 2016); maximum duration of follow up for ORR was 34 months.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Group 2 was used for all efficacy analyses per protocol.

| End point values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | Group 2 Veliparib + TMZ | |
|-----------------------------------|--|--|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 80 | 72 | 70 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 61.3 (49.7 to 71.9) | 77.8 (66.4 to 86.7) | 28.6 (18.4 to 40.6) | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib |

| | |
|---|---------------------------|
| | + Carboplatin/ Paclitaxel |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.027 ^[7] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[7] - P-value is from Cochran-Mantel-Haenszel test stratified by estrogen receptor/progesterone receptor status and prior cytotoxic therapy use.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Group 2 Placebo + Carboplatin/ Paclitaxel v Group 2 Veliparib + TMZ |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 ^[8] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[8] - P-value is from Cochran-Mantel-Haenszel test stratified by estrogen receptor/progesterone receptor status and prior cytotoxic therapy use.

Secondary: Change From Baseline at Week 18 in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy Module (EORTC QLQ-CIPN20) Sensory Subscale Score

| | |
|-----------------|--|
| End point title | Change From Baseline at Week 18 in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy Module (EORTC QLQ-CIPN20) Sensory Subscale Score ^[9] |
|-----------------|--|

End point description:

EORTC QLQ-CIPN20 sensory subscale score was calculated following the standard scoring algorithm, transformed to a 0 (low quality of life) to 100 (best quality of life) scale. A positive change from baseline indicates improvement.

Group 2: All randomized participants with suspected deleterious or deleterious BRCA1 or BRCA2 mutation determined by sponsor core lab. Participants with a baseline and post baseline value. Per protocol, this outcome measure was not planned for the Veliparib + TMZ arm.

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

End point timeframe:

Baseline, Week 18

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Group 2 was used for all efficacy analyses per protocol. No analysis was planned for the Velparib + TMZ arm for this endpoint per protocol.

| End point values | Group 2 Placebo + Carboplatin/ Paclitaxel | Group 2 Veliparib + Carboplatin/ Paclitaxel | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 69 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 13.94 (± 14.123) | 11.24 (± 13.954) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Group 2 Veliparib + Carboplatin/ Paclitaxel v Group 2 Placebo + Carboplatin/ Paclitaxel |
| Number of subjects included in analysis | 131 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.354 ^[10] |
| Method | ANCOVA |
| Parameter estimate | Least Squares (LS) Mean of Difference |
| Point estimate | -2.302 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.2 |
| upper limit | 2.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.476 |

Notes:

[10] - ANCOVA with treatment arm and baseline value as covariate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 30 days after last dose of study drug. Median duration of treatment for Placebo + Carboplatin/Paclitaxel, Veliparib + Carboplatin/Paclitaxel, and Veliparib + TMZ arms were 70 days, 84 days, and 42 days, respectively.

Adverse event reporting additional description:

As Treated population: all randomized participants who took at least 1 dose of study drug (veliparib/placebo), analyzed by the actual treatment that participant received.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Group 1 Placebo + Carboplatin/ Paclitaxel |
|-----------------------|---|

Reporting group description:

Placebo BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|-----------------------|--|
| Reporting group title | Group 1 Veliparib + Carboplatin/Paclitaxel |
|-----------------------|--|

Reporting group description:

Veliparib 80 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|-----------------------|-------------------------|
| Reporting group title | Group 1 Veliparib + TMZ |
|-----------------------|-------------------------|

Reporting group description:

Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m² QD Days 1 through 5 in each 28-day cycle.

| | |
|-----------------------|--|
| Reporting group title | Group 2 Placebo + Carboplatin/Paclitaxel |
|-----------------------|--|

Reporting group description:

Placebo BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|-----------------------|--|
| Reporting group title | Group 2 Veliparib + Carboplatin/Paclitaxel |
|-----------------------|--|

Reporting group description:

Veliparib 120 mg BID Days 1 through 7 plus carboplatin target AUC 6 administered on Day 3 of each 21-day cycle and paclitaxel 175 mg/m² administered on Day 3 of each 21-day cycle.

| | |
|-----------------------|-------------------------|
| Reporting group title | Group 2 Veliparib + TMZ |
|-----------------------|-------------------------|

Reporting group description:

Veliparib 40 mg BID Days 1 through 7 plus TMZ 150 to 200 mg/m² QD Days 1 through 5 in each 28-day cycle.

| Serious adverse events | Group 1 Placebo + Carboplatin/ Paclitaxel | Group 1 Veliparib + Carboplatin/Paclitaxel | Group 1 Veliparib + TMZ |
|---|---|--|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| number of deaths (all causes) | 2 | 1 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|--|---------------|---------------|---------------|
| BREAST CANCER METASTATIC | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| THROMBOPHLEBITIS SUPERFICIAL | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DISEASE PROGRESSION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYREXIA | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSпноEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOTHORAX | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|---------------|---------------|
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENTAL STATUS CHANGES | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EJECTION FRACTION DECREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OXYGEN SATURATION DECREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| FEMORAL NECK FRACTURE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCEDURAL HYPOTENSION | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECALL PHENOMENON | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THORACIC VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC TAMPONADE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| CENTRAL NERVOUS SYSTEM LESION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHAGE INTRACRANIAL | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEIZURE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOCAL CORD PARALYSIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHADENOPATHY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIA | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---------------|---------------|---------------|
| BILE DUCT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATOTOXICITY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| URINARY RETENTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PATHOLOGICAL FRACTURE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BETA HAEMOLYTIC STREPTOCOCCAL INFECTION | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BREAST CELLULITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMPHYSEMA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MASTITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OTITIS MEDIA | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Group 2 Placebo + Carboplatin/Paclitaxel | Group 2 Veliparib + Carboplatin/Paclitaxel | Group 2 Veliparib + TMZ |
|---|--|--|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 96 (27.08%) | 32 / 93 (34.41%) | 16 / 93 (17.20%) |
| number of deaths (all causes) | 64 | 58 | 76 |
| number of deaths resulting from adverse events | 2 | 3 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BREAST CANCER METASTATIC | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 0 / 93 (0.00%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| CANCER PAIN | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 5 / 93 (5.38%) | 4 / 93 (4.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| Vascular disorders | | | |
| THROMBOPHLEBITIS SUPERFICIAL | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| DISEASE PROGRESSION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| FATIGUE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| PYREXIA | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 4 / 93 (4.30%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSпноEA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| EPISTAXIS | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOTHORAX | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENTAL STATUS CHANGES | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 | | | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| EJECTION FRACTION DECREASED | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| OXYGEN SATURATION DECREASED | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| 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 | | | |
| FEMORAL NECK FRACTURE | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| FEMUR FRACTURE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCEDURAL HYPOTENSION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| RECALL PHENOMENON | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| THORACIC VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| CARDIAC TAMPONADE | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| Nervous system disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| CENTRAL NERVOUS SYSTEM LESION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| HAEMORRHAGE INTRACRANIAL | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| SEIZURE | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| SYNCOPE | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 1 / 93 (1.08%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOCAL CORD PARALYSIS | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 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 | 0 / 96 (0.00%) | 2 / 93 (2.15%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 7 / 93 (7.53%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 1 / 2 | 5 / 7 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHADENOPATHY | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 2 / 93 (2.15%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 3 / 93 (3.23%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 1 / 93 (1.08%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 96 (1.04%) | 1 / 93 (1.08%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| BILE DUCT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| HEPATOTOXICITY | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 | | | |
| URINARY RETENTION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| PATHOLOGICAL FRACTURE | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| Infections and infestations | | | |
| BACTERAEemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| BETA HAEMOLYTIC STREPTOCOCCAL INFECTION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| BREAST CELLULITIS | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 2 / 93 (2.15%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| DIVERTICULITIS | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| EMPYEMA | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| 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 ZOSTER | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| MASTITIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| 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 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (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 UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (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 |
| Metabolism and nutrition disorders | | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOCALCAEMIA | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 96 (0.00%) | 0 / 93 (0.00%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| 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 | Group 1 Placebo + Carboplatin/ Paclitaxel | Group 1 Veliparib + Carboplatin/ Paclitaxel | Group 1 Veliparib + TMZ |
|---|--|--|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | 1 / 1 (100.00%) | 1 / 1 (100.00%) |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HOT FLUSH | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 0 | 1 |
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CHILLS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALAISE | | | |

| | | | |
|---|---------------|-----------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| BREAST PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPNOEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |

| | | | |
|--------------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINORRHOEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INSOMNIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| WEIGHT INCREASED | | | |

| | | | |
|---|----------------------|--------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Injury, poisoning and procedural complications CONTUSION subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| INFUSION RELATED REACTION subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Cardiac disorders TACHYCARDIA subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Nervous system disorders DISTURBANCE IN ATTENTION subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| DIZZINESS subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 |
| DYSGEUSIA subjects affected / exposed occurrences (all) | 2 / 2 (100.00%) 2 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| HEADACHE subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 |
| HYPOAESTHESIA subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| LETHARGY subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 |
| NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| PARAESTHESIA | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 13 | 3 | 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 5 | 2 |
| Ear and labyrinth disorders | | | |
| EAR PAIN | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| DRY EYE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LACRIMATION INCREASED | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VISION BLURRED | | | |

| | | | |
|---------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 1 | 2 |
| DRY MOUTH | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MELAENA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| NAUSEA | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 2 | 3 |
| STOMATITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| DERMATITIS ACNEIFORM | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ERYTHEMA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| URTICARIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|----------------|-----------------|---------------|
| ARTHRALGIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| EAR INFECTION | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GASTROENTERITIS | | | |

| | | | |
|------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| INFLUENZA | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|-----------------------------------|--|--|-------------------------|
| Non-serious adverse events | Group 2 Placebo + Carboplatin/Paclitaxel | Group 2 Veliparib + Carboplatin/Paclitaxel | Group 2 Veliparib + TMZ |
|-----------------------------------|--|--|-------------------------|

| | | | |
|---|------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 93 / 96 (96.88%) | 93 / 93 (100.00%) | 91 / 93 (97.85%) |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 5 / 96 (5.21%) | 3 / 93 (3.23%) | 6 / 93 (6.45%) |
| occurrences (all) | 5 | 4 | 10 |
| HOT FLUSH | | | |
| subjects affected / exposed | 8 / 96 (8.33%) | 14 / 93 (15.05%) | 11 / 93 (11.83%) |
| occurrences (all) | 12 | 22 | 13 |
| HYPERTENSION | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 2 / 93 (2.15%) | 5 / 93 (5.38%) |
| occurrences (all) | 6 | 2 | 7 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 15 / 96 (15.63%) | 23 / 93 (24.73%) | 17 / 93 (18.28%) |
| occurrences (all) | 29 | 61 | 59 |
| CHILLS | | | |
| subjects affected / exposed | 3 / 96 (3.13%) | 7 / 93 (7.53%) | 2 / 93 (2.15%) |
| occurrences (all) | 3 | 8 | 3 |
| FATIGUE | | | |
| subjects affected / exposed | 57 / 96 (59.38%) | 47 / 93 (50.54%) | 44 / 93 (47.31%) |
| occurrences (all) | 141 | 93 | 76 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 5 / 93 (5.38%) | 3 / 93 (3.23%) |
| occurrences (all) | 5 | 8 | 4 |
| MALAISE | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 3 / 93 (3.23%) | 5 / 93 (5.38%) |
| occurrences (all) | 2 | 4 | 5 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 7 / 96 (7.29%) | 9 / 93 (9.68%) | 3 / 93 (3.23%) |
| occurrences (all) | 10 | 10 | 3 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 6 / 96 (6.25%) | 6 / 93 (6.45%) | 1 / 93 (1.08%) |
| occurrences (all) | 6 | 6 | 1 |
| OEDEMA PERIPHERAL | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 14 / 96 (14.58%) 18 | 13 / 93 (13.98%) 18 | 3 / 93 (3.23%) 5 |
| PAIN subjects affected / exposed occurrences (all) | 4 / 96 (4.17%) 7 | 14 / 93 (15.05%) 20 | 5 / 93 (5.38%) 5 |
| PYREXIA subjects affected / exposed occurrences (all) | 18 / 96 (18.75%) 23 | 15 / 93 (16.13%) 16 | 9 / 93 (9.68%) 12 |
| Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all) | 16 / 96 (16.67%) 26 | 18 / 93 (19.35%) 24 | 0 / 93 (0.00%) 0 |
| Reproductive system and breast disorders BREAST PAIN subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 6 | 1 / 93 (1.08%) 1 | 1 / 93 (1.08%) 1 |
| Respiratory, thoracic and mediastinal disorders COUGH subjects affected / exposed occurrences (all) | 15 / 96 (15.63%) 23 | 21 / 93 (22.58%) 27 | 13 / 93 (13.98%) 23 |
| DYSPNOEA subjects affected / exposed occurrences (all) | 22 / 96 (22.92%) 28 | 14 / 93 (15.05%) 16 | 8 / 93 (8.60%) 11 |
| EPISTAXIS subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 7 | 7 / 93 (7.53%) 8 | 3 / 93 (3.23%) 8 |
| OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all) | 2 / 96 (2.08%) 2 | 7 / 93 (7.53%) 8 | 2 / 93 (2.15%) 2 |
| RHINORRHOEA subjects affected / exposed occurrences (all) | 3 / 96 (3.13%) 4 | 8 / 93 (8.60%) 10 | 3 / 93 (3.23%) 3 |
| Psychiatric disorders ANXIETY subjects affected / exposed occurrences (all) | 7 / 96 (7.29%) 7 | 10 / 93 (10.75%) 13 | 5 / 93 (5.38%) 9 |

| | | | |
|--|------------------|------------------|------------------|
| DEPRESSION | | | |
| subjects affected / exposed | 6 / 96 (6.25%) | 7 / 93 (7.53%) | 4 / 93 (4.30%) |
| occurrences (all) | 7 | 8 | 4 |
| INSOMNIA | | | |
| subjects affected / exposed | 23 / 96 (23.96%) | 14 / 93 (15.05%) | 20 / 93 (21.51%) |
| occurrences (all) | 26 | 16 | 21 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 10 / 96 (10.42%) | 13 / 93 (13.98%) | 6 / 93 (6.45%) |
| occurrences (all) | 17 | 20 | 6 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 10 / 96 (10.42%) | 10 / 93 (10.75%) | 10 / 93 (10.75%) |
| occurrences (all) | 12 | 16 | 12 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 5 / 93 (5.38%) | 5 / 93 (5.38%) |
| occurrences (all) | 1 | 11 | 5 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 0 / 93 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 5 / 93 (5.38%) | 1 / 93 (1.08%) |
| occurrences (all) | 1 | 12 | 2 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 6 / 96 (6.25%) | 4 / 93 (4.30%) | 3 / 93 (3.23%) |
| occurrences (all) | 8 | 5 | 3 |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 2 / 93 (2.15%) | 1 / 93 (1.08%) |
| occurrences (all) | 5 | 5 | 1 |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 2 / 93 (2.15%) | 5 / 93 (5.38%) |
| occurrences (all) | 4 | 2 | 5 |
| INFUSION RELATED REACTION | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 5 / 96 (5.21%) 10 | 5 / 93 (5.38%) 10 | 0 / 93 (0.00%) 0 |
| Cardiac disorders TACHYCARDIA subjects affected / exposed occurrences (all) | 5 / 96 (5.21%) 6 | 2 / 93 (2.15%) 2 | 0 / 93 (0.00%) 0 |
| Nervous system disorders DISTURBANCE IN ATTENTION subjects affected / exposed occurrences (all) | 0 / 96 (0.00%) 0 | 0 / 93 (0.00%) 0 | 0 / 93 (0.00%) 0 |
| DIZZINESS subjects affected / exposed occurrences (all) | 18 / 96 (18.75%) 28 | 23 / 93 (24.73%) 31 | 7 / 93 (7.53%) 8 |
| DYSGEUSIA subjects affected / exposed occurrences (all) | 12 / 96 (12.50%) 34 | 18 / 93 (19.35%) 19 | 12 / 93 (12.90%) 12 |
| HEADACHE subjects affected / exposed occurrences (all) | 31 / 96 (32.29%) 41 | 34 / 93 (36.56%) 61 | 27 / 93 (29.03%) 50 |
| HYPOAESTHESIA subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 7 | 4 / 93 (4.30%) 4 | 2 / 93 (2.15%) 2 |
| LETHARGY subjects affected / exposed occurrences (all) | 0 / 96 (0.00%) 0 | 1 / 93 (1.08%) 1 | 0 / 93 (0.00%) 0 |
| NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all) | 34 / 96 (35.42%) 64 | 42 / 93 (45.16%) 60 | 7 / 93 (7.53%) 7 |
| PARAESTHESIA subjects affected / exposed occurrences (all) | 17 / 96 (17.71%) 32 | 17 / 93 (18.28%) 24 | 4 / 93 (4.30%) 4 |
| PERIPHERAL SENSORY NEUROPATHY subjects affected / exposed occurrences (all) | 22 / 96 (22.92%) 47 | 31 / 93 (33.33%) 64 | 4 / 93 (4.30%) 5 |
| Blood and lymphatic system disorders | | | |

| | | | |
|-----------------------------|------------------|------------------|------------------|
| ANAEMIA | | | |
| subjects affected / exposed | 49 / 96 (51.04%) | 53 / 93 (56.99%) | 26 / 93 (27.96%) |
| occurrences (all) | 113 | 139 | 52 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 27 / 96 (28.13%) | 28 / 93 (30.11%) | 16 / 93 (17.20%) |
| occurrences (all) | 88 | 112 | 55 |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 8 / 93 (8.60%) | 7 / 93 (7.53%) |
| occurrences (all) | 4 | 30 | 8 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 70 / 96 (72.92%) | 68 / 93 (73.12%) | 46 / 93 (49.46%) |
| occurrences (all) | 373 | 402 | 211 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 65 / 96 (67.71%) | 66 / 93 (70.97%) | 72 / 93 (77.42%) |
| occurrences (all) | 239 | 312 | 187 |
| Ear and labyrinth disorders | | | |
| EAR PAIN | | | |
| subjects affected / exposed | 3 / 96 (3.13%) | 4 / 93 (4.30%) | 3 / 93 (3.23%) |
| occurrences (all) | 8 | 4 | 3 |
| VERTIGO | | | |
| subjects affected / exposed | 5 / 96 (5.21%) | 2 / 93 (2.15%) | 2 / 93 (2.15%) |
| occurrences (all) | 6 | 3 | 2 |
| Eye disorders | | | |
| DRY EYE | | | |
| subjects affected / exposed | 5 / 96 (5.21%) | 4 / 93 (4.30%) | 4 / 93 (4.30%) |
| occurrences (all) | 6 | 4 | 6 |
| LACRIMATION INCREASED | | | |
| subjects affected / exposed | 5 / 96 (5.21%) | 4 / 93 (4.30%) | 2 / 93 (2.15%) |
| occurrences (all) | 7 | 6 | 2 |
| VISION BLURRED | | | |
| subjects affected / exposed | 7 / 96 (7.29%) | 12 / 93 (12.90%) | 1 / 93 (1.08%) |
| occurrences (all) | 7 | 15 | 1 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 16 / 96 (16.67%) | 20 / 93 (21.51%) | 15 / 93 (16.13%) |
| occurrences (all) | 19 | 23 | 24 |
| ABDOMINAL PAIN UPPER | | | |

| | | | |
|----------------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 7 / 96 (7.29%) | 11 / 93 (11.83%) | 7 / 93 (7.53%) |
| occurrences (all) | 14 | 15 | 14 |
| CONSTIPATION | | | |
| subjects affected / exposed | 28 / 96 (29.17%) | 38 / 93 (40.86%) | 38 / 93 (40.86%) |
| occurrences (all) | 49 | 57 | 57 |
| DIARRHOEA | | | |
| subjects affected / exposed | 25 / 96 (26.04%) | 37 / 93 (39.78%) | 19 / 93 (20.43%) |
| occurrences (all) | 44 | 63 | 27 |
| DRY MOUTH | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 6 / 93 (6.45%) | 8 / 93 (8.60%) |
| occurrences (all) | 4 | 6 | 8 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 15 / 96 (15.63%) | 9 / 93 (9.68%) | 5 / 93 (5.38%) |
| occurrences (all) | 23 | 17 | 5 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 2 / 93 (2.15%) | 6 / 93 (6.45%) |
| occurrences (all) | 1 | 2 | 7 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 5 / 93 (5.38%) | 0 / 93 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 4 / 96 (4.17%) | 9 / 93 (9.68%) | 4 / 93 (4.30%) |
| occurrences (all) | 4 | 14 | 4 |
| MELAENA | | | |
| subjects affected / exposed | 0 / 96 (0.00%) | 1 / 93 (1.08%) | 1 / 93 (1.08%) |
| occurrences (all) | 0 | 1 | 1 |
| NAUSEA | | | |
| subjects affected / exposed | 56 / 96 (58.33%) | 66 / 93 (70.97%) | 69 / 93 (74.19%) |
| occurrences (all) | 133 | 152 | 166 |
| STOMATITIS | | | |
| subjects affected / exposed | 11 / 96 (11.46%) | 11 / 93 (11.83%) | 5 / 93 (5.38%) |
| occurrences (all) | 20 | 15 | 6 |
| TOOTHACHE | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 5 / 93 (5.38%) | 3 / 93 (3.23%) |
| occurrences (all) | 5 | 5 | 3 |

| | | | |
|--|------------------------|------------------------|------------------------|
| VOMITING subjects affected / exposed occurrences (all) | 22 / 96 (22.92%) 36 | 26 / 93 (27.96%) 41 | 40 / 93 (43.01%) 81 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA subjects affected / exposed occurrences (all) | 55 / 96 (57.29%) 69 | 61 / 93 (65.59%) 79 | 10 / 93 (10.75%) 13 |
| DERMATITIS ACNEIFORM subjects affected / exposed occurrences (all) | 2 / 96 (2.08%) 2 | 3 / 93 (3.23%) 3 | 0 / 93 (0.00%) 0 |
| ERYTHEMA subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 7 | 6 / 93 (6.45%) 7 | 1 / 93 (1.08%) 1 |
| PRURITUS subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 7 | 12 / 93 (12.90%) 16 | 9 / 93 (9.68%) 9 |
| RASH subjects affected / exposed occurrences (all) | 17 / 96 (17.71%) 23 | 7 / 93 (7.53%) 10 | 5 / 93 (5.38%) 7 |
| URTICARIA subjects affected / exposed occurrences (all) | 2 / 96 (2.08%) 2 | 0 / 93 (0.00%) 0 | 1 / 93 (1.08%) 1 |
| Renal and urinary disorders | | | |
| DYSURIA subjects affected / exposed occurrences (all) | 4 / 96 (4.17%) 4 | 5 / 93 (5.38%) 5 | 1 / 93 (1.08%) 2 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA subjects affected / exposed occurrences (all) | 31 / 96 (32.29%) 45 | 34 / 93 (36.56%) 62 | 14 / 93 (15.05%) 18 |
| BACK PAIN subjects affected / exposed occurrences (all) | 23 / 96 (23.96%) 40 | 28 / 93 (30.11%) 43 | 24 / 93 (25.81%) 32 |
| BONE PAIN subjects affected / exposed occurrences (all) | 12 / 96 (12.50%) 16 | 21 / 93 (22.58%) 37 | 6 / 93 (6.45%) 6 |

| | | | |
|-----------------------------|------------------|------------------|------------------|
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 9 / 96 (9.38%) | 10 / 93 (10.75%) | 6 / 93 (6.45%) |
| occurrences (all) | 9 | 14 | 6 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 2 / 96 (2.08%) | 3 / 93 (3.23%) | 1 / 93 (1.08%) |
| occurrences (all) | 3 | 3 | 1 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 7 / 96 (7.29%) | 4 / 93 (4.30%) | 7 / 93 (7.53%) |
| occurrences (all) | 7 | 5 | 8 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 7 / 96 (7.29%) | 14 / 93 (15.05%) | 8 / 93 (8.60%) |
| occurrences (all) | 8 | 16 | 8 |
| MYALGIA | | | |
| subjects affected / exposed | 20 / 96 (20.83%) | 32 / 93 (34.41%) | 8 / 93 (8.60%) |
| occurrences (all) | 38 | 56 | 9 |
| NECK PAIN | | | |
| subjects affected / exposed | 3 / 96 (3.13%) | 4 / 93 (4.30%) | 2 / 93 (2.15%) |
| occurrences (all) | 4 | 4 | 3 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 23 / 96 (23.96%) | 17 / 93 (18.28%) | 13 / 93 (13.98%) |
| occurrences (all) | 39 | 55 | 15 |
| Infections and infestations | | | |
| EAR INFECTION | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 0 / 93 (0.00%) | 0 / 93 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 1 / 96 (1.04%) | 4 / 93 (4.30%) | 2 / 93 (2.15%) |
| occurrences (all) | 1 | 4 | 2 |
| INFLUENZA | | | |
| subjects affected / exposed | 3 / 96 (3.13%) | 3 / 93 (3.23%) | 4 / 93 (4.30%) |
| occurrences (all) | 5 | 4 | 4 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 12 / 96 (12.50%) | 12 / 93 (12.90%) | 5 / 93 (5.38%) |
| occurrences (all) | 13 | 18 | 5 |
| SINUSITIS | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 7 / 96 (7.29%) 7 | 5 / 93 (5.38%) 6 | 1 / 93 (1.08%) 1 |
| UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) | 10 / 96 (10.42%) 11 | 20 / 93 (21.51%) 28 | 14 / 93 (15.05%) 17 |
| URINARY TRACT INFECTION subjects affected / exposed occurrences (all) | 9 / 96 (9.38%) 14 | 12 / 93 (12.90%) 13 | 13 / 93 (13.98%) 13 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE subjects affected / exposed occurrences (all) | 20 / 96 (20.83%) 27 | 22 / 93 (23.66%) 30 | 21 / 93 (22.58%) 29 |
| DEHYDRATION subjects affected / exposed occurrences (all) | 0 / 96 (0.00%) 0 | 3 / 93 (3.23%) 3 | 0 / 93 (0.00%) 0 |
| HYPERGLYCAEMIA subjects affected / exposed occurrences (all) | 5 / 96 (5.21%) 7 | 3 / 93 (3.23%) 4 | 1 / 93 (1.08%) 1 |
| HYPOKALAEMIA subjects affected / exposed occurrences (all) | 6 / 96 (6.25%) 7 | 9 / 93 (9.68%) 12 | 1 / 93 (1.08%) 1 |
| HYPOMAGNESAEMIA subjects affected / exposed occurrences (all) | 11 / 96 (11.46%) 18 | 17 / 93 (18.28%) 21 | 2 / 93 (2.15%) 2 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 16 March 2012 | Modified the dose of veliparib/placebo to 120 mg BID for subjects randomized to the C/P treatment arms as the recommended Phase 2 dose based on the currently available data from the Cancer Treatment Evaluation Program 7967 and GOG 9923 studies. |
| 28 January 2013 | Allowed for broader eligibility while maintaining patient characteristics consistent with the trial intent and modified secondary efficacy endpoints and clarified definition of CBR to include all intent-to-treat (ITT) subjects and ORR to include only subjects with at least 1 measurable lesion at baseline. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported