



## Clinical trial results:

### A Phase 2, 2-Stage, 2-Cohort Study of Talazoparib (BMN 673) Administered to Germline BRCA Mutation Subjects with Locally Advanced and/or Metastatic Breast Cancer

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-003076-12 |
| Trial protocol           | GB ES          |
| Global end of trial date |                |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1                |
| This version publication date  | 17 September 2017 |
| First version publication date | 17 September 2017 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | 673-201 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |                              |
|------------------------------------|------------------------------|
| ISRCTN number                      | -                            |
| ClinicalTrials.gov id (NCT number) | NCT02034916                  |
| WHO universal trial number (UTN)   | -                            |
| Other trial identifiers            | Alias Study Number: C3441008 |

Notes:

#### Sponsors

|                              |                                                                                                              |
|------------------------------|--------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Pfizer, Inc.                                                                                                 |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017                                                         |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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                                       | Interim           |
| Date of interim/final analysis                       | 01 September 2016 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 01 September 2016 |
| Global end of trial reached?                         | No                |

Notes:

## General information about the trial

Main objective of the trial:

To determine the objective response rate (ORR) for each cohort treated with talazoparib as a single agent. The ORR would be based on confirmed responses as defined by Response Evaluation Criteria in Solid Tumors (RECIST).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 08 May 2014 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | France: 15         |
| Country: Number of subjects enrolled | Germany: 18        |
| Country: Number of subjects enrolled | Spain: 11          |
| Country: Number of subjects enrolled | United Kingdom: 15 |
| Country: Number of subjects enrolled | United States: 25  |
| Worldwide total number of subjects   | 84                 |
| EEA total number of subjects         | 59                 |

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)                      | 70 |
| From 65 to 84 years                       | 14 |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

In this study, enrollment of subjects was to be done in 2 stages for each of the two cohorts. Sufficient responses in each cohort were observed such that enrollment could proceed to Stage 2 for both cohorts. However, due to Sponsor decision, enrollment in the overall trial was terminated early.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |                            |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes                        |
| <b>Arm title</b>             | Cohort 1: Talazoparib 1 mg |

Arm description:

Subjects who responded to a prior platinum-containing treatment for metastatic breast cancer, received talazoparib 1.0 milligram (mg) orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Talazoparib      |
| Investigational medicinal product code |                  |
| Other name                             | BMN 673, MDV3800 |
| Pharmaceutical forms                   | Capsule          |
| Routes of administration               | Oral use         |

Dosage and administration details:

Talazoparib 1 mg was administered orally, once daily.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Cohort 2: Talazoparib 1 mg |
|------------------|----------------------------|

Arm description:

Subjects with more than 2 prior non-platinum chemotherapy treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Prior adjuvant or neo-adjuvant therapy with a platinum was allowed if first disease recurrence was for more than 6 months since last dose of adjuvant/neo-adjuvant platinum treatment. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Talazoparib      |
| Investigational medicinal product code |                  |
| Other name                             | BMN 673, MDV3800 |
| Pharmaceutical forms                   | Capsule          |
| Routes of administration               | Oral use         |

Dosage and administration details:

Talazoparib 1 mg was administered orally, once daily.

| <b>Number of subjects in period 1</b>   | Cohort 1:<br>Talazoparib 1 mg | Cohort 2:<br>Talazoparib 1 mg |
|-----------------------------------------|-------------------------------|-------------------------------|
| Started                                 | 49                            | 35                            |
| Treated                                 | 48                            | 35                            |
| Completed                               | 0                             | 0                             |
| Not completed                           | 49                            | 35                            |
| Consent withdrawn by subject            | 1                             | 1                             |
| Ongoing as of data cutoff (01 Sep 2016) | 15                            | 20                            |
| Death                                   | 32                            | 13                            |
| Lost to follow-up                       | 1                             | 1                             |

## Baseline characteristics

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Cohort 1: Talazoparib 1 mg |
|-----------------------|----------------------------|

Reporting group description:

Subjects who responded to a prior platinum-containing treatment for metastatic breast cancer, received talazoparib 1.0 milligram (mg) orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Cohort 2: Talazoparib 1 mg |
|-----------------------|----------------------------|

Reporting group description:

Subjects with more than 2 prior non-platinum chemotherapy treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Prior adjuvant or neo-adjuvant therapy with a platinum was allowed if first disease recurrence was for more than 6 months since last dose of adjuvant/neo-adjuvant platinum treatment. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

| Reporting group values                                | Cohort 1:<br>Talazoparib 1 mg | Cohort 2:<br>Talazoparib 1 mg | Total |
|-------------------------------------------------------|-------------------------------|-------------------------------|-------|
| Number of subjects                                    | 49                            | 35                            | 84    |
| Age categorical<br>Units: Subjects                    |                               |                               |       |
| In utero                                              | 0                             | 0                             | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                             | 0                             | 0     |
| Newborns (0-27 days)                                  | 0                             | 0                             | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0                             | 0                             | 0     |
| Children (2-11 years)                                 | 0                             | 0                             | 0     |
| Adolescents (12-17 years)                             | 0                             | 0                             | 0     |
| Adults (18-64 years)                                  | 42                            | 28                            | 70    |
| From 65-84 years                                      | 7                             | 7                             | 14    |
| 85 years and over                                     | 0                             | 0                             | 0     |
| Age Continuous<br>Units: years                        |                               |                               |       |
| arithmetic mean                                       | 50.1                          | 53.4                          |       |
| standard deviation                                    | ± 11.48                       | ± 11.05                       | -     |
| Gender, Male/Female<br>Units: Subjects                |                               |                               |       |
| Female                                                | 48                            | 34                            | 82    |
| Male                                                  | 1                             | 1                             | 2     |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Cohort 1: Talazoparib 1 mg     |
| Reporting group description:<br>Subjects who responded to a prior platinum-containing treatment for metastatic breast cancer, received talazoparib 1.0 milligram (mg) orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.                                                                                                                                                                                                                                                                                                                                    |                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Cohort 2: Talazoparib 1 mg     |
| Reporting group description:<br>Subjects with more than 2 prior non-platinum chemotherapy treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Prior adjuvant or neo-adjuvant therapy with a platinum was allowed if first disease recurrence was for more than 6 months since last dose of adjuvant/neo-adjuvant platinum treatment. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.                                                                                                                                                     |                                |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | All Subjects: Talazoparib 1 mg |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Sub-group analysis             |
| Subject analysis set description:<br>Subjects, who either responded to a prior platinum-containing treatment for metastatic breast cancer or had more than 2 prior non-platinum chemotherapy treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. For the subjects with non-platinum chemotherapy, prior adjuvant or neo-adjuvant therapy with a platinum was allowed if first disease recurrence was for more than 6 months since last dose of adjuvant/neo-adjuvant platinum treatment. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter. |                                |

### Primary: Objective Response Rate (ORR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Objective Response Rate (ORR) <sup>[1]</sup> |
| End point description:<br>ORR: Percentage of subjects with a confirmed best overall complete response (CR) or partial response (PR) according to response evaluation criteria in solid tumors version 1.1 (RECIST 1.1), evaluated by an independent radiology facility (IRF). CR: Disappearance of all non-nodal target and non-target lesions, including target and non-target lymph nodes reduction to less than 10 millimeter (mm) in short axis. PR: Greater than or equal to ( $\geq$ ) 30 percent (%) decrease in sum of diameters of target lesions, compared to the sum at baseline. Tumor-evaluable population (TEP) included all treated subjects who had a baseline and at least 1 post-baseline tumor assessment or who discontinued the study before first scheduled post-baseline tumor scan plus (+) 1 week window. |                                              |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                      |
| End point timeframe:<br>From randomization until data cutoff date (01 Sep 2016)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                              |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was reported for this endpoint.

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 48                               | 35                               |  |  |
| Units: percentage of subjects    |                                  |                                  |  |  |
| number (confidence interval 95%) | 20.8 (10.47 to<br>34.99)         | 37.1 (21.47 to<br>55.08)         |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Benefit Rate-24 (CBR-24)

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Clinical Benefit Rate-24 (CBR-24) |
|-----------------|-----------------------------------|

End point description:

CBR24: Percentage of subjects with a best overall response of confirmed CR, confirmed PR or stable disease (SD) sustained for at least 24 weeks, as assessed by IRF using RECIST 1.1. CR: Disappearance of all non-nodal target and non-target lesions, including target and non-target lymph nodes reduction to less than 10 mm in short axis. PR:  $\geq 30\%$  decrease in sum of diameters of target lesions, compared to the sum at baseline. SD: Neither PR nor progression of disease (PD) criteria met. SD follow PR only when sum increases by less than 20% from the nadir, but previously seen 30% decrease from baseline no longer hold. PD:  $\geq 20\%$  increase ( $\geq 5$  mm absolute increase) in the sum of target lesion measurements, compared to the smallest sum on study (including baseline), or unequivocal progression of non-target lesions, evaluated as a whole, such that it is clear that treatment has failed and disease is progressing, regardless of the status of the target lesions. Analysis was done on TEP.

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

End point timeframe:

From randomization until data cutoff date (01 Sep 2016)

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 48                               | 35                               |  |  |
| Units: percentage of subjects    |                                  |                                  |  |  |
| number (confidence interval 95%) | 27.1 (15.28 to<br>41.85)         | 45.7 (28.83 to<br>63.35)         |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR)

|                 |                            |
|-----------------|----------------------------|
| End point title | Duration of Response (DOR) |
|-----------------|----------------------------|

End point description:

DOR: Time from first documentation of CR or PR, to PD by IRF using RECIST 1.1, or to death (any cause), whichever occurred first. CR: Disappearance of all non-nodal target, non-target lesions (lymph nodes reduction to less than ( $<$ ) 10 mm in short axis). PR:  $\geq 30\%$  decrease in sum of diameters of target lesions, compared baseline sum. PD:  $\geq 20\%$  increase ( $\geq 5$  mm absolute increase) in sum of target lesion, compared to smallest sum, or unequivocal progression of non-target lesions, regardless target lesions. Subjects with no PD or death were censored at last tumor assessment prior to on or before of new anticancer therapy or before data cutoff. Analysis was done on TEP. Here 'Number of subjects analyzed' signifies subjects evaluable for this endpoint and '99999' signifies data not available

as upper limit of 95% confidence interval (CI) was not reached due to very less number of subjects and insufficient events at data cutoff.

|                                                                                                                                                                                                                           |           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                                                                                                            | Secondary |
| End point timeframe:                                                                                                                                                                                                      |           |
| From first documentation of CR or PR until PD, last tumor assessment without PD before new anticancer treatment initiation or death due to any cause, whichever occurred first (up to the data cutoff date [01 Sep 2016]) |           |

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 10                               | 13                               |  |  |
| Units: months                    |                                  |                                  |  |  |
| median (confidence interval 95%) | 5.8 (2.8 to 99999)               | 3.8 (2.8 to 10.1)                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression Free Survival (PFS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Progression Free Survival (PFS) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                 |
| PFS: Time, in months, from the first dose of study drug to the first documentation of PD by investigator assessment using RECIST 1.1 or death due to any cause on or before the data cutoff date, whichever occurred first. PD: $\geq 20\%$ increase ( $\geq 5$ mm absolute increase) in the sum of target lesion measurements, compared to the smallest sum on study (including baseline), or unequivocal progression of non-target lesions, evaluated as a whole, such that it is clear that treatment has failed and disease is progressing, regardless of the status of the target lesions. Subjects with no PFS event at the analysis were censored at last tumor assessment date prior to data cutoff or date of new anticancer treatment initiation, whichever occurred first. ITT population involved all enrolled subjects including subjects who were not treated. |                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                       |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                 |
| From first dose of study drug until PD, last tumor assessment without PD before new anticancer treatment initiation or death due to any cause, whichever occurred first (up to the data cutoff date [01 Sep 2016])                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 49                               | 35                               |  |  |
| Units: months                    |                                  |                                  |  |  |
| median (confidence interval 95%) | 4 (2.8 to 5.4)                   | 5.6 (5.5 to 7.8)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival (OS)

|                 |                       |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

OS was defined as the time from first dose of study drug to death due to any cause. For subjects without a death date at the time of data cutoff or permanently lost to follow-up, OS was right-censored at the date the subject was last known to be alive on or before the data cutoff date. ITT population. Here '99999' signifies data not available due to insufficient number of events at data cutoff.

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

End point timeframe:

From first dose of study drug until death due to any cause (up to the data cutoff date [01 Sep 2016])

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 49                               | 35                               |  |  |
| Units: months                    |                                  |                                  |  |  |
| median (confidence interval 95%) | 11.8 (8.8 to<br>15)              | 16.5 (10.1 to<br>99999)          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; an important medical event or reaction, including events requiring medical intervention to prevent worsening to any of the previously noted seriousness criteria. A treatment emergent AE was defined as an event that emerged during the treatment period that was absent before treatment, or worsened during the treatment period relative to the pretreatment state. AEs included both serious and non-serious AEs. Safety population included all subjects who received at least 1 dose of talazoparib.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values            | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed | 48                               | 35                               |  |  |
| Units: subjects             |                                  |                                  |  |  |
| AEs                         | 47                               | 34                               |  |  |
| SAEs                        | 16                               | 7                                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs)

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

A treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. A treatment-related SAE was a treatment-related AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; an important medical event or reaction, including events requiring medical intervention to prevent worsening to any of the previously noted seriousness criteria. Safety population included all subjects who received at least 1 dose of talazoparib. Here 'Number of subjects analyzed' signifies subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values            | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed | 47                               | 34                               |  |  |
| Units: subjects             |                                  |                                  |  |  |
| AEs                         | 46                               | 33                               |  |  |
| SAEs                        | 7                                | 3                                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Outcome in Response to Adverse Events (AEs)

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Number of Subjects With Outcome in Response to Adverse Events (AEs) |
|-----------------|---------------------------------------------------------------------|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Outcome of an AE was response to a question answered by the investigator: 'Is the AE leading to study discontinuation or death?' as 'yes'. Safety population included all subjects who received at least 1 dose of talazoparib. Here 'Number of subjects analyzed' signifies subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values                          | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-------------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type                        | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed               | 47                               | 34                               |  |  |
| Units: subjects                           |                                  |                                  |  |  |
| AEs leading to study drug discontinuation | 4                                | 1                                |  |  |
| AEs leading to death                      | 4                                | 0                                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Toxicity Grades Increase of 2 or More in Laboratory Parameters

|                 |                                                                                        |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Toxicity Grades Increase of 2 or More in Laboratory Parameters |
|-----------------|----------------------------------------------------------------------------------------|

End point description:

Laboratory tests included hematology (hemoglobin [low], leucocytes [low], lymphocytes [low], neutrophils [low], platelets [low]) and serum chemistry (alanine aminotransferase [high], albumin [low], alkaline phosphatase [high], aspartate aminotransferase [high], bilirubin [high], calcium [low], glucose [high], magnesium [low], phosphate [low], potassium [high], potassium [low], sodium [high], sodium [low]). Toxicity grades were evaluated based on national cancer institute- common terminology criteria for adverse events (NCI-CTCAE) version 4.03. Number of subjects with increase of 2 or more CTCAE toxicity grades above baseline, for hematology and chemistry laboratory parameters is reported in this endpoint. Safety population included all subjects who received at least 1 dose of talazoparib.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values                  | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type                | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed       | 48                               | 35                               |  |  |
| Units: subjects                   |                                  |                                  |  |  |
| Hemoglobin (low)                  | 19                               | 16                               |  |  |
| Leukocytes (low)                  | 16                               | 15                               |  |  |
| Lymphocytes (low)                 | 14                               | 4                                |  |  |
| Neutrophils (low)                 | 20                               | 17                               |  |  |
| Platelets (low)                   | 21                               | 10                               |  |  |
| Alanine aminotransferase (high)   | 3                                | 2                                |  |  |
| Albumin (low)                     | 3                                | 0                                |  |  |
| Alkaline phosphatase (high)       | 1                                | 1                                |  |  |
| Aspartate aminotransferase (high) | 2                                | 1                                |  |  |
| Bilirubin (high)                  | 2                                | 0                                |  |  |
| Calcium (low)                     | 4                                | 1                                |  |  |
| Glucose (high)                    | 1                                | 1                                |  |  |
| Magnesium (low)                   | 1                                | 0                                |  |  |
| Phosphate (low)                   | 6                                | 2                                |  |  |
| Potassium (high)                  | 1                                | 0                                |  |  |
| Potassium (low)                   | 2                                | 0                                |  |  |
| Sodium (high)                     | 1                                | 0                                |  |  |
| Sodium (low)                      | 0                                | 1                                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Change From Baseline in Vital Signs

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Clinically Significant Change From Baseline in Vital Signs |
|-----------------|------------------------------------------------------------------------------------|

End point description:

Criteria for clinically significant vital sign changes: 1) Blood pressure: systolic blood pressure (SBP):  $\geq 30$  millimeters of mercury (mmHg) increase from baseline, diastolic blood pressure (DBP):  $\geq 20$  mmHg decrease from baseline; 2) Heart rate (HR): absolute HR  $> 120$  beats per minute (bpm) and  $> 30$  bpm increase from baseline, absolute HR  $< 50$  bpm and  $> 20$  bpm decrease from baseline; 3) Weight:  $> 10\%$  decrease from baseline. Number of subjects with any clinically significant change from baseline for blood pressure, heart rate and weight are reported in this endpoint. Safety population included all subjects who received at least 1 dose of talazoparib.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values            | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed | 48                               | 35                               |  |  |
| Units: subjects             |                                  |                                  |  |  |
| Blood pressure (SBP or DBP) | 20                               | 18                               |  |  |
| HR                          | 2                                | 0                                |  |  |
| Weight                      | 4                                | 1                                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinically Significant Change From Baseline in Physical Findings

|                 |                                                                                          |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Clinically Significant Change From Baseline in Physical Findings |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

Physical examination included examination of the head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal, musculoskeletal, and neurological systems. The examination assessed the subjects for any potential changes in general appearance, the respiratory and cardiovascular systems, as well as towards subject reported symptoms. Findings were considered to be clinically significant based on investigator's decision. ITT population involved all enrolled subjects including subjects who were not treated.

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

End point timeframe:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

| End point values            | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed | 49                               | 35                               |  |  |
| Units: subjects             | 0                                | 0                                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Atleast 1 Concomitant Medication

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Number of Subjects With Atleast 1 Concomitant Medication |
|-----------------|----------------------------------------------------------|

End point description:

Number of subjects taking any non-study medications, therapies, including herbal supplements during the treatment-emergent period for the management of an adverse event or for the treatment of any other disease. Safety population included all subjects who received at least 1 dose of talazoparib.

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

End point timeframe:

From first dose of study drug up to 30 days after the last dose or before initiation of a new anticancer treatment, whichever occurred first (up to the data cutoff date [01 Sep 2016])

| End point values            | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed | 48                               | 35                               |  |  |
| Units: subjects             | 48                               | 34                               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Trough Concentration Versus Time Summary of Talazoparib

|                 |                                                         |
|-----------------|---------------------------------------------------------|
| End point title | Trough Concentration Versus Time Summary of Talazoparib |
|-----------------|---------------------------------------------------------|

End point description:

Concentrations below the limit of quantitation values less than or equal to ( $\leq$ ) 25 picogram per milliliter (pg/mL) were set as zero. Pharmacokinetic (PK) population included all subjects who received at least 1 dose of talazoparib and had evaluable PK assessments. Here 'n' signifies subjects evaluable for each specified categories.

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

End point timeframe:

Predose on Day 1 of cycle 1, 2, 3 and 4

| End point values                     | All Subjects:<br>Talazoparib 1<br>mg |  |  |  |
|--------------------------------------|--------------------------------------|--|--|--|
| Subject group type                   | Subject analysis set                 |  |  |  |
| Number of subjects analysed          | 83                                   |  |  |  |
| Units: pg/mL                         |                                      |  |  |  |
| arithmetic mean (standard deviation) |                                      |  |  |  |
| Day 1 of Cycle 1 (n = 82)            | 10.3 ( $\pm$ 93.3)                   |  |  |  |
| Day 1 of Cycle 2 (n = 70)            | 4220 ( $\pm$ 2510)                   |  |  |  |
| Day 1 of Cycle 3 (n = 68)            | 3990 ( $\pm$ 2840)                   |  |  |  |
| Day 1 of Cycle 4 (n = 60)            | 3090 ( $\pm$ 2170)                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Time to Deterioration in Global Health Status/Quality of Life

**(QOL) and Functional Status as Assessed by European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30)**

|                 |                                                                                                                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time to Deterioration in Global Health Status/Quality of Life (QOL) and Functional Status as Assessed by European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

Time to deterioration was defined as the time from baseline to day to death, first occurrence of progression, or a  $\geq 10$  point change from baseline in any of the functional status score and global health status/QOL score based on the EORTC-QLQ-C30, whichever occurred first. EORTC-QLQ-C30 questionnaire is a standardized instrument developed to assess the quality of life of people with cancer. EORTC-QLQ-C30 functional subscale includes 5 items: physical, role, emotional, cognitive, and social functioning. All of the single items of functional status subscale measures and global health status/QOL subscale range from 0 to 100, where higher scores represent a better level of functioning/quality of life. ITT population involved all enrolled subjects including subjects who were not treated.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

**End point timeframe:**

Baseline up to death, disease progression or end of treatment (30 days after last dose of study drug or before initiation of a new anticancer therapy, whichever occurred first [up to data cutoff date: 01 Sep 2016])

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 49                               | 35                               |  |  |
| Units: months                    |                                  |                                  |  |  |
| median (confidence interval 95%) |                                  |                                  |  |  |
| Global Health Status/QOL         | 2.8 (2.1 to 3)                   | 5.5 (4.2 to 5.7)                 |  |  |
| Physical Functioning             | 3.1 (2.1 to 4.6)                 | 5.6 (5.3 to 7.7)                 |  |  |
| Role Functioning                 | 2.1 (1.4 to 2.8)                 | 4.2 (2.1 to 5.5)                 |  |  |
| Emotional Functioning            | 2.7 (2 to 2.8)                   | 5.5 (4.3 to 5.6)                 |  |  |
| Cognitive Functioning            | 2.7 (1.6 to 3.2)                 | 4.2 (2.8 to 5.5)                 |  |  |
| Social Functioning               | 2.2 (1.4 to 2.9)                 | 5.3 (4.1 to 5.6)                 |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Other pre-specified: Time to Deterioration in Disease Specific Symptoms as Assessed by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Breast Cancer Module (EORTC-QLQ-BR23)**

|                 |                                                                                                                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time to Deterioration in Disease Specific Symptoms as Assessed by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Breast Cancer Module (EORTC-QLQ-BR23) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

Time to deterioration was defined as the time from baseline to day to death, first occurrence of progression, or a  $\geq 10$  point change from baseline in any of the symptom score based on the EORTC-QLQ-BR23, whichever occurred first. EORTC-QLQ-BR23 is a disease-specific module for breast cancer developed as a supplement for the EORTC-QLQ-C30 to assess the quality of life of subjects with breast cancer. EORTC-QLQ-BR23 symptoms subscale includes 4 items: systemic therapy side effects, breast symptoms, arm symptoms, upset by hair loss. Each item is rated by choosing 1 of 4 possible responses

that record the level of intensity (1= not at all, 2= a little, 3= quite a bit, and 4= very much) within each scale. ITT population involved all enrolled subjects including subjects who were not treated.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline up to death, disease progression or end of treatment (30 days after last dose of study drug or before initiation of a new anticancer therapy, whichever occurred first [up to data cutoff date: 01 Sep 2016])

| End point values                 | Cohort 1:<br>Talazoparib 1<br>mg | Cohort 2:<br>Talazoparib 1<br>mg |  |  |
|----------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type               | Reporting group                  | Reporting group                  |  |  |
| Number of subjects analysed      | 49                               | 35                               |  |  |
| Units: months                    |                                  |                                  |  |  |
| median (confidence interval 95%) |                                  |                                  |  |  |
| Systemic Therapy Side Effects    | 2.8 (2.3 to 4)                   | 5.5 (4.1 to 5.6)                 |  |  |
| Breast Symptoms                  | 3.1 (2.5 to 4.6)                 | 5.6 (5.3 to 7.7)                 |  |  |
| Arm Symptoms                     | 2.6 (2 to 3.7)                   | 4.2 (2.8 to 5.5)                 |  |  |
| Upset by Hair Loss               | 4 (2.7 to 5.4)                   | 5.6 (5.3 to 7.7)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after the last dose of study drug or before initiation of a new anticancer treatment, whichever occurred first (up to data cutoff date [01 Sep 2016])

Adverse event reporting additional description:

Same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study. AEs and SAEs were collected for safety population.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Cohort 1: Talazoparib 1 mg |
|-----------------------|----------------------------|

Reporting group description:

Subjects who responded to a prior platinum-containing treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Cohort 2: Talazoparib 1 mg |
|-----------------------|----------------------------|

Reporting group description:

Subjects with more than 2 prior non-platinum chemotherapy treatment for metastatic breast cancer, received talazoparib 1.0 mg orally, once daily for 21 days in repeated 21-day cycles until disease progression, occurrence of unacceptable toxicity or permanent treatment discontinuation. Prior adjuvant or neo-adjuvant therapy with a platinum was allowed if first disease recurrence was for more than 6 months since last dose of adjuvant/neo-adjuvant platinum treatment. Subjects were followed-up for survival and new anticancer treatment at every 60 days after the last dose of study drug for the first year, every 90 days thereafter.

| Serious adverse events                                              | Cohort 1:<br>Talazoparib 1 mg | Cohort 2:<br>Talazoparib 1 mg |  |
|---------------------------------------------------------------------|-------------------------------|-------------------------------|--|
| Total subjects affected by serious adverse events                   |                               |                               |  |
| subjects affected / exposed                                         | 16 / 48 (33.33%)              | 7 / 35 (20.00%)               |  |
| number of deaths (all causes)                                       | 32                            | 13                            |  |
| number of deaths resulting from adverse events                      | 4                             | 0                             |  |
| Investigations                                                      |                               |                               |  |
| Platelet count decreased                                            |                               |                               |  |
| subjects affected / exposed                                         | 1 / 48 (2.08%)                | 1 / 35 (2.86%)                |  |
| occurrences causally related to treatment / all                     | 1 / 1                         | 1 / 1                         |  |
| deaths causally related to treatment / all                          | 0 / 0                         | 0 / 0                         |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                               |                               |  |
| Neoplasm progression                                                |                               |                               |  |

|                                                 |                                                |                |  |
|-------------------------------------------------|------------------------------------------------|----------------|--|
| subjects affected / exposed                     | 3 / 48 (6.25%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 2 / 2                                          | 0 / 0          |  |
| Breast cancer metastatic                        |                                                |                |  |
| subjects affected / exposed                     | 2 / 48 (4.17%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1                                          | 0 / 0          |  |
| Silicon granuloma                               |                                                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0                                          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                                                |                |  |
| Transfusion reaction                            |                                                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0                                          | 0 / 0          |  |
| Surgical and medical procedures                 |                                                |                |  |
| Lipoinjection                                   |                                                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0                                          | 0 / 0          |  |
| Salpingo-oophorectomy                           | Additional description: Gender specific event. |                |  |
| alternative assessment type: Systematic         |                                                |                |  |
| subjects affected / exposed <sup>[1]</sup>      | 1 / 47 (2.13%)                                 | 0 / 34 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0                                          | 0 / 0          |  |
| Nervous system disorders                        |                                                |                |  |
| Central nervous system lesion                   |                                                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)                                 | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0                                          | 0 / 0          |  |
| Presyncope                                      |                                                |                |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 48 (2.08%)  | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Syncope                                         |                 |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)  | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |
| Anaemia                                         |                 |                |  |
| subjects affected / exposed                     | 5 / 48 (10.42%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 4 / 5           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Thrombocytopenia                                |                 |                |  |
| subjects affected / exposed                     | 2 / 48 (4.17%)  | 1 / 35 (2.86%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Anaemia of malignant disease                    |                 |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)  | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal disorders                      |                 |                |  |
| Oesophagitis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)  | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| Pleural effusion                                |                 |                |  |
| subjects affected / exposed                     | 3 / 48 (6.25%)  | 2 / 35 (5.71%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dyspnoea                                        |                 |                |  |
| subjects affected / exposed                     | 2 / 48 (4.17%)  | 2 / 35 (5.71%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Atelectasis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary embolism                              |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Anxiety                                         |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Arthralgia                                      |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Bronchopneumonia                                |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenic sepsis                              |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 35 (2.86%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Hypokalaemia                                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 35 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is a gender specific event.

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

| <b>Non-serious adverse events</b>                     | Cohort 1:<br>Talazoparib 1 mg | Cohort 2:<br>Talazoparib 1 mg |  |
|-------------------------------------------------------|-------------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events |                               |                               |  |
| subjects affected / exposed                           | 47 / 48 (97.92%)              | 34 / 35 (97.14%)              |  |
| Vascular disorders                                    |                               |                               |  |
| Hot flush                                             |                               |                               |  |
| subjects affected / exposed                           | 3 / 48 (6.25%)                | 3 / 35 (8.57%)                |  |
| occurrences (all)                                     | 3                             | 3                             |  |
| Lymphoedema                                           |                               |                               |  |
| subjects affected / exposed                           | 3 / 48 (6.25%)                | 2 / 35 (5.71%)                |  |
| occurrences (all)                                     | 3                             | 2                             |  |
| General disorders and administration site conditions  |                               |                               |  |
| Asthenia                                              |                               |                               |  |
| subjects affected / exposed                           | 3 / 48 (6.25%)                | 10 / 35 (28.57%)              |  |
| occurrences (all)                                     | 7                             | 21                            |  |
| Axillary pain                                         |                               |                               |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)                | 2 / 35 (5.71%)                |  |
| occurrences (all)                                     | 0                             | 3                             |  |
| Fatigue                                               |                               |                               |  |
| subjects affected / exposed                           | 29 / 48 (60.42%)              | 8 / 35 (22.86%)               |  |
| occurrences (all)                                     | 35                            | 15                            |  |
| Mucosal inflammation                                  |                               |                               |  |
| subjects affected / exposed                           | 4 / 48 (8.33%)                | 2 / 35 (5.71%)                |  |
| occurrences (all)                                     | 5                             | 2                             |  |
| Non-cardiac chest pain                                |                               |                               |  |
| subjects affected / exposed                           | 3 / 48 (6.25%)                | 0 / 35 (0.00%)                |  |
| occurrences (all)                                     | 7                             | 0                             |  |
| Oedema peripheral                                     |                               |                               |  |

|                                                                                        |                       |                       |  |
|----------------------------------------------------------------------------------------|-----------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                       | 1 / 48 (2.08%)<br>1   | 5 / 35 (14.29%)<br>8  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 48 (2.08%)<br>1   | 4 / 35 (11.43%)<br>4  |  |
| Respiratory, thoracic and mediastinal disorders                                        |                       |                       |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                              | 9 / 48 (18.75%)<br>9  | 6 / 35 (17.14%)<br>7  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                           | 9 / 48 (18.75%)<br>11 | 9 / 35 (25.71%)<br>16 |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 48 (4.17%)<br>2   | 2 / 35 (5.71%)<br>2   |  |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 48 (2.08%)<br>1   | 2 / 35 (5.71%)<br>2   |  |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 48 (2.08%)<br>1   | 2 / 35 (5.71%)<br>3   |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 48 (0.00%)<br>0   | 2 / 35 (5.71%)<br>2   |  |
| Psychiatric disorders                                                                  |                       |                       |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 48 (2.08%)<br>1   | 2 / 35 (5.71%)<br>2   |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                           | 5 / 48 (10.42%)<br>5  | 3 / 35 (8.57%)<br>4   |  |
| Investigations                                                                         |                       |                       |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 48 (2.08%)<br>3   | 3 / 35 (8.57%)<br>6   |  |
| Aspartate aminotransferase increased                                                   |                       |                       |  |

|                                                                                           |                       |                        |  |
|-------------------------------------------------------------------------------------------|-----------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                          | 4 / 48 (8.33%)<br>4   | 2 / 35 (5.71%)<br>5    |  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)            | 5 / 48 (10.42%)<br>11 | 5 / 35 (14.29%)<br>16  |  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)              | 7 / 48 (14.58%)<br>29 | 5 / 35 (14.29%)<br>16  |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                      | 3 / 48 (6.25%)<br>3   | 0 / 35 (0.00%)<br>0    |  |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)      | 3 / 48 (6.25%)<br>13  | 5 / 35 (14.29%)<br>12  |  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)      | 2 / 48 (4.17%)<br>2   | 2 / 35 (5.71%)<br>2    |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all) | 6 / 48 (12.50%)<br>7  | 1 / 35 (2.86%)<br>1    |  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 48 (2.08%)<br>1   | 3 / 35 (8.57%)<br>3    |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                              | 9 / 48 (18.75%)<br>14 | 10 / 35 (28.57%)<br>16 |  |
| Neuralgia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 48 (0.00%)<br>0   | 2 / 35 (5.71%)<br>2    |  |
| Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 48 (4.17%)<br>2   | 4 / 35 (11.43%)<br>5   |  |
| Blood and lymphatic system disorders                                                      |                       |                        |  |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| Anaemia                     |                  |                  |  |
| subjects affected / exposed | 23 / 48 (47.92%) | 19 / 35 (54.29%) |  |
| occurrences (all)           | 67               | 84               |  |
| Leukopenia                  |                  |                  |  |
| subjects affected / exposed | 7 / 48 (14.58%)  | 6 / 35 (17.14%)  |  |
| occurrences (all)           | 17               | 21               |  |
| Lymphopenia                 |                  |                  |  |
| subjects affected / exposed | 2 / 48 (4.17%)   | 4 / 35 (11.43%)  |  |
| occurrences (all)           | 3                | 8                |  |
| Neutropenia                 |                  |                  |  |
| subjects affected / exposed | 10 / 48 (20.83%) | 12 / 35 (34.29%) |  |
| occurrences (all)           | 36               | 36               |  |
| Thrombocytopenia            |                  |                  |  |
| subjects affected / exposed | 18 / 48 (37.50%) | 9 / 35 (25.71%)  |  |
| occurrences (all)           | 49               | 34               |  |
| Gastrointestinal disorders  |                  |                  |  |
| Abdominal discomfort        |                  |                  |  |
| subjects affected / exposed | 1 / 48 (2.08%)   | 2 / 35 (5.71%)   |  |
| occurrences (all)           | 1                | 2                |  |
| Abdominal distension        |                  |                  |  |
| subjects affected / exposed | 1 / 48 (2.08%)   | 3 / 35 (8.57%)   |  |
| occurrences (all)           | 1                | 3                |  |
| Abdominal pain              |                  |                  |  |
| subjects affected / exposed | 7 / 48 (14.58%)  | 7 / 35 (20.00%)  |  |
| occurrences (all)           | 8                | 11               |  |
| Abdominal pain upper        |                  |                  |  |
| subjects affected / exposed | 2 / 48 (4.17%)   | 6 / 35 (17.14%)  |  |
| occurrences (all)           | 3                | 10               |  |
| Constipation                |                  |                  |  |
| subjects affected / exposed | 9 / 48 (18.75%)  | 6 / 35 (17.14%)  |  |
| occurrences (all)           | 10               | 15               |  |
| Diarrhoea                   |                  |                  |  |
| subjects affected / exposed | 17 / 48 (35.42%) | 10 / 35 (28.57%) |  |
| occurrences (all)           | 24               | 18               |  |
| Dry mouth                   |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 48 (0.00%)   | 2 / 35 (5.71%)   |  |
| occurrences (all)                               | 0                | 2                |  |
| Dyspepsia                                       |                  |                  |  |
| subjects affected / exposed                     | 5 / 48 (10.42%)  | 3 / 35 (8.57%)   |  |
| occurrences (all)                               | 5                | 4                |  |
| Nausea                                          |                  |                  |  |
| subjects affected / exposed                     | 20 / 48 (41.67%) | 15 / 35 (42.86%) |  |
| occurrences (all)                               | 24               | 22               |  |
| Stomatitis                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 48 (6.25%)   | 1 / 35 (2.86%)   |  |
| occurrences (all)                               | 3                | 1                |  |
| Toothache                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 48 (0.00%)   | 2 / 35 (5.71%)   |  |
| occurrences (all)                               | 0                | 2                |  |
| Vomiting                                        |                  |                  |  |
| subjects affected / exposed                     | 10 / 48 (20.83%) | 7 / 35 (20.00%)  |  |
| occurrences (all)                               | 19               | 13               |  |
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Alopecia                                        |                  |                  |  |
| subjects affected / exposed                     | 11 / 48 (22.92%) | 7 / 35 (20.00%)  |  |
| occurrences (all)                               | 11               | 7                |  |
| Dry skin                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)   | 3 / 35 (8.57%)   |  |
| occurrences (all)                               | 1                | 4                |  |
| Erythema                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 48 (0.00%)   | 3 / 35 (8.57%)   |  |
| occurrences (all)                               | 0                | 4                |  |
| Pruritus                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 48 (2.08%)   | 3 / 35 (8.57%)   |  |
| occurrences (all)                               | 1                | 4                |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Arthralgia                                      |                  |                  |  |
| subjects affected / exposed                     | 7 / 48 (14.58%)  | 7 / 35 (20.00%)  |  |
| occurrences (all)                               | 9                | 9                |  |
| Back pain                                       |                  |                  |  |

|                                   |                  |                 |  |
|-----------------------------------|------------------|-----------------|--|
| subjects affected / exposed       | 11 / 48 (22.92%) | 7 / 35 (20.00%) |  |
| occurrences (all)                 | 12               | 10              |  |
| Bone pain                         |                  |                 |  |
| subjects affected / exposed       | 0 / 48 (0.00%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                 | 0                | 2               |  |
| Muscle spasms                     |                  |                 |  |
| subjects affected / exposed       | 4 / 48 (8.33%)   | 4 / 35 (11.43%) |  |
| occurrences (all)                 | 4                | 4               |  |
| Musculoskeletal chest pain        |                  |                 |  |
| subjects affected / exposed       | 3 / 48 (6.25%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                 | 4                | 2               |  |
| Musculoskeletal pain              |                  |                 |  |
| subjects affected / exposed       | 1 / 48 (2.08%)   | 3 / 35 (8.57%)  |  |
| occurrences (all)                 | 1                | 3               |  |
| Neck pain                         |                  |                 |  |
| subjects affected / exposed       | 0 / 48 (0.00%)   | 3 / 35 (8.57%)  |  |
| occurrences (all)                 | 0                | 5               |  |
| Pain in extremity                 |                  |                 |  |
| subjects affected / exposed       | 2 / 48 (4.17%)   | 3 / 35 (8.57%)  |  |
| occurrences (all)                 | 2                | 4               |  |
| Infections and infestations       |                  |                 |  |
| Gingivitis                        |                  |                 |  |
| subjects affected / exposed       | 0 / 48 (0.00%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                 | 0                | 3               |  |
| Influenza                         |                  |                 |  |
| subjects affected / exposed       | 3 / 48 (6.25%)   | 0 / 35 (0.00%)  |  |
| occurrences (all)                 | 3                | 0               |  |
| Lower respiratory tract infection |                  |                 |  |
| subjects affected / exposed       | 3 / 48 (6.25%)   | 0 / 35 (0.00%)  |  |
| occurrences (all)                 | 3                | 0               |  |
| Nasopharyngitis                   |                  |                 |  |
| subjects affected / exposed       | 9 / 48 (18.75%)  | 5 / 35 (14.29%) |  |
| occurrences (all)                 | 11               | 6               |  |
| Pharyngitis                       |                  |                 |  |
| subjects affected / exposed       | 0 / 48 (0.00%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                 | 0                | 2               |  |

|                                    |                  |                 |  |
|------------------------------------|------------------|-----------------|--|
| Rhinitis                           |                  |                 |  |
| subjects affected / exposed        | 4 / 48 (8.33%)   | 1 / 35 (2.86%)  |  |
| occurrences (all)                  | 4                | 1               |  |
| Sinusitis                          |                  |                 |  |
| subjects affected / exposed        | 1 / 48 (2.08%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                  | 1                | 2               |  |
| Upper respiratory tract infection  |                  |                 |  |
| subjects affected / exposed        | 3 / 48 (6.25%)   | 5 / 35 (14.29%) |  |
| occurrences (all)                  | 3                | 6               |  |
| Metabolism and nutrition disorders |                  |                 |  |
| Decreased appetite                 |                  |                 |  |
| subjects affected / exposed        | 11 / 48 (22.92%) | 9 / 35 (25.71%) |  |
| occurrences (all)                  | 12               | 13              |  |
| Hyperglycaemia                     |                  |                 |  |
| subjects affected / exposed        | 2 / 48 (4.17%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                  | 2                | 4               |  |
| Hypomagnesaemia                    |                  |                 |  |
| subjects affected / exposed        | 3 / 48 (6.25%)   | 0 / 35 (0.00%)  |  |
| occurrences (all)                  | 3                | 0               |  |
| Hyponatraemia                      |                  |                 |  |
| subjects affected / exposed        | 1 / 48 (2.08%)   | 2 / 35 (5.71%)  |  |
| occurrences (all)                  | 1                | 3               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 15 December 2015 | To add liver safety monitoring guidelines in accordance with United States Food and Drug Administration (US FDA) Guidance for Industry Drug-Induced Liver Injury: Premarketing Clinical Evaluation (2009).<br>To update the dose modification guidelines taking into consideration the type of toxicity. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported