



Clinical trial results:

An Open Label, Single Arm, Multicentre Study to Assess the Clinical Effectiveness and Safety of Lynparza (Olaparib) Capsules Maintenance Monotherapy in Platinum Sensitive Relapsed Somatic or Germline BRCA Mutated Ovarian Cancer Patients who are in Complete or Partial Response Following Platinum based Chemotherapy (ORZORA)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2015-000734-30 |
| Trial protocol | GB CZ ES HU BG PL |
| Global end of trial date | 17 December 2021 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 11 October 2022 |
| First version publication date | 11 October 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D0816C00012 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02476968 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85 |
| Public contact | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 June 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 December 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy by Investigator-assessed progression-free survival (PFS) according to modified Response Evaluation Criteria In Solid Tumours (RECIST) v1.1 in patients with somatic breast cancer susceptibility gene mutated (sBRCAm) ovarian cancer.

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy by Investigator-assessed PFS according to RECIST v1.1 in patients with BRCAm ovarian cancer.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 28 September 2015 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 32 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Bulgaria: 34 |
| Country: Number of subjects enrolled | Canada: 13 |
| Country: Number of subjects enrolled | Czechia: 23 |
| Country: Number of subjects enrolled | Spain: 28 |
| Country: Number of subjects enrolled | United Kingdom: 35 |
| Country: Number of subjects enrolled | Hungary: 17 |
| Country: Number of subjects enrolled | Italy: 17 |
| Country: Number of subjects enrolled | Poland: 14 |
| Worldwide total number of subjects | 181 |
| EEA total number of subjects | 133 |

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) | 108 |
| From 65 to 84 years | 73 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in patients with platinum sensitive relapsed high grade epithelial ovarian (including fallopian tube or primary peritoneal) cancer, who were in complete or partial response to platinum-based chemotherapy.

Pre-assignment

Screening details:

181 patients enrolled and assigned to olaparib: 145 with breast cancer susceptibility gene mutation (BRCAm) status (87 with germline mutations [gBRCAm], 55 with somatic mutations [sBRCAm] and 3 with undetermined BRCAm status), 33 with BRCA-independent homologous recombination repair mutation (HRRm[^]) status, and 3 enrolled in error (unassigned).

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 |
| Arm title | Overall BRCAm |

Arm description:

Patients received olaparib capsules orally 400 milligrams (mg) twice daily. Patients in this cohort had BRCAm status, comprising of those with sBRCAm or gBRCAm disease, as well as any patients where the germline or somatic BRCA mutation status was not determined.

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

Dosage and administration details:

Patients were administered eight 50 mg olaparib capsules (i.e, 400 mg), which were to be taken twice daily at the same time each day approximately 12 hours apart with approximately 240 milliliter (mL) of water.

| | |
|------------------|-------------------|
| Arm title | HRRm [^] |
|------------------|-------------------|

Arm description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this exploratory cohort had a qualifying mutation in any of the 13 genes involved in the HRR pathway (excluding BRCA1 and BRCA2) (i.e, BRCA-independent HRRm[^]).

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

Dosage and administration details:

Patients were administered eight 50 mg olaparib capsules (i.e, 400 mg), which were to be taken twice daily at the same time each day approximately 12 hours apart with approximately 240 mL of water.

| | |
|------------------|--|
| Arm title | Unassigned (not BRCAm, not HRRm [^]) |
|------------------|--|

Arm description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort were not classified

as being a part of either the BRCaM group or the HRRm⁺ group and were enrolled in error.

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

Dosage and administration details:

Patients were administered eight 50 mg olaparib capsules (i.e, 400 mg), which were to be taken twice daily at the same time each day approximately 12 hours apart with approximately 240 mL of water.

| Number of subjects in period 1 | Overall BRCaM | HRRm ⁺ | Unassigned (not BRCaM, not HRRm ⁺) |
|------------------------------------|---------------|-------------------|--|
| | | | |
| Started | 145 | 33 | 3 |
| Received treatment | 143 | 32 | 2 |
| Completed | 50 | 15 | 0 |
| Not completed | 95 | 18 | 3 |
| Patient decision | 37 | 8 | - |
| Eligibility criteria not fulfilled | - | - | 1 |
| Death | 48 | 8 | 1 |
| Unspecified | - | 2 | - |
| Lost to follow-up | 10 | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Overall BRCaM |
| Reporting group description: | |
| Patients received olaparib capsules orally 400 milligrams (mg) twice daily. Patients in this cohort had BRCaM status, comprising of those with sBRCaM or gBRCaM disease, as well as any patients where the germline or somatic BRCA mutation status was not determined. | |
| Reporting group title | HRRm^ |
| Reporting group description: | |
| Patients received olaparib capsules orally 400 mg twice daily. Patients in this exploratory cohort had a qualifying mutation in any of the 13 genes involved in the HRR pathway (excluding BRCA1 and BRCA2) (i.e, BRCA-independent HRRm^). | |
| Reporting group title | Unassigned (not BRCaM, not HRRm^) |
| Reporting group description: | |
| Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort were not classified as being a part of either the BRCaM group or the HRRm^ group and were enrolled in error. | |

| Reporting group values | Overall BRCaM | HRRm^ | Unassigned (not BRCaM, not HRRm^) |
|----------------------------|---------------|-------|-----------------------------------|
| Number of subjects | 145 | 33 | 3 |
| Age Categorical | | | |
| Units: Participants | | | |
| <35 years | 0 | 0 | 0 |
| ≥35 to <50 years | 29 | 3 | 0 |
| ≥50 to <65 years | 61 | 13 | 2 |
| ≥65 to <80 years | 54 | 17 | 1 |
| ≥80 years | 1 | 0 | 0 |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 145 | 33 | 3 |
| Male | 0 | 0 | 0 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 142 | 31 | 3 |
| Asian | 2 | 1 | 0 |
| Other | 1 | 0 | 0 |
| Unknown or Not Reported | 0 | 1 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | 1 | 0 |
| Not Hispanic or Latino | 142 | 31 | 3 |
| Unknown or Not Reported | 0 | 1 | 0 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 181 | | |
| Age Categorical | | | |
| Units: Participants | | | |
| <35 years | 0 | | |
| ≥35 to <50 years | 32 | | |

| | | | |
|----------------------------|-----|--|--|
| ≥50 to <65 years | 76 | | |
| ≥65 to <80 years | 72 | | |
| ≥80 years | 1 | | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 181 | | |
| Male | 0 | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 176 | | |
| Asian | 3 | | |
| Other | 1 | | |
| Unknown or Not Reported | 1 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | | |
| Not Hispanic or Latino | 176 | | |
| Unknown or Not Reported | 1 | | |

End points

End points reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Overall BRCAM |
| Reporting group description: Patients received olaparib capsules orally 400 milligrams (mg) twice daily. Patients in this cohort had BRCAM status, comprising of those with sBRCAM or gBRCAM disease, as well as any patients where the germline or somatic BRCA mutation status was not determined. | |
| Reporting group title | HRRm^ |
| Reporting group description: Patients received olaparib capsules orally 400 mg twice daily. Patients in this exploratory cohort had a qualifying mutation in any of the 13 genes involved in the HRR pathway (excluding BRCA1 and BRCA2) (i.e, BRCA-independent HRRm^). | |
| Reporting group title | Unassigned (not BRCAM, not HRRm^) |
| Reporting group description: Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort were not classified as being a part of either the BRCAM group or the HRRm^ group and were enrolled in error. | |
| Subject analysis set title | sBRCAM |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort had sBRCAM disease (i.e. confirmed somatic mutation). | |

Primary: Progression-Free Survival (PFS)

| | |
|--|---|
| End point title | Progression-Free Survival (PFS) ^{[1][2]} |
| End point description: The PFS was defined as the time from the date of enrolment until date of objective radiological disease progression (assessed by the Investigator via, RECIST version 1.1), or death (by any cause in absence of disease progression) regardless of whether the patient withdrew from therapy or received another anti-cancer therapy prior to disease progression. Objective progression was defined as at least a 20% increase in the sum of the diameters of the target lesions (compared to previous minimum sum) and an absolute increase of > 5 millimeters, or an overall non-target lesion assessment of progression or a new lesion. The data cut-off (DCO) for the primary analysis of the study occurred after approximately 60% maturity of PFS in the sBRCAM and all BRCAM patient populations. The FAS included all enrolled patients who were assigned olaparib. The primary endpoint results for PFS assessment included only BRCAM and sBRCAM patients. | |
| End point type | Primary |
| End point timeframe: Tumour assessments at baseline then every 12 weeks relative to date of enrolment until RECIST 1.1-defined progression. Assessed until primary analysis DCO of 17 April 2020 (up to maximum of 55 months). | |
| 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 participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint. [2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint. | |

| End point values | Overall BRCaM | sBRCaM | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 18.0 (14.3 to 22.1) | 16.6 (12.4 to 22.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS); Assessed at Primary Analysis

| | |
|-----------------|--|
| End point title | Overall Survival (OS); Assessed at Primary Analysis ^[3] |
|-----------------|--|

End point description:

The OS was defined as the time from the date of enrolment until death due to any cause regardless of whether the patient withdrew from therapy or received another anti-cancer therapy. Any patient not known to have died at the time of analysis was censored based on the last recorded date on which the patient was known to be alive. Pre-specified analysis of OS was performed at the time of primary analysis of PFS; a further analysis of OS was performed after approximately 60% maturity of OS in the sBRCaM and all BRCaM patient populations (and reported as a separate outcome measure). The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for OS assessment included only BRCaM and sBRCaM patients. 9999 indicates that the median and upper limit 95% confidence interval (CI) could not be calculated as it was not reached.

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

End point timeframe:

From baseline until death due to any cause. Assessed until primary analysis DCO of 17 April 2020 (up to maximum of 55 months).

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCaM reporting group and sBRCaM subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCaM | sBRCaM | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 47.6 (36.1 to 9999) | 9999 (33.2 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Second Progression (PFS2) or Death; Assessed at Primary Analysis

| | |
|-----------------|---|
| End point title | Time to Second Progression (PFS2) or Death; Assessed at Primary Analysis ^[4] |
|-----------------|---|

End point description:

The PFS2 was defined as the time from the date of enrolment to the earliest progression event subsequent to that used for the primary variable PFS or death (by any cause) in the absence of

progression. Patients whose progression event for PFS was death had this counted as a progression event for PFS2 also. The date of second progression was recorded by the Investigator and defined according to local standard clinical practice and could involve any of the following: objective radiological, symptomatic, cancer antigen-125 (CA-125) progression or death. Pre-specified analysis of PFS2 was performed at the time of the primary analysis; a further analysis of PFS2 was performed at the final analysis (and reported as a separate outcome measure). The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for PFS2 assessment included only BRCAM and sBRCAM patients.

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

End point timeframe:

Tumour assessments (and blood samples for CA-125, if applicable) at baseline then every 12 weeks relative to date of enrolment until second progression. Assessed until primary analysis DCO of 17 April 2020 (up to maximum of 55 months).

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAM | sBRCAM | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 30.9 (24.7 to 40.0) | 24.7 (21.8 to 36.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Subsequent Therapy (Treatment) or Death (TFST); Assessed at Primary Analysis

| | |
|-----------------|---|
| End point title | Time to First Subsequent Therapy (Treatment) or Death (TFST); Assessed at Primary Analysis ^[5] |
|-----------------|---|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAM and sBRCAM ovarian cancer by assessment of TFST. The TFST was defined as the time from the date of enrolment to the earlier of first subsequent anti-cancer therapy start date (excluding radiotherapy), or death date. Pre-specified analysis of TFST was performed at the time of the primary analysis; a further analysis of TFST was performed at the final analysis (and reported as a separate outcome measure). The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for TFST assessment included only BRCAM and sBRCAM patients. 9999 indicates that the upper limit 95% CI could not be calculated as it was not reached.

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

End point timeframe:

From enrolment to first subsequent therapy or death. Assessed every 12 weeks following treatment discontinuation. Assessed until primary analysis DCO of 17 April 2020 (up to maximum of 55 months).

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 37.6 (23.5 to 47.6) | 31.5 (19.5 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Second Subsequent Therapy (Treatment) or Death (TSST); Assessed at Primary Analysis

| | |
|-----------------|--|
| End point title | Time to Second Subsequent Therapy (Treatment) or Death (TSST); Assessed at Primary Analysis ^[6] |
|-----------------|--|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of TSST. The TSST was defined as the time from the date of enrolment to the earlier of the date of second subsequent anti-cancer therapy start date, or death date. Pre-specified analysis of TSST was performed at the time of the primary analysis; a further analysis of TSST was performed at the final analysis (and reported as a separate outcome measure). The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for TSST assessment included only BRCAm and sBRCAm patients. 9999 indicates that the median and upper limit 95% CI could not be calculated as they were not reached.

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

End point timeframe:

From enrolment to second subsequent therapy or death. Assessed every 12 weeks following treatment discontinuation. Assessed until primary analysis DCO of 17 April 2020 (up to maximum of 55 months).

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 47.6 (29.4 to 9999) | 9999 (24.7 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Discontinuation of Treatment or Death (TDT)

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|-----------------|--|
| End point title | Time to Discontinuation of Treatment or Death (TDT) ^[7] |
|-----------------|--|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of TDT. The TDT was defined as the time from the date of enrolment to the earlier of the date of study treatment discontinuation or death. The FAS

included all enrolled patients who were assigned olaparib. The secondary endpoint results for TDT assessment included only BRCAM and sBRCAM patients.

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

End point timeframe:

From enrolment to study treatment discontinuation or death (up to maximum of 6 years).

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAM | sBRCAM | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 19.8 (14.3 to 22.9) | 19.0 (13.5 to 22.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Cancer Therapy - Ovarian (FACT-O) Trial Outcome Index (TOI) Scores Over Time; Assessed at Primary Analysis

| | |
|-----------------|--|
| End point title | Change from Baseline in Functional Assessment of Cancer Therapy - Ovarian (FACT-O) Trial Outcome Index (TOI) Scores Over Time; Assessed at Primary Analysis ^[8] |
|-----------------|--|

End point description:

The Quality of Life (QoL) of patients with BRCAM and sBRCAM ovarian cancer was assessed by FACT-O TOI. The TOI score was derived from the sum of the scores of the 25 items included in the physical well-being (7 items), functional well-being (7 items), and additional concerns ovarian cancer subscale (11 items) of the FACT-O questionnaire version 4. The FACT-O TOI score ranges from 0-100, with a higher score indicating better QoL. A change (increase or decrease) in score of at least 10 points from baseline was defined as clinically meaningful. A positive change in score from baseline indicates an improvement. The FAS-FACT-O-TOI population included all enrolled patients who were assigned olaparib excluding patients who did not have FACT-O TOI score at baseline and patients who did not have any FACT-O TOI score post-baseline. The secondary endpoint results for FACT-O TOI assessment included only BRCAM and sBRCAM patients. Here, n= number of participants analysed in each analysis set.

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

End point timeframe:

Baseline, Day 29 (Week 4), then every 12 weeks for 24 months or DCO (17 April 2020) for primary analysis, whichever came first. QoL questionnaires also collected at discontinuation of study treatment visit and 30 days post last dose.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAM reporting group and sBRCAM subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|---|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 131 | 50 | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4, n=126, 47 | -2.2 (± 9.82) | -1.9 (± 9.59) | | |
| Week 16, n=91, 31 | -1.3 (± 10.04) | -0.3 (± 10.85) | | |
| Week 28, n=82, 30 | 1.2 (± 9.44) | 3.2 (± 10.25) | | |
| Week 40, n=80, 28 | 1.6 (± 10.72) | 4.1 (± 10.48) | | |
| Week 52, n=70, 24 | 3.2 (± 9.03) | 4.9 (± 7.84) | | |
| Week 64, n=60, 23 | 1.8 (± 9.88) | 0.8 (± 9.72) | | |
| Week 76, n=57, 20 | 1.4 (± 9.27) | 0.3 (± 9.83) | | |
| Week 88, n=46, 15 | 2.0 (± 9.97) | 1.5 (± 10.86) | | |
| Week 100, n=34, 11 | -0.2 (± 9.41) | -3.5 (± 7.54) | | |
| Discontinuation of olaparib visit, n=36, 16 | -4.7 (± 13.00) | -7.4 (± 15.53) | | |
| 30 days post discontinuation, n=52, 24 | -8.0 (± 13.45) | -4.3 (± 13.36) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Scores Over Time; Assessed at Primary Analysis

| | |
|-----------------|--|
| End point title | Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Scores Over Time; Assessed at Primary Analysis ^[9] |
|-----------------|--|

End point description:

To assess the QoL of patients with BRCAm and sBRCAm ovarian cancer by evaluation of FACIT-F. The FACIT-F is a 13-item questionnaire to assess patients' fatigue experience and its impact on their daily lives over the past 7 days. The FACIT-F total score ranges from 0-52, with a higher score indicating a lower level of fatigue (and better QoL). Changes in scores of ≥3 points were defined to be clinically meaningful. A positive change in score from baseline indicates an improvement. The FAS-FACIT-F population included all enrolled patients who were assigned olaparib excluding patients who did not have FACIT-F total score at baseline and patients who did not have any FACIT-F total score post-baseline. The secondary endpoint results for FACIT-F assessment included only BRCAm and sBRCAm patients. Here, n= number of patients analysed at specific timepoint.

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

End point timeframe:

At baseline, Day 29 (Week 4), then every 12 weeks for 24 months or DCO (17 April 2020) for primary analysis, whichever came first. QoL questionnaires also collected at discontinuation of study treatment visit and 30 days post last dose.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|--|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 136 | 53 | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4, n=130, 48 | -2.9 (± 8.21) | -2.9 (± 7.58) | | |
| Week 16, n=95, 34 | -2.5 (± 7.54) | -2.7 (± 9.26) | | |
| Week 28, n= 83, 31 | -1.2 (± 7.95) | -0.6 (± 7.25) | | |
| Week 40, n= 83, 31 | -0.3 (± 7.91) | 0.9 (± 7.02) | | |
| Week 52, n= 76, 29 | 0.6 (± 7.43) | 1.3 (± 7.25) | | |
| Week 64, n= 65, 25 | 0.8 (± 7.26) | 0.5 (± 8.47) | | |
| Week 76, n= 58, 21 | -0.3 (± 8.57) | -1.1 (± 8.74) | | |
| Week 88, n= 46, 14 | 0.3 (± 8.45) | -0.9 (± 5.81) | | |
| Week 100, n= 34, 11 | -0.4 (± 8.59) | -1.3 (± 8.75) | | |
| Discontinuation of olaparib visit, n=37,16 | -2.3 (± 9.01) | -2.7 (± 9.32) | | |
| 30 days post discontinuation, n=53,24 | -5.2 (± 11.16) | -3.8 (± 9.65) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Living Index-Emesis (FLIE) Questionnaire Total Scores Over Time; Assessed at Primary Analysis

| | |
|-----------------|--|
| End point title | Change from Baseline in Functional Living Index-Emesis (FLIE) Questionnaire Total Scores Over Time; Assessed at Primary Analysis ^[10] |
|-----------------|--|

End point description:

The FLIE captures the impact of nausea and vomiting on patient's QoL. The FLIE consists of 18 items (9 nausea-specific and 9 vomiting-specific items), rated from 1 to 7. Two domain scores and a total score are derived; the total score ranges 18-126 and a higher score indicates a lower impact (and better QoL). A positive change in score from baseline indicates an improvement. The FAS-FLIE population included all enrolled patients who were assigned olaparib excluding patients who did not have FLIE total score at baseline and patients who did not have any FLIE total score post-baseline. The secondary endpoint results for FLIE assessment included only BRCAm and sBRCAm patients. Here, n= number of patients analysed at specific timepoint.

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

End point timeframe:

At baseline, weekly until Day 29 (Week 4), then every 12 weeks for 24 months or DCO (17 April 2020) for primary analysis, whichever came first. FLIE questionnaires also collected at discontinuation of study treatment visit and 30 days post last dose.

Notes:

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

Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|---|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 114 | 46 | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1, n= 105, 42 | -6.1 (± 18.62) | -1.6 (± 18.28) | | |
| Week 2, n= 101, 39 | -4.5 (± 18.40) | -2.6 (± 15.97) | | |
| Week 3, n= 102, 40 | -4.1 (± 14.57) | -3.9 (± 13.23) | | |
| Week 4, n= 103, 39 | -4.8 (± 18.48) | -5.4 (± 19.92) | | |
| Week 16, n= 80, 29 | -2.3 (± 11.50) | -6.3 (± 11.00) | | |
| Week 28, n= 73, 28 | -1.6 (± 13.87) | -3.0 (± 7.94) | | |
| Week 40, n= 72, 28 | -0.1 (± 14.07) | -3.2 (± 14.56) | | |
| Week 52, n= 64, 26 | 0.9 (± 14.41) | -1.9 (± 11.64) | | |
| Week 64, n= 54, 23 | -0.2 (± 15.93) | -1.0 (± 20.77) | | |
| Week 76, n= 49, 19 | 0.9 (± 14.14) | 0.6 (± 6.60) | | |
| Week 88, n= 42, 14 | 2.2 (± 10.04) | -1.3 (± 9.29) | | |
| Week 100, n= 32, 11 | 0.4 (± 10.37) | 0.1 (± 13.19) | | |
| Discontinuation of olaparib visit,n=28,12 | -0.7 (± 20.17) | -8.8 (± 21.57) | | |
| 30 days post discontinuation,n=39,18 | -5.2 (± 17.02) | -5.6 (± 15.69) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS; Assessed at Final Analysis

| | |
|-----------------|--|
| End point title | OS; Assessed at Final Analysis ^[11] |
|-----------------|--|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of OS. The OS was defined as the time from the date of enrolment until death due to any cause regardless of whether the patient withdrew from therapy or received another anti-cancer therapy. Any patient not known to have died at the time of analysis was censored based on the last recorded date on which the patient was known to be alive. The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for OS assessment included only BRCAm and sBRCAm patients. 9999 indicates that the upper limit 95% CI could not be calculated as it was not reached.

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

End point timeframe:

From baseline until death due to any cause (up to maximum of 6 years).

Notes:

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

Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 46.8 (37.9 to 54.4) | 43.2 (31.7 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS2 or Death; Assessed at Final Analysis

| | |
|-----------------|---|
| End point title | PFS2 or Death; Assessed at Final Analysis ^[12] |
|-----------------|---|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of PFS2. The PFS2 was defined as the time from the date of enrolment to the earliest progression event subsequent to that used for the primary variable PFS or death (by any cause) in the absence of progression. Patients whose progression event for PFS was death had this counted as a progression event for PFS2 also. The date of second progression was recorded by the Investigator and defined according to local standard clinical practice and could involve any of the following: objective radiological, symptomatic, CA-125 progression or death. The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for PFS2 assessment included only BRCAm and sBRCAm patients.

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

End point timeframe:

Tumour assessments (and blood samples for CA-125, if applicable) at baseline then every 12 weeks relative to date of enrolment until second progression (up to maximum of 6 years).

Notes:

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

Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 34.0 (29.3 to 44.2) | 29.3 (23.7 to 44.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: TFST; Assessed at Final Analysis

| | |
|-----------------|--|
| End point title | TFST; Assessed at Final Analysis ^[13] |
|-----------------|--|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of TFST. The TFST was defined as the time from the date of enrolment to the earlier of first subsequent anti-cancer therapy start date (excluding

radiotherapy), or death date. The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for TFST assessment included only BRCAm and sBRCAm patients. 9999 indicates that the upper limit 95% CI could not be calculated as it was not reached.

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

End point timeframe:

From enrolment to first subsequent therapy or death. Assessed every 12 weeks following treatment discontinuation (up to maximum of 6 years).

Notes:

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

Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 32.1 (25.8 to 40.0) | 31.7 (18.0 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: TSST; Assessed at Final Analysis

| | |
|-----------------|--|
| End point title | TSST; Assessed at Final Analysis ^[14] |
|-----------------|--|

End point description:

To assess the real-world clinical effectiveness of olaparib maintenance monotherapy in patients with BRCAm and sBRCAm ovarian cancer by assessment of TSST. The TSST was defined as the time from the date of enrolment to the earlier of the date of second subsequent anti-cancer therapy start date, or death date. The FAS included all enrolled patients who were assigned olaparib. The secondary endpoint results for TSST assessment included only BRCAm and sBRCAm patients. 9999 indicates that the upper limit 95% CI could not be calculated as it was not reached.

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

End point timeframe:

From enrolment to second subsequent therapy or death. Assessed every 12 weeks following treatment discontinuation (up to maximum 6 years).

Notes:

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

Justification: Only participants treated in Overall BRCAm reporting group and sBRCAm subject analysis set were analyzed for the primary endpoint.

| End point values | Overall BRCAm | sBRCAm | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 145 | 55 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 38.4 (31.5 to 9999) | 32.1 (25.8 to 44.7) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of olaparib up to and including 30 days following the date of discontinuation of olaparib. Maximum timeframe of approximately 6 years.

Adverse event reporting additional description:

Adverse events are reported for the safety analysis set which included all patients who received at least one dose of olaparib. Total number of deaths was determined for patients in the FAS (enrolled and assigned olaparib).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | gBRCAM |
|-----------------------|--------|

Reporting group description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort had gBRCAM disease (i.e, confirmed germline mutation).

| | |
|-----------------------|--------|
| Reporting group title | sBRCAM |
|-----------------------|--------|

Reporting group description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort had sBRCAM disease (i.e, confirmed somatic mutation).

| | |
|-----------------------|---------------|
| Reporting group title | Overall BRCAM |
|-----------------------|---------------|

Reporting group description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort had BRCAM status, comprising of those with sBRCAM or gBRCAM disease, as well as any patients where the germline or somatic BRCA mutation status was not determined.

| | |
|-----------------------|-------------------|
| Reporting group title | HRRm [^] |
|-----------------------|-------------------|

Reporting group description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this exploratory cohort had a qualifying mutation in any of the 13 genes involved in the HRR pathway (excluding BRCA1 and BRCA2) (i.e, BRCA-independent HRRm[^]).

| | |
|-----------------------|--|
| Reporting group title | Unassigned (not BRCAM, not HRRm [^]) |
|-----------------------|--|

Reporting group description:

Patients received olaparib capsules orally 400 mg twice daily. Patients in this cohort were not classified as being a part of either the BRCAM group or the HRRm[^] group and were enrolled in error.

| Serious adverse events | gBRCAM | sBRCAM | Overall BRCAM |
|---|------------------|------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 87 (31.03%) | 13 / 55 (23.64%) | 40 / 143 (27.97%) |
| number of deaths (all causes) | 40 | 28 | 68 |
| number of deaths resulting from adverse events | 4 | 0 | 4 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 87 (2.30%) | 0 / 55 (0.00%) | 2 / 143 (1.40%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| Burkitt's lymphoma | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 1 / 55 (1.82%) | 2 / 143 (1.40%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Sudden death | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 55 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 0 / 55 (0.00%) | 3 / 143 (2.10%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |

| | | | |
|---|----------------|----------------|------------------|
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 55 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 87 (8.05%) | 5 / 55 (9.09%) | 12 / 143 (8.39%) |
| occurrences causally related to treatment / all | 9 / 10 | 5 / 6 | 14 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 55 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 55 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Glaucoma | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric vein thrombosis | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Colonic abscess | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 55 (1.82%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 55 (0.00%) | 0 / 143 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 0 / 55 (0.00%) | 3 / 143 (2.10%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------------------------|--|
| Serious adverse events | HRRm^ | Unassigned (not BRCam, not HRRm^) | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | 1 / 2 (50.00%) | |
| number of deaths (all causes) | 14 | 2 | |

| | | | |
|---|----------------|---------------|--|
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burkitt's lymphoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (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 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 10 / 10 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesenteric vein thrombosis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 2 (50.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Subileus | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Colonic abscess | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | gBRCaM | sBRCaM | Overall BRCaM |
|--|------------------|------------------|--------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 79 / 87 (90.80%) | 51 / 55 (92.73%) | 131 / 143 (91.61%) |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 3 / 55 (5.45%) | 6 / 143 (4.20%) |
| occurrences (all) | 3 | 3 | 6 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 13 / 87 (14.94%) | 11 / 55 (20.00%) | 24 / 143 (16.78%) |
| occurrences (all) | 19 | 14 | 33 |
| Fatigue | | | |
| subjects affected / exposed | 38 / 87 (43.68%) | 22 / 55 (40.00%) | 60 / 143 (41.96%) |
| occurrences (all) | 46 | 25 | 71 |
| Influenza like illness | | | |
| subjects affected / exposed | 7 / 87 (8.05%) | 2 / 55 (3.64%) | 9 / 143 (6.29%) |
| occurrences (all) | 8 | 2 | 10 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 3 / 55 (5.45%) | 4 / 143 (2.80%) |
| occurrences (all) | 1 | 3 | 4 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 6 / 55 (10.91%) | 6 / 143 (4.20%) |
| occurrences (all) | 0 | 8 | 8 |
| Peripheral swelling | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 2 / 55 (3.64%) | 7 / 143 (4.90%) |
| occurrences (all) | 5 | 3 | 8 |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 87 (6.90%) | 2 / 55 (3.64%) | 8 / 143 (5.59%) |
| occurrences (all) | 9 | 4 | 13 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 9 / 87 (10.34%) | 5 / 55 (9.09%) | 14 / 143 (9.79%) |
| occurrences (all) | 12 | 5 | 17 |

| | | | |
|--|------------------------|---------------------|------------------------|
| Dyspnoea subjects affected / exposed occurrences (all) | 10 / 87 (11.49%) 26 | 4 / 55 (7.27%) 8 | 14 / 143 (9.79%) 34 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 3 / 87 (3.45%) 5 | 1 / 55 (1.82%) 1 | 4 / 143 (2.80%) 6 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 4 | 3 / 55 (5.45%) 3 | 7 / 143 (4.90%) 7 |
| Depression subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 4 | 3 / 55 (5.45%) 3 | 7 / 143 (4.90%) 7 |
| Insomnia subjects affected / exposed occurrences (all) | 7 / 87 (8.05%) 7 | 4 / 55 (7.27%) 4 | 11 / 143 (7.69%) 11 |
| Irritability subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 143 (0.00%) 0 |
| Personality change subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 143 (0.00%) 0 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 7 / 87 (8.05%) 11 | 1 / 55 (1.82%) 1 | 8 / 143 (5.59%) 12 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 8 / 87 (9.20%) 21 | 3 / 55 (5.45%) 3 | 11 / 143 (7.69%) 24 |
| Glomerular filtration rate decreased subjects affected / exposed occurrences (all) | 2 / 87 (2.30%) 2 | 3 / 55 (5.45%) 5 | 5 / 143 (3.50%) 7 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 5 / 87 (5.75%) 8 | 2 / 55 (3.64%) 3 | 7 / 143 (4.90%) 11 |
| Platelet count decreased | | | |

| | | | |
|---|------------------------|------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 5 / 87 (5.75%) 6 | 1 / 55 (1.82%) 1 | 6 / 143 (4.20%) 7 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 5 / 87 (5.75%) 14 | 2 / 55 (3.64%) 7 | 7 / 143 (4.90%) 21 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 1 / 87 (1.15%) 2 | 1 / 55 (1.82%) 3 | 2 / 143 (1.40%) 5 |
| Injury, poisoning and procedural complications Foot fracture subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 143 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 13 / 87 (14.94%) 21 | 2 / 55 (3.64%) 3 | 15 / 143 (10.49%) 24 |
| Dysgeusia subjects affected / exposed occurrences (all) | 8 / 87 (9.20%) 10 | 3 / 55 (5.45%) 3 | 11 / 143 (7.69%) 13 |
| Headache subjects affected / exposed occurrences (all) | 11 / 87 (12.64%) 16 | 3 / 55 (5.45%) 11 | 14 / 143 (9.79%) 27 |
| Taste disorder subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 143 (0.00%) 0 |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 2 / 87 (2.30%) 2 | 2 / 55 (3.64%) 4 | 4 / 143 (2.80%) 6 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 38 / 87 (43.68%) 56 | 20 / 55 (36.36%) 32 | 58 / 143 (40.56%) 88 |
| Leukopenia subjects affected / exposed occurrences (all) | 6 / 87 (6.90%) 6 | 2 / 55 (3.64%) 2 | 8 / 143 (5.59%) 8 |
| Neutropenia | | | |

| | | | |
|----------------------------------|------------------|------------------|-------------------|
| subjects affected / exposed | 12 / 87 (13.79%) | 4 / 55 (7.27%) | 16 / 143 (11.19%) |
| occurrences (all) | 16 | 10 | 26 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 6 / 55 (10.91%) | 11 / 143 (7.69%) |
| occurrences (all) | 5 | 7 | 12 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 6 / 87 (6.90%) | 2 / 55 (3.64%) | 8 / 143 (5.59%) |
| occurrences (all) | 7 | 2 | 9 |
| Abdominal pain | | | |
| subjects affected / exposed | 11 / 87 (12.64%) | 12 / 55 (21.82%) | 23 / 143 (16.08%) |
| occurrences (all) | 11 | 20 | 31 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 0 / 55 (0.00%) | 3 / 143 (2.10%) |
| occurrences (all) | 4 | 0 | 4 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 9 / 87 (10.34%) | 4 / 55 (7.27%) | 13 / 143 (9.09%) |
| occurrences (all) | 13 | 6 | 19 |
| Constipation | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 8 / 55 (14.55%) | 13 / 143 (9.09%) |
| occurrences (all) | 6 | 9 | 15 |
| Diarrhoea | | | |
| subjects affected / exposed | 15 / 87 (17.24%) | 9 / 55 (16.36%) | 24 / 143 (16.78%) |
| occurrences (all) | 16 | 11 | 27 |
| Dyspepsia | | | |
| subjects affected / exposed | 14 / 87 (16.09%) | 8 / 55 (14.55%) | 23 / 143 (16.08%) |
| occurrences (all) | 27 | 10 | 38 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 0 / 55 (0.00%) | 3 / 143 (2.10%) |
| occurrences (all) | 5 | 0 | 5 |
| Nausea | | | |
| subjects affected / exposed | 49 / 87 (56.32%) | 28 / 55 (50.91%) | 78 / 143 (54.55%) |
| occurrences (all) | 86 | 36 | 123 |
| Vomiting | | | |
| subjects affected / exposed | 24 / 87 (27.59%) | 15 / 55 (27.27%) | 39 / 143 (27.27%) |
| occurrences (all) | 41 | 28 | 69 |

| | | | |
|--|------------------------|----------------------|-------------------------|
| Haemorrhoids subjects affected / exposed occurrences (all) | 1 / 87 (1.15%) 2 | 0 / 55 (0.00%) 0 | 1 / 143 (0.70%) 2 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 7 / 87 (8.05%) 9 | 4 / 55 (7.27%) 4 | 11 / 143 (7.69%) 13 |
| Pruritus subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 5 | 3 / 55 (5.45%) 3 | 7 / 143 (4.90%) 8 |
| Rash subjects affected / exposed occurrences (all) | 3 / 87 (3.45%) 3 | 3 / 55 (5.45%) 3 | 6 / 143 (4.20%) 6 |
| Renal and urinary disorders | | | |
| Pollakiuria subjects affected / exposed occurrences (all) | 3 / 87 (3.45%) 3 | 2 / 55 (3.64%) 2 | 5 / 143 (3.50%) 5 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 11 / 87 (12.64%) 15 | 6 / 55 (10.91%) 8 | 17 / 143 (11.89%) 23 |
| Back pain subjects affected / exposed occurrences (all) | 7 / 87 (8.05%) 11 | 4 / 55 (7.27%) 4 | 11 / 143 (7.69%) 15 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 1 / 55 (1.82%) 2 | 1 / 143 (0.70%) 2 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 4 | 5 / 55 (9.09%) 6 | 9 / 143 (6.29%) 10 |
| Myalgia subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 5 | 1 / 55 (1.82%) 1 | 5 / 143 (3.50%) 6 |
| Pain in extremity subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 7 | 2 / 55 (3.64%) 2 | 6 / 143 (4.20%) 9 |

| | | | |
|------------------------------------|------------------|-----------------|-------------------|
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 7 / 87 (8.05%) | 0 / 55 (0.00%) | 7 / 143 (4.90%) |
| occurrences (all) | 13 | 0 | 13 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 87 (10.34%) | 3 / 55 (5.45%) | 12 / 143 (8.39%) |
| occurrences (all) | 12 | 4 | 16 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 55 (0.00%) | 1 / 143 (0.70%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 3 / 55 (5.45%) | 3 / 143 (2.10%) |
| occurrences (all) | 0 | 3 | 3 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 87 (2.30%) | 6 / 55 (10.91%) | 8 / 143 (5.59%) |
| occurrences (all) | 3 | 6 | 9 |
| Urinary tract infection | | | |
| subjects affected / exposed | 6 / 87 (6.90%) | 6 / 55 (10.91%) | 12 / 143 (8.39%) |
| occurrences (all) | 10 | 13 | 23 |
| Bronchitis | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 1 / 55 (1.82%) | 6 / 143 (4.20%) |
| occurrences (all) | 6 | 1 | 7 |
| Herpes zoster | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 0 / 55 (0.00%) | 3 / 143 (2.10%) |
| occurrences (all) | 3 | 0 | 3 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 10 / 87 (11.49%) | 7 / 55 (12.73%) | 17 / 143 (11.89%) |
| occurrences (all) | 10 | 8 | 18 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 6 / 87 (6.90%) | 2 / 55 (3.64%) | 8 / 143 (5.59%) |
| occurrences (all) | 20 | 2 | 22 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 2 / 87 (2.30%) | 3 / 55 (5.45%) | 5 / 143 (3.50%) |
| occurrences (all) | 2 | 3 | 5 |

| | | | |
|-----------------------------------|-------|-----------------|--|
| Non-serious adverse events | HRRm^ | Unassigned (not | |
|-----------------------------------|-------|-----------------|--|

| | | BRCAm, not HRRm^) | |
|---|------------------|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 32 (90.63%) | 1 / 2 (50.00%) | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 15 / 32 (46.88%) | 1 / 2 (50.00%) | |
| occurrences (all) | 18 | 1 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |

| | | | |
|--------------------------------------|-----------------|----------------|--|
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | 0 / 2 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Irritability | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Personality change | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Glomerular filtration rate decreased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 2 (50.00%) | |
| occurrences (all) | 1 | 1 | |
| Platelet count decreased | | | |

| | | | |
|--|------------------|----------------|--|
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 0 / 2 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Headache | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | 0 / 2 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 11 / 32 (34.38%) | 1 / 2 (50.00%) | |
| occurrences (all) | 16 | 1 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neutropenia | | | |

| | | | |
|----------------------------------|------------------|----------------|--|
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 8 / 32 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 0 / 2 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 32 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 0 / 2 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 1 / 2 (50.00%) | |
| occurrences (all) | 2 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 19 / 32 (59.38%) | 0 / 2 (0.00%) | |
| occurrences (all) | 30 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 32 (31.25%) | 1 / 2 (50.00%) | |
| occurrences (all) | 25 | 1 | |

| | | | |
|--|---------------------|--------------------|--|
| Haemorrhoids subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | 0 / 2 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | 0 / 2 (0.00%) 0 | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 1 | 0 / 2 (0.00%) 0 | |
| Rash subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | 0 / 2 (0.00%) 0 | |
| Renal and urinary disorders | | | |
| Pollakiuria subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 1 | 0 / 2 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 2 (0.00%) 0 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | 0 / 2 (0.00%) 0 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | 0 / 2 (0.00%) 0 | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 2 (0.00%) 0 | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 2 | 0 / 2 (0.00%) 0 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 4 | 0 / 2 (0.00%) 0 | |

| | | | |
|------------------------------------|-----------------|---------------|--|
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 December 2015 | Editorial change to improve clarity on study conduct, maintain consistency of information across protocol sections in line with revised AZ standard guidance. Expected proportion of patient populations specified. Revision of enrolment/screening procedures. Protocol compliance in European Union specified. Mutation testing details specified. Study design and flow chart updated. Co-primary endpoints finalised and details for their assessment specified. Secondary endpoints finalised and details for their assessment specified. Safety and exploratory objectives specified. Enrolment and screening procedures updated. Exclusion/inclusion criteria updated. Text added to align with Investigator's Brochure. Details specified for follow-up visits after discontinuation. Details related to tumour breast cancer susceptibility gene mutation testing specified. Removal of haemorrhage from Adverse event of special interest (AESI) list. Details about radiological assessments specified. Details of tumour samples required during central BRCA testing and exploratory testing specified. Steps for determination of mutation status aligned with revised screening procedures. Details on consent withdrawal and sample traceability updated. Details of BRACAnalysis® revised. Details for AESI updated. Drug interactions updated. Expected PFS/death events revised. Variables specified in the analysis sets. Details added for the efficacy analysis set. Secondary outcome measures specified to align with primary outcome measures and further details added. Details specified further for questionnaires/scales. Details for primary and QoL variable analyses, and sensitivity analyses updated. |
| 30 July 2016 | New exploratory cohort added. New exploratory objective and related outcomes measures added. Inclusion criteria updated. Collection of samples updated in tables. Screening procedure for exploratory HRRm^ cohort updated and details specified for circulating tumour deoxyribonucleic acid (ctDNA) analysis. Section added to provide further details for ctDNA analysis. Details of sample collection for exploratory analysis and ctDNA analysis added. Definitions and details of analysis sets updated. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

All patients in the FAS (enrolled and assigned olaparib) were included in the baseline characteristics data. For 17 patients in the FAS, only year of birth was reported. Therefore, age at enrollment imputed using year of birth.

Notes: