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
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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)

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

subjects affected / exposed	5 / 87 (5.75%)	1 / 55 (1.82%)	6 / 143 (4.20%)
occurrences (all)	6	1	7
White blood cell count decreased			
subjects affected / exposed	5 / 87 (5.75%)	2 / 55 (3.64%)	7 / 143 (4.90%)
occurrences (all)	14	7	21
Blood bilirubin increased			
subjects affected / exposed	1 / 87 (1.15%)	1 / 55 (1.82%)	2 / 143 (1.40%)
occurrences (all)	2	3	5
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 55 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 87 (14.94%)	2 / 55 (3.64%)	15 / 143 (10.49%)
occurrences (all)	21	3	24
Dysgeusia			
subjects affected / exposed	8 / 87 (9.20%)	3 / 55 (5.45%)	11 / 143 (7.69%)
occurrences (all)	10	3	13
Headache			
subjects affected / exposed	11 / 87 (12.64%)	3 / 55 (5.45%)	14 / 143 (9.79%)
occurrences (all)	16	11	27
Taste disorder			
subjects affected / exposed	0 / 87 (0.00%)	0 / 55 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 87 (2.30%)	2 / 55 (3.64%)	4 / 143 (2.80%)
occurrences (all)	2	4	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	38 / 87 (43.68%)	20 / 55 (36.36%)	58 / 143 (40.56%)
occurrences (all)	56	32	88
Leukopenia			
subjects affected / exposed	6 / 87 (6.90%)	2 / 55 (3.64%)	8 / 143 (5.59%)
occurrences (all)	6	2	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	1 / 87 (1.15%)	0 / 55 (0.00%)	1 / 143 (0.70%)
occurrences (all)	2	0	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 87 (8.05%)	4 / 55 (7.27%)	11 / 143 (7.69%)
occurrences (all)	9	4	13
Pruritus			
subjects affected / exposed	4 / 87 (4.60%)	3 / 55 (5.45%)	7 / 143 (4.90%)
occurrences (all)	5	3	8
Rash			
subjects affected / exposed	3 / 87 (3.45%)	3 / 55 (5.45%)	6 / 143 (4.20%)
occurrences (all)	3	3	6
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	3 / 87 (3.45%)	2 / 55 (3.64%)	5 / 143 (3.50%)
occurrences (all)	3	2	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 87 (12.64%)	6 / 55 (10.91%)	17 / 143 (11.89%)
occurrences (all)	15	8	23
Back pain			
subjects affected / exposed	7 / 87 (8.05%)	4 / 55 (7.27%)	11 / 143 (7.69%)
occurrences (all)	11	4	15
Muscle spasms			
subjects affected / exposed	0 / 87 (0.00%)	1 / 55 (1.82%)	1 / 143 (0.70%)
occurrences (all)	0	2	2
Musculoskeletal pain			
subjects affected / exposed	4 / 87 (4.60%)	5 / 55 (9.09%)	9 / 143 (6.29%)
occurrences (all)	4	6	10
Myalgia			
subjects affected / exposed	4 / 87 (4.60%)	1 / 55 (1.82%)	5 / 143 (3.50%)
occurrences (all)	5	1	6
Pain in extremity			
subjects affected / exposed	4 / 87 (4.60%)	2 / 55 (3.64%)	6 / 143 (4.20%)
occurrences (all)	7	2	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 occurrences (all)	2 / 32 (6.25%) 2	0 / 2 (0.00%) 0	
Hypertension subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 2 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 2 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	15 / 32 (46.88%) 18	1 / 2 (50.00%) 1	
Influenza like illness subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 2 (0.00%) 0	
Mucosal inflammation subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 2 (0.00%) 0	
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 2 (0.00%) 0	
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 2 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 2 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	6 / 32 (18.75%) 6	0 / 2 (0.00%) 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	2 / 32 (6.25%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 32 (9.38%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 32 (3.13%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	3 / 32 (9.38%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Muscle spasms			
subjects affected / exposed	2 / 32 (6.25%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	3 / 32 (9.38%)	0 / 2 (0.00%)	
occurrences (all)	4	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: