Clinical trial results:
A Phase IIIb, Single-arm, Open-label Multicentre Study of Olaparib Monotherapy in the Treatment of HER2-ve Metastatic Breast Cancer Patients with Germline or Somatic BRCA1/2 Mutations

Summary

EudraCT number	2017-001054-34
Trial protocol	DE GB ES HU FR PL BG IT
Global end of trial date	08 October 2021

Results information

Result version number	v1 (current)
This version publication date	25 October 2022
First version publication date	25 October 2022

Trial information

Trial identification

Sponsor protocol code	D0816C00018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03286842
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	NA, NA, United States, NA
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, 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	15 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer patients in a real-world setting through assessment of progression-free survival in germline BRCA mutated patients

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 ICH/GCP, applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Italy: 43
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Turkey: 21
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Taiwan: 1
Worldwide total number of subjects	255
EEA total number of subjects	156

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)	232
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in this study from 17-January-2018 to 21-March-2019 in 125 sites in 15 countries.

Pre-assignment

Screening details:

Participants who met the inclusion and none of the exclusion criteria were enrolled to the study. All study assessments were performed as per the schedule of assessment.

Period 1

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

Arms

Arm title	Olaparib

Arm description:

Participants received olaparib 300 mg tablets orally twice daily continuously given as 2 x 150 mg twice daily.

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Peritumoral use

Dosage and administration details:

Participants were administered olaparib 300 mg tablets orally twice daily continuously given as 2 x 150 mg twice daily.

Number of subjects in period 1	Olaparib
Started	255
Completed	0
Not completed	255
Participants ongoing in the study	80
Excluding COVID-19	3
Death	142
Withdrawal by participant	28
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib
Reporting group description:	
Participants received olaparib 300 mg tablets orally twice daily continuously given as 2 x 150 mg twice daily.	

Reporting group values	Olaparib	Total	
Number of subjects	255	255	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	232	232	
From 65-84 years	23	23	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	46.3		
standard deviation	± 11.34	-	
Sex: Female, Male Units: Participants			
Female	251	251	
Male	4	4	
Race (NIH/OMB) Units: Subjects			
White	177	177	
American Indian or Alaska Native	1	1	
Asian	23	23	
Black or African American	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
Other	0	0	
Missing	52	52	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13	13	
Not Hispanic or Latino	190	190	
Missing	52	52	

Subject analysis sets	
Subject analysis set title	Olaparib gBRCAm cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received olaparib 300mg twice daily given as 150mg x 2 tablets orally twice daily continuously.

Subject analysis set title	Olaparib sBRCAm cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received olaparib 300mg twice daily given as 150mg x 2 tablets orally twice daily continuously.

Reporting group values	Olaparib gBRCAm cohort	Olaparib sBRCAm cohort	
Number of subjects	252	3	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	230	2	
From 65-84 years	22	1	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	46.2		
standard deviation	± 11.30	±	
Sex: Female, Male Units: Participants			
Female	248	3	
Male	4	0	
Race (NIH/OMB) Units: Subjects			
White	177	0	
American Indian or Alaska Native	1	0	
Asian	22	1	
Black or African American	2	0	
Native Hawaiian or Other Pacific Islander	0	0	
Other	0	0	
Missing	50	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13	0	
Not Hispanic or Latino	189	1	
Missing	50	2	

End points

End points reporting groups

Reporting group title	Olaparib
Reporting group description: Participants received olaparib 300 mg tablets orally twice daily continuously given as 2 x 150 mg twice daily.	
Subject analysis set title	Olaparib gBRCAm cohort
Subject analysis set type	Full analysis
Subject analysis set description: Participants received olaparib 300mg twice daily given as 150mg x 2 tablets orally twice daily continuously.	
Subject analysis set title	Olaparib sBRCAm cohort
Subject analysis set type	Full analysis
Subject analysis set description: Participants received olaparib 300mg twice daily given as 150mg x 2 tablets orally twice daily continuously.	

Primary: Progression-free survival (PFS) in real-world setting in germline BRCA mutated participants

End point title	Progression-free survival (PFS) in real-world setting in germline BRCA mutated participants[1]
End point description: The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting through assessment of PFS in germline BRCA mutated patients was evaluated. PS was defined as the time from first dose of olaparib to the date of progression or death from any cause regardless of whether the patient withdraws from therapy or receives another anticancer therapy prior to progression.	
End point type	Primary
End point timeframe: At every visit until the earliest of disease progression, death or end of study (up to 3.9 years)	

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: Statistical Analyses were not performed for the outcome measures.

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	8.18 (6.97 to 9.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) in germline BRCA mutated participants

End point title	Overall survival (OS) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of overall survival in germline BRCA mutated participants was determined. OS is defined as the time from first dose of olaparib to the date of death from any cause.

End point type	Secondary

End point timeframe:

At every visit and until death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	24.94 (21.06 to 28.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first subsequent treatment or death (TFST) in germline BRCA mutated participants

End point title	Time to first subsequent treatment or death (TFST) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of time to use of subsequent therapies, second progression, and study treatment discontinuation in germline BRCA mutated participants was determined. TFST is defined as the time from first dose of olaparib to first subsequent treatment commencement or death if this occurs before commencement of first subsequent treatment.

End point type	Secondary

End point timeframe:

At every visit until start of first subsequent anticancer treatment or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	9.40 (8.61 to 10.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to second subsequent treatment or death (TSST) in germline BRCA mutated participants

End point title	Time to second subsequent treatment or death (TSST) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of time to use of subsequent therapies, second progression, and study treatment discontinuation in germline BRCA mutated participants was determined. TSST is defined as the time from first dose of olaparib to second subsequent treatment commencement or death if this occurs before commencement of second subsequent treatment.

End point type	Secondary

End point timeframe:

At every visit until start of second subsequent anticancer treatment or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	14.72 (13.50 to 17.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to study treatment discontinuation or death (TDT) in germline BRCA mutated participants

End point title	Time to study treatment discontinuation or death (TDT) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of time to use of subsequent therapies, second progression, and study treatment discontinuation in germline BRCA mutated patients was determined. TDT is defined as the time from first dose of olaparib to study treatment discontinuation or death if this occurs before discontinuation of study treatment.

End point type	Secondary

End point timeframe:

At every visit and until discontinuation of study treatment or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	7.98 (6.90 to 8.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to second progression or death (PFS2) in germline BRCA mutated participants

End point title	Time to second progression or death (PFS2) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of time to use of subsequent therapies, second progression, and study treatment discontinuation in germline BRCA mutated participants was determined. PFS2 is defined as the time from first dose of olaparib to the earliest progression event subsequent to that used for the primary variable PFS or death from any cause.

End point type	Secondary

End point timeframe:

At every visit until second progression or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: months				
median (confidence interval 95%)				
gBRCAm cohort	14.49 (13.17 to 17.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate (CRR) in germline BRCA mutated participants

End point title	Clinical response rate (CRR) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of clinical response rate and duration of clinical response in germline BRCA mutated participants was determined. CRR is defined as the proportion of patients assessed by the Investigator as responding.

End point type	Secondary

End point timeframe:

At every visit until disease progression or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: Percentage of participants				
number (confidence interval 95%)	49.6 (43.3 to 55.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with adverse events (AEs) and serious adverse events (SAEs)

End point description:

The safety and tolerability of olaparib treatment in HER2-ve metastatic breast cancer patients in a real-word setting was evaluated. LTD = leading to discontinuation CRT = causally related to treatment

End point type	Secondary

End point timeframe:

From Screening (Day -28 to Day -1) until post DCO [up to 3.9 years]

End point values	Olaparib gBRCAm cohort			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Participants				
Any AE	243			
Any AE CRT	214			
Any AE of CTCAE grade ≥ 3	69			
Any AE of CTCAE grade ≥ 3, CRT	44			
Any AE with outcome = death	0			
Any AE with outcome = death, CRT	0			
Any SAE (including death)	32			
Any SAE (including death), CRT	10			
Any AE LTD of study treatment	16			
Any AE LTD of study treatment, CRT	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of clinical response (DoCR) in germline BRCA mutated participants

End point title	Duration of clinical response (DoCR) in germline BRCA mutated participants

End point description:

The clinical effectiveness of olaparib treatment in HER2-ve metastatic breast cancer participants in a real-world setting by assessment of clinical response rate and duration of clinical response in germline BRCA mutated participants was determined. DoCR is defined as the time from the date the Investigator first assessed the patient as responding to the date the Investigator assessed the patient as progressing or the date of death from any cause.

End point type	Secondary

End point timeframe:

At every visit until disease progression or death or end of study (up to 3.9 years)

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: Months				
median (inter-quartile range (Q1-Q3))				
gBRCAm cohort	8.0 (4.2 to 18.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Screening (Day -28 to -1) until post DCO [up to 3.9 years].	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Olaparib
Reporting group description: Participants received olaparib 150mg tablets orally twice daily continuously.	

Serious adverse events	Olaparib		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 255 (12.94%)		
number of deaths (all causes)	142		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer stage 0, with cancer in situ			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	2 / 255 (0.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pleurisy				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Psychiatric decompensation				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Anxiety			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
General physical condition abnormal			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation necrosis			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			

subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 255 (2.75%)		
occurrences causally related to treatment / all	6 / 10		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	2 / 255 (0.78%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus paralytic			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 255 (0.78%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders				
Back pain				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle spasms				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
COVID-19				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest wall abscess				
subjects affected / exposed	1 / 255 (0.39%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			

Influenza			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
H1N1 influenza			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	1 / 255 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Olaparib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	246 / 255 (96.47%)		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	14 / 255 (5.49%)		
occurrences (all)	18		
Nervous system disorders			
Dizziness			
subjects affected / exposed	23 / 255 (9.02%)		
occurrences (all)	28		
Dysgeusia			
subjects affected / exposed	16 / 255 (6.27%)		
occurrences (all)	18		
Headache			
subjects affected / exposed	47 / 255 (18.43%)		
occurrences (all)	103		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	22 / 255 (8.63%)		
occurrences (all)	37		
Anaemia			
subjects affected / exposed	98 / 255 (38.43%)		
occurrences (all)	168		
Neutropenia			
subjects affected / exposed	40 / 255 (15.69%)		
occurrences (all)	65		
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	70 / 255 (27.45%)		
occurrences (all)	94		
Fatigue			
subjects affected / exposed	59 / 255 (23.14%)		
occurrences (all)	84		
Pyrexia			
subjects affected / exposed	31 / 255 (12.16%)		
occurrences (all)	43		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	21 / 255 (8.24%)		
occurrences (all)	25		
Constipation			
subjects affected / exposed	30 / 255 (11.76%)		
occurrences (all)	37		
Abdominal pain upper			
subjects affected / exposed	19 / 255 (7.45%)		
occurrences (all)	31		
Nausea			
subjects affected / exposed	140 / 255 (54.90%)		
occurrences (all)	236		
Vomiting			
subjects affected / exposed	67 / 255 (26.27%)		
occurrences (all)	111		
Dyspepsia			
subjects affected / exposed	25 / 255 (9.80%)		
occurrences (all)	30		
Diarrhoea			
subjects affected / exposed	53 / 255 (20.78%)		
occurrences (all)	72		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	21 / 255 (8.24%)		
occurrences (all)	24		
Cough			

subjects affected / exposed	35 / 255 (13.73%)		
occurrences (all)	40		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 255 (5.88%)		
occurrences (all)	15		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	39 / 255 (15.29%)		
occurrences (all)	55		
Back pain			
subjects affected / exposed	28 / 255 (10.98%)		
occurrences (all)	32		
Myalgia			
subjects affected / exposed	17 / 255 (6.67%)		
occurrences (all)	17		
Pain in extremity			
subjects affected / exposed	21 / 255 (8.24%)		
occurrences (all)	24		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	13 / 255 (5.10%)		
occurrences (all)	14		
Urinary tract infection			
subjects affected / exposed	16 / 255 (6.27%)		
occurrences (all)	22		
Nasopharyngitis			
subjects affected / exposed	14 / 255 (5.49%)		
occurrences (all)	17		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	31 / 255 (12.16%)		
occurrences (all)	36		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2018	The protocol was expanded to include a cohort of patients with somatic BRCA mutations (sBRCAm).
22 October 2020	The contraceptive language was updated based on feedback from the Czech Republic regulatory authority. Myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) were changed from important potential risks to important identified risks due to a change in risks related to olaparib. Clarification of post study access in the form of transition to a roll-over study (ROSY-O), continuous supply within this trial, or switching to commercial drug.
19 April 2021	The second time point for statistical analysis has been extended to Q2/Q3 2021 due to longer than expected survival. Based on the current death event rate, at least~ 130 deaths (~52% maturity) are predicted to have occurred by this date. In order to reduce the burden on patients in terms of schedule of assessments, the follow-up after data cut-off (DCO) was reduced. Patients still receiving treatment with olaparib will have the option of continuing to receive olaparib as part of the roll over ROSY-O study (NCT04421963). Acceptable non-hormonal and hormonal birth control methods were updated following Investigator Brochure update.

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.

Due to insufficient number of patients in sBRCA cohort, the outcome measures were not calculated.

Notes: