Clinical trial results:
Randomized, Double-Blind, Phase III Trial of Olaparib vs. Placebo in Patients with Advanced FIGO Stage IIIB – IV High Grade Serous or Endometrioid Ovarian, Fallopian Tube, or Peritoneal Cancer treated with standard First-Line Treatment, Combining Platinum-Taxane Chemotherapy and Bevacizumab Concurrent with Chemotherapy and in Maintenance

Summary

EudraCT number	2014-004027-52
Trial protocol	DE AT BE ES DK SE FI IT
Global end of trial date	22 March 2022

Results information

Result version number	v1 (current)
This version publication date	14 February 2024
First version publication date	14 February 2024
Summary attachment (see zip file)	Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer (NEJMoa1911361.pdf)

Trial information

Trial identification

Sponsor protocol code	GINECO-OV125b

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02477644
WHO universal trial number (UTN)	-
Other trial identifiers	ENGOT-ov25: ENGOT

Notes:

Sponsors

Sponsor organisation name	ARCAGY-RESEARCH
Sponsor organisation address	8 Rue Lamennais, PARIS, France, 75008
Public contact	Project Manager, Sophie BRUTTO, ARCAGY-RESEARCH, +33 184 85 20 20, reglementaire@arcagy.org
Scientific contact	Project Manager, Sophie BRUTTO, ARCAGY-RESEARCH, +33 184 85 20 20, reglementaire@arcagy.org

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	22 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2019
Global end of trial reached?	Yes
Global end of trial date	22 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy by progression free survival (PFS1) investigator based according to modified Response Evaluation Criteria in Solid Tumors (RECIST version 1.1) of olaparib maintenance compared to placebo in high grade epithelial ovarian, fallopian tube, or peritoneal cancer that are in clinical complete response or partial response following first line platinum-taxane based chemotherapy plus bevacizumab, and planned to receive bevacizumab in the maintenance phase.

Protection of trial subjects:

The study will be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements.
The Informed Consent Form will incorporate (or, in some cases, be accompanied by a separate document incorporating) wording that complies with relevant data protection and privacy legislation.
ARCAGY Research will not provide individual genotype results to patient, her family members, any insurance company, any employer, general physician or any other third party, unless required to do so by law.
The exception to the above is the result of the tBRCA test; this will be made available to the investigator and patient.
Extra precautions are taken to preserve confidentiality and prevent genetic data being linked to the identity of the patient. In exceptional circumstances, however, certain individuals might see both the genetic data and the personal identifiers of a patient. For example, in the case of a medical emergency, a sponsor physician or an investigator might know a patient’s identity and also have access to her genetic data. Also Regulatory authorities may require access to the relevant files, though the patient’s medical information and the genetic files would remain physically separate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 55
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Austria: 28
Country: Number of subjects enrolled	Belgium: 20

Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 327
Country: Number of subjects enrolled	Germany: 251
Country: Number of subjects enrolled	Italy: 85
Country: Number of subjects enrolled	Monaco: 2
Country: Number of subjects enrolled	Japan: 24
Worldwide total number of subjects	806
EEA total number of subjects	780

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)	514
From 65 to 84 years	289
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Of the 1222 patients enrolled into the study (ie, gave informed consent), 416 patients were not randomised, with 326 patients not meeting the eligibility criteria.
Of the 806 patients randomised into the study, 535 olaparib patients and 267 placebo patients received study treatment (olaparib or placebo) in addition to bevacizumab

Pre-assignment

Screening details:

Patients were randomised using an Interactive Voice Response System (IVRS)/Interactive Web Response System in a 2:1 ratio (olaparib:matching placebo) to receive either olaparib tablets orally 300 mg twice daily (bd) or matching placebo, in addition to bevacizumab.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A : Olaparib

Arm description:

Olaparib

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

Dosage and administration details:

Olaparib tablets per os 300 mg twice daily,

Arm title	Arm B : Placebo

Arm description:

Placebo

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

Dosage and administration details:

Placebo tablets per os 300 mg twice daily.

Number of subjects in period 1	Arm A : Olaparib	Arm B : Placebo
Started	537	269
Completed	230	105
Not completed	307	164
Consent withdrawn by subject	15	6
Lost to follow-up	6	-
Lack of efficacy	286	158

Baseline characteristics

Reporting groups	
Reporting group title	Arm A : Olaparib
Reporting group description: Olaparib	
Reporting group title	Arm B : Placebo
Reporting group description: Placebo	

Reporting group values	Arm A : Olaparib	Arm B : Placebo	Total
Number of subjects	537	269	806
Age categorical Units: Subjects			
Adults (18-64 years)	332	182	514
From 65-84 years	204	85	289
85 years and over	1	2	3
Age continuous Units: years			
median	61	60	
full range (min-max)	32 to 87	26 to 85	-
Gender categorical Units: Subjects			
Female	537	269	806
Male	0	0	0
Performance status Units: Subjects			
ECOG 0	378	189	567
ECOG 1	153	76	229
Missing	6	4	10
Primary tumour location Units: Subjects			
Ovary	456	238	694
Fallopian tubes	39	11	50
Primary peritoneal	42	20	62
Histology Units: Subjects			
Serous	519	253	772
Endometrioid	12	8	20
Other	6	8	14
FIGO Stage Units: Subjects			
III	378	186	564
IV	159	83	242
History of cytoreductive surgery Units: Subjects			
No surgery	38	21	59
Upfront surgery - Residual macroscopic disease	111	53	164

Upfront surgery - No residual macroscopic disease	160	85	245
Interval surgery - Residual macroscopic disease	65	35	100
Interval surgery - No residual macroscopic disease	163	75	238
Response after surgery/platinum-based chemotherapy Units: Subjects			
No evidence of disease	290	141	431
Complete response	106	53	159
Partial response	141	75	216
Normal serum Ca-125 level Units: Subjects			
Yes	463	234	697
No	74	34	108
Missing	0	1	1
Deleterious tumor BRCA mutation Units: Subjects			
Yes	161	80	241
No	376	189	565
Tumor HRD status Units: Subjects			
Positive	255	132	387
Negative	192	85	277
Unknow	90	52	142

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Baseline characteristics and efficacy data will be described on the Intent-to-treat (ITT) population. The Intent-to-treat (ITT) population is defined as all patients randomized in the trial, regardless of whether they actually received treatment. The treatment groups will be analyzed as randomized. FAS: all randomised patients analysed on an ITT basis.

Reporting group values	ITT		
Number of subjects	806		
Age categorical Units: Subjects			
Adults (18-64 years)	514		
From 65-84 years	289		
85 years and over	3		
Age continuous Units: years			
median	61		
full range (min-max)	26 to 87		
Gender categorical Units: Subjects			
Female	806		
Male	0		

Performance status Units: Subjects			
ECOG 0	567		
ECOG 1	229		
Missing	10		
Primary tumour location Units: Subjects			
Ovary	694		
Fallopian tubes	50		
Primary peritoneal	62		
Histology Units: Subjects			
Serous	772		
Endometrioid	20		
Other	14		
FIGO Stage Units: Subjects			
III	564		
IV	242		
History of cytoreductive surgery Units: Subjects			
No surgery	59		
Upfront surgery - Residual macroscopic disease	164		
Upfront surgery - No residual macroscopic disease	245		
Interval surgery - Residual macroscopic disease	100		
Interval surgery - No residual macroscopic disease	238		
Response after surgery/platinum-based chemotherapy Units: Subjects			
No evidence of disease	431		
Complete response	159		
Partial response	216		
Normal serum Ca-125 level Units: Subjects			
Yes	697		
No	108		
Missing	1		
Deleterious tumor BRCA mutation Units: Subjects			
Yes	241		
No	565		
Tumor HRD status Units: Subjects			
Positive	387		
Negative	277		
Unknow	142		

End points

End points reporting groups

Reporting group title	Arm A : Olaparib
Reporting group description: Olaparib	
Reporting group title	Arm B : Placebo
Reporting group description: Placebo	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Baseline characteristics and efficacy data will be described on the Intent-to-treat (ITT) population. The Intent-to-treat (ITT) population is defined as all patients randomized in the trial, regardless of whether they actually received treatment. The treatment groups will be analyzed as randomized. FAS: all randomised patients analysed on an ITT basis.	

Primary: Progression free survival in ITT population

End point title	Progression free survival in ITT population
End point description: Time from randomization to disease prgression according to RECIST1.1 or death whatever occurs first.	
End point type	Primary
End point timeframe: At disease progression	

End point values	Arm A : Olaparib	Arm B : Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	537	269		
Units: months				
median (confidence interval 95%)	22.1 (21.8 to 24.1)	16.6 (15.4 to 18.6)		

Statistical analyses

Statistical analysis title	Median PFS
Statistical analysis description: Log-rank test stratified on first line treatment outcome and tBRCA status	
Comparison groups	Arm A : Olaparib v Arm B : Placebo
Number of subjects included in analysis	806
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.72

Secondary: Second Progression free survival (PFS2) in ITT population

End point title	Second Progression free survival (PFS2) in ITT population

End point description:

Time from the date of randomization to the earliest of the progression event subsequent to that used for the primary variable PFS1, or date of death

End point type	Secondary

End point timeframe:

When 411 events had been observed in ITT population, OR after a maximum duration of 1 year following the PFS1 analysis, whichever occurs first.

End point values	Arm A : Olaparib	Arm B : Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	537	269		
Units: Months				
median (confidence interval 95%)	36.5 (32.2 to 42.6)	32.6 (28.3 to 35.1)		

Statistical analyses

Statistical analysis title	Median PFS

Statistical analysis description:

Log-rank test stratified on first line treatment outcome and tBRCA status

Comparison groups	Arm A : Olaparib v Arm B : Placebo
Number of subjects included in analysis	806
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0125
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.95

Secondary: Overall survival in ITT population

End point title	Overall survival in ITT population

End point description:

Time from the date of randomization until death due to any cause.

End point type	Secondary

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	Arm A : Olaparib	Arm B : Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	537	269		
Units: Months				
median (confidence interval 95%)	56.5 (49.8 to 62.2)	51.6 (43.0 to 55.7)		

Statistical analyses

Statistical analysis title	Median OS

Statistical analysis description:

Log-rank test stratified on first line treatment outcome and tBRCA status

Comparison groups	Arm A : Olaparib v Arm B : Placebo
Number of subjects included in analysis	806
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4118
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.12

Other pre-specified: Progression free survival in tBRCA mutated patients

End point title	Progression free survival in tBRCA mutated patients

End point description:

End point type	Other pre-specified

End point timeframe:
When 458 events had been observed on ITT population

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	237[1]			
Units: Hazard ratio				
number (confidence interval 95%)	0.31 (0.2 to 0.47)			

Notes:
[1] - Patients with tumor BRCA mutation (tBRCAm)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression free survival in tBRCA wild type patients

End point title	Progression free survival in tBRCA wild type patients

End point description:

End point type	Other pre-specified

End point timeframe:
When 458 events had been observed on ITT population

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	569[2]			
Units: Hazard ratio				
number (confidence interval 95%)	0.71 (0.58 to 0.88)			

Notes:
[2] - Patients with no tumor BRCA mutation (tBRCAwt)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression free survival in HRD negative patients

End point title	Progression free survival in HRD negative patients

End point description:

End point type	Other pre-specified

End point timeframe:
When 458 events had been observed on ITT population

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	419			
Units: months				
median (confidence interval 95%)	0.92 (0.72 to 1.17)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression free survival in HRD positive including tBRCAm patients

End point title	Progression free survival in HRD positive including tBRCAm patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 458 events had been observed on ITT population

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	387			
Units: months				
median (confidence interval 95%)	0.33 (0.25 to 0.45)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression free survival in HRD positive, excluding tBRCAm patients

End point title	Progression free survival in HRD positive, excluding tBRCAm patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 458 events had been observed on ITT population

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: months				
median (confidence interval 95%)	0.43 (0.28 to 0.66)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Second Progression free survival (PFS2) in HRD positive, including tBRCAm patients

End point title	Second Progression free survival (PFS2) in HRD positive, including tBRCAm patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 411 events had been observed in ITT population, OR after a maximum duration of 1 year following the PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	387			
Units: Hazard ratio				
number (confidence interval 95%)	0.56 (0.41 to 0.77)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Second Progression free survival (PFS2) in HRD positive, excluding tBRCAm patients

End point title	Second Progression free survival (PFS2) in HRD positive, excluding tBRCAm patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 411 events had been observed in ITT population, OR after a maximum duration of 1 year following the PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Hazard ratio				
number (confidence interval 95%)	0.6 (0.38 to 0.96)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Second Progression free survival (PFS2) in HRD negative patients

End point title	Second Progression free survival (PFS2) in HRD negative patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 411 events had been observed in ITT population, OR after a maximum duration of 1 year following the PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	419			
Units: Hazard ratio				
number (confidence interval 95%)	0.98 (0.77 to 1.27)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall survival (OS) in HRD positive, including tBRCAm patients

End point title	Overall survival (OS) in HRD positive, including tBRCAm patients

End point description:

Time from the date of randomization until death due to any cause.

End point type	Other pre-specified

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	387			
Units: Hazard ratio				
number (confidence interval 95%)	0.62 (0.45 to 0.85)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall survival (OS) in tBRCAm patients

End point title	Overall survival (OS) in tBRCAm patients

End point description:

Time from the date of randomization until death due to any cause.

End point type	Other pre-specified

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	237			
Units: Hazard ratio				
number (confidence interval 95%)	0.6 (0.39 to 0.93)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall survival (OS) in HRD positive, excluding tBRCAm patients

End point title	Overall survival (OS) in HRD positive, excluding tBRCAm patients

End point description:

Time from the date of randomization until death due to any cause.

End point type	Other pre-specified

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Hazard ratio				
number (confidence interval 95%)	0.71 (0.45 to 1.13)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall survival (OS) in HRD negative patients (excluding unknown)

End point title	Overall survival (OS) in HRD negative patients (excluding unknown)

End point description:

Time from the date of randomization until death due to any cause.

End point type	Other pre-specified

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Hazard ratio				
number (confidence interval 95%)	1.19 (0.88 to 1.63)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall survival (OS) in HRD negative patients

End point title	Overall survival (OS) in HRD negative patients

End point description:

Time from the date of randomization until death due to any cause.

End point type	Other pre-specified

End point timeframe:

Final OS analysis is planned to be performed when the OS data are approximately 60% mature OR after a 3-year duration from the main PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	419			
Units: Hazard ratio				
number (confidence interval 95%)	1.14 (0.89 to 1.48)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Second Progression free survival (PFS2) in tBRCAm patients

End point title	Second Progression free survival (PFS2) in tBRCAm patients

End point description:

End point type	Other pre-specified

End point timeframe:

When 411 events had been observed in ITT population, OR after a maximum duration of 1 year following the PFS1 analysis, whichever occurs first.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	237			
Units: Hazard ratio				
number (confidence interval 95%)	0.53 (0.34 to 0.83)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first subsequent therapy (TFST) in ITT population

End point title	Time to first subsequent therapy (TFST) in ITT population

End point description:

Time from randomization to first subsequent therapy or death (TFST)
FST is defined as the time from the date of randomization to the earliest of the date of anti-cancer therapy start date following study treatment discontinuation, or death. Subsequent therapies intended

to control ovarian cancer will be reported. Any patient not known to have died at the time of the analysis and not known to have had a further intervention of this type will be censored at the last known time to have not received subsequent therapy, i.e. the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of first subsequent therapy or death (TFST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	806			
Units: Hazard ratio				
number (confidence interval 95%)	0.63 (0.54 to 0.75)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first subsequent therapy (TFST) in HRD positive including tBRCAm patients

End point title	Time to first subsequent therapy (TFST) in HRD positive including tBRCAm patients

End point description:

Time from randomization to first subsequent therapy or death (TFST)
FST is defined as the time from the date of randomization to the earliest of the date of anti-cancer therapy start date following study treatment discontinuation, or death. Subsequent therapies intended to control ovarian cancer will be reported. Any patient not known to have died at the time of the analysis and not known to have had a further intervention of this type will be censored at the last known time to have not received subsequent therapy, i.e. the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of first subsequent therapy or death (TFST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	387			
Units: Hazard ratio				
number (confidence interval 95%)	0.41 (0.32 to 0.52)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first subsequent therapy (TFST) in HRD positive, excluding tBRCAm patients

End point title	Time to first subsequent therapy (TFST) in HRD positive, excluding tBRCAm patients

End point description:

Time from randomization to first subsequent therapy or death (TFST)
FST is defined as the time from the date of randomization to the earliest of the date of anti-cancer therapy start date following study treatment discontinuation, or death. Subsequent therapies intended to control ovarian cancer will be reported. Any patient not known to have died at the time of the analysis and not known to have had a further intervention of this type will be censored at the last known time to have not received subsequent therapy, i.e. the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of first subsequent therapy or death (TFST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Hazard ratio				
number (confidence interval 95%)	0.48 (0.32 to 0.7)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first subsequent therapy (TFST) in HRD negative patients (excluding unknown)

End point title	Time to first subsequent therapy (TFST) in HRD negative patients (excluding unknown)

End point description:

Time from randomization to first subsequent therapy or death (TFST)
FST is defined as the time from the date of randomization to the earliest of the date of anti-cancer therapy start date following study treatment discontinuation, or death. Subsequent therapies intended to control ovarian cancer will be reported. Any patient not known to have died at the time of the analysis and not known to have had a further intervention of this type will be censored at the last known time to have not received subsequent therapy, i.e. the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of first subsequent therapy or death (TFST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Hazard Ratio				
number (confidence interval 95%)	1.03 (0.79 to 1.36)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first subsequent therapy (TFST) in tBRCA mutated patients

End point title	Time to first subsequent therapy (TFST) in tBRCA mutated patients

End point description:

Time from randomization to first subsequent therapy or death (TFST)
FST is defined as the time from the date of randomization to the earliest of the date of anti-cancer therapy start date following study treatment discontinuation, or death. Subsequent therapies intended to control ovarian cancer will be reported. Any patient not known to have died at the time of the analysis and not known to have had a further intervention of this type will be censored at the last known time to have not received subsequent therapy, i.e. the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of first subsequent therapy or death (TFST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	237			
Units: Hazard Ratio				
number (confidence interval 95%)	0.47 (0.34 to 0.65)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to second subsequent therapy (TSST) in ITT population

End point title	Time to second subsequent therapy (TSST) in ITT population

End point description:

Time to start of second subsequent therapy or death (TSST) will be defined as the time from the date of randomization to the earliest of the date of event defined as start of a second subsequent anti-cancer therapy following study treatment discontinuation, or death (by any cause in the absence of start of a second new anti-cancer therapy). Patient not known to have died at the time of the analysis and not known to have started a second new anticancer therapy will be censored at the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of second subsequent therapy or death (TSST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	806			
Units: Hazard ratio				
number (confidence interval 95%)	0.77 (0.65 to 0.92)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to second subsequent therapy (TSST) in HRD positive including tBRCAm patients

End point title	Time to second subsequent therapy (TSST) in HRD positive including tBRCAm patients

End point description:

Time to start of second subsequent therapy or death (TSST) will be defined as the time from the date of randomization to the earliest of the date of event defined as start of a second subsequent anti-cancer therapy following study treatment discontinuation, or death (by any cause in the absence of start of a second new anti-cancer therapy). Patient not known to have died at the time of the analysis and not known to have started a second new anticancer therapy will be censored at the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of second subsequent therapy or death (TSST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	387			
Units: Hazard ratio				
number (confidence interval 95%)	0.51 (0.39 to 0.68)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to second subsequent therapy (TSST) in HRD positive, excluding tBRCAm patients

End point title	Time to second subsequent therapy (TSST) in HRD positive,

	excluding tBRCAm patients

End point description:

Time to start of second subsequent therapy or death (TSST) will be defined as the time from the date of randomization to the earliest of the date of event defined as start of a second subsequent anti-cancer therapy following study treatment discontinuation, or death (by any cause in the absence of start of a second new anti-cancer therapy). Patient not known to have died at the time of the analysis and not known to have started a second new anticancer therapy will be censored at the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of second subsequent therapy or death (TSST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: Hazard ratio				
number (confidence interval 95%)	0.63 (0.42 to 0.96)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to second subsequent therapy (TSST) in HRD negative patients (excluding unknown)

End point title	Time to second subsequent therapy (TSST) in HRD negative patients (excluding unknown)

End point description:

Time to start of second subsequent therapy or death (TSST) will be defined as the time from the date of randomization to the earliest of the date of event defined as start of a second subsequent anti-cancer therapy following study treatment discontinuation, or death (by any cause in the absence of start of a second new anti-cancer therapy). Patient not known to have died at the time of the analysis and not known to have started a second new anticancer therapy will be censored at the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of second subsequent therapy or death (TSST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Hazard Ratio				
number (confidence interval 95%)	1.15 (0.87 to 1.54)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to second subsequent therapy (TSST) in tBRCA mutated patients

End point title	Time to second subsequent therapy (TSST) in tBRCA mutated patients

End point description:

Time to start of second subsequent therapy or death (TSST) will be defined as the time from the date of randomization to the earliest of the date of event defined as start of a second subsequent anti-cancer therapy following study treatment discontinuation, or death (by any cause in the absence of start of a second new anti-cancer therapy). Patient not known to have died at the time of the analysis and not known to have started a second new anticancer therapy will be censored at the last follow-up visit where this was confirmed.

End point type	Other pre-specified

End point timeframe:

Time to start of second subsequent therapy or death (TSST) will be assessed at the time of OS analysis

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	237			
Units: Hazard ratio				
number (confidence interval 95%)	0.51 (0.35 to 0.74)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events will be collected from initiation of study drug throughout the treatment period and up to and including the 30-day follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Arm A: Olaparib

Reporting group description:

Experimental arm

Reporting group title	Arm B : Placebo

Reporting group description:

Control arm

Serious adverse events	Arm A: Olaparib	Arm B : Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	168 / 535 (31.40%)	84 / 267 (31.46%)	
number of deaths (all causes)	289	159	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	2 / 535 (0.37%)	3 / 267 (1.12%)	
occurrences causally related to treatment / all	2 / 2	1 / 3	
deaths causally related to treatment / all	1 / 1	1 / 1	
Basal cell carcinoma			

subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	7 / 535 (1.31%)	3 / 267 (1.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis autoimmune			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	3 / 535 (0.56%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			

subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	2 / 535 (0.37%)	3 / 267 (1.12%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Neoplasm malignant			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus polyp			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric cancer			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Coronary artery disease			

subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery dissection			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	51 / 535 (9.53%)	35 / 267 (13.11%)	
occurrences causally related to treatment / all	11 / 81	4 / 62	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			

subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cementoplasty			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eventration repair			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Allergic oedema			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast complication associated with device			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 535 (0.56%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oedema peripheral			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 535 (0.56%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic dermatomyositis			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic rupture			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 535 (0.37%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	3 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Interstitial lung disease			

subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 535 (0.75%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	1 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	3 / 535 (0.56%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			

subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site infection			
subjects affected / exposed	0 / 535 (0.00%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute pulmonary oedema			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 535 (0.00%)	4 / 267 (1.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prinzmetal angina			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Cerebral haemorrhage			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Acute myeloid leukaemia			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Aplastic anaemia			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Anaemia			
subjects affected / exposed	33 / 535 (6.17%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	42 / 44	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cold type haemolytic anaemia			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythroblastosis			

subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic disorder			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	3 / 535 (0.56%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye infection			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 535 (0.75%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 535 (0.00%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 535 (0.37%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	4 / 535 (0.75%)	4 / 267 (1.50%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	8 / 535 (1.50%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	1 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			

subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Melaena			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 535 (0.00%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	8 / 535 (1.50%)	3 / 267 (1.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 535 (0.00%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			

subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urogenital fistula			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myalgia			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	1 / 535 (0.19%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta haemolytic streptococcal infection			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONA VIRUS INFECTION			
subjects affected / exposed	0 / 535 (0.00%)	2 / 267 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Cytomegalovirus infection			
subjects affected / exposed	2 / 535 (0.37%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	3 / 535 (0.56%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 535 (0.37%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			

subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PILONIDAL CYST			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 535 (0.56%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 535 (0.19%)	0 / 267 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 535 (0.00%)	1 / 267 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2.8 %

Non-serious adverse events	Arm A: Olaparib	Arm B : Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	531 / 535 (99.25%)	256 / 267 (95.88%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	245 / 535 (45.79%)	160 / 267 (59.93%)	
occurrences (all)	665	471	
Nervous system disorders			
Headache			
subjects affected / exposed	73 / 535 (13.64%)	36 / 267 (13.48%)	
occurrences (all)	130	82	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	219 / 535 (40.93%)	27 / 267 (10.11%)	
occurrences (all)	692	33	
Lymphopenia			
subjects affected / exposed	126 / 535 (23.55%)	25 / 267 (9.36%)	
occurrences (all)	339	50	
Leukopenia			
subjects affected / exposed	95 / 535 (17.76%)	26 / 267 (9.74%)	
occurrences (all)	174	37	
Neutropenia			
subjects affected / exposed	95 / 535 (17.76%)	42 / 267 (15.73%)	
occurrences (all)	137	49	
Thrombocytopenia			
subjects affected / exposed	32 / 535 (5.98%)	7 / 267 (2.62%)	
occurrences (all)	76	8	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	283 / 535 (52.90%)	86 / 267 (32.21%)	
occurrences (all)	601	159	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	285 / 535 (53.27%)	58 / 267 (21.72%)	
occurrences (all)	601	96	
Vomiting			

subjects affected / exposed	117 / 535 (21.87%)	29 / 267 (10.86%)	
occurrences (all)	233	47	
Diarrhoea			
subjects affected / exposed	98 / 535 (18.32%)	45 / 267 (16.85%)	
occurrences (all)	181	72	
Abdominal pain			
subjects affected / exposed	103 / 535 (19.25%)	53 / 267 (19.85%)	
occurrences (all)	167	86	
Constipation			
subjects affected / exposed	53 / 535 (9.91%)	28 / 267 (10.49%)	
occurrences (all)	66	39	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	31 / 535 (5.79%)	40 / 267 (14.98%)	
occurrences (all)	47	62	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	116 / 535 (21.68%)	64 / 267 (23.97%)	
occurrences (all)	167	123	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	79 / 535 (14.77%)	27 / 267 (10.11%)	
occurrences (all)	149	37	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2015	• Initial corrected (administrative correction) • Collect of QoL questionnaires and Pharmaco-economy information until 2 years (calculated from 1st study drug administration).
14 January 2016	• Update of the list of special interest events (adding "Pneumonitis"), • Update of the flow chart according to study schedule, • Modification of the translational research on blood samples, • Administrative correction.
15 February 2016	• Modification of selection criteria I-5 and I-8, • Modification on CT scan/RMI schedule.
06 January 2017	• New Statistical hypothesis with increase of the randomized patients number (and prolongation of inclusion period) • Modification of the Sponsor's name • Review of anemia's management • Addition of a new exploratory objective • Administrative update • Correction of typographical errors
22 December 2017	• Removal of the Interim Efficacy Analyses • Frequency's modification of haemotology tests • Administrative update
03 October 2018	• Addition of details in the description of exploratory endpoints analyses • Corrections regarding the Japanese cohort • Addition of clarifications regarding the end of study treatment • Addition of details for the collection of some data • Administrative update
28 February 2019	• Modification of statistical methodology with addition of interim PFS2/OS analysis at the same time as final PFS1 analysis • Addition of visits during the Follow up of patient • Addition of clarification regarding the SAE declaration • Addition of details regarding the declaration to MR0O1 • Corrections to typographical errors • Administrative update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31851799

http://www.ncbi.nlm.nih.gov/pubmed/33372675

http://www.ncbi.nlm.nih.gov/pubmed/34378365

http://www.ncbi.nlm.nih.gov/pubmed/34952708

http://www.ncbi.nlm.nih.gov/pubmed/36067615

http://www.ncbi.nlm.nih.gov/pubmed/34597975

http://www.ncbi.nlm.nih.gov/pubmed/36564284

http://www.ncbi.nlm.nih.gov/pubmed/36634389

http://www.ncbi.nlm.nih.gov/pubmed/38129136

http://www.ncbi.nlm.nih.gov/pubmed/37211045

http://www.ncbi.nlm.nih.gov/pubmed/36716415