Clinical trial results:
A GINECO phase II trial assessing the safety and efficacy of the Bevacizumab (FKB238), Olaparib (MEDI 4736) and Durvalumab combination in patients with advanced epithelial ovarian cancer in relapse: BOLD

Summary

EudraCT number	2018-002281-39
Trial protocol	FR
Global end of trial date	31 May 2023

Results information

Result version number	v1 (current)
This version publication date	10 April 2025
First version publication date	10 April 2025

Trial information

Trial identification

Sponsor protocol code	GINECO-OV238

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ARCAGY-GINECO
Sponsor organisation address	8 rue Lamennais , Paris, France,
Public contact	Michèle TORRES-MACQUE, ARCAGY-GINECO, 33 142348323, reglementaire@arcagy.org
Scientific contact	Michèle TORRES-MACQUE, ARCAGY-GINECO, 33 142348323, 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	12 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2021
Global end of trial reached?	Yes
Global end of trial date	31 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is the rate of clinical and radiological non-progressive disease, as assessed by immune-related response criteria (irRC) (Wolchok et al. 2009) :

- At 3 months in the PRR cohort
- At 6 months in the PSR cohort

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki. The trial was conducted in agreement with the International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP).

Background therapy:

Bevacizumab and olaparib have already been tested on 12 patients in a phase I trial at their usual doses (10 mg/kg q2w and 400 mg bid – 50 mg capsules -, respectively), and no DLTs were observed (Dean et al., 2012). The addition of an anti-VEGF small molecule, cediranib, to olaparib doubled the median PFS in a randomized phase II trial in patients with platinum sensitive relapse, with a manageable safety profile (Liu et al., 2014).

A recently reported phase I trial established the RDP2D of Durvalumab and Olaparib – 150 mg tablets –, when given in combination, at 1500 mg every 4 weeks, and 300 mg bid, respectively (Lee et al. 2017). In addition, the ENGOT/GINECO PAOLA phase III trial is currently evaluating the combination of Olaparib and Bevacizumab as first-line maintenance after platinum-paclitaxel combination, in patients with advanced high-grade serous ovarian carcinoma. Under the hypothesis of a survival benefit in favor of this combination, it would also be of interest to assess the value of adding Durvalumab in order to improve the efficacy of the overall combination.

There are no trials to date assessing anti-VEGF in combination with anti-PARP and anti-PDL1 therapy.

Beside additive efficacy, a synergistic effect could be expected :
• Between bevacizumab and durvalumab, through normalization of blood vessel and potentiation of immunologic infiltration.
• Between olaparib and durvalumab, through cytotoxicity-mediated release of antigens and impairment of mutation repair mechanisms, thereby increasing neoantigen loads.
• Between olaparib and bevacizumab, through tumor environment modulation and signaling of DNA damage inhibition, which has already been tested with the anti-VEGF cediranib.

Evidence for comparator:

The lifetime risk of ovarian cancer is around 1 to 2% in developed countries (Jayson et al., 2014). While there are effective treatment options that significantly prolong survival, advanced ovarian cancer (AOC) is still mostly a fatal disease, which requires additional therapeutic options. After first-line cytoreductive surgery and chemotherapy, 70 % of patients achieving complete remission will relapse. In patients with platinum sensitive relapse, long remissions may be obtained by platinum containing chemotherapy regimens and, in some cases, by surgery. Bevacizumab is indicated in first-relapse, in patients who did not previously receive this drug. Olaparib is SoC for mBRCA ½ PSR maintenance patients. However, relapsing AOC is no longer a curable disease and iterative relapses usually occur. In patients with platinum resistant disease, non-platinum cytotoxic agents such as paclitaxel, liposomal doxorubicin, or topotecan are indicated, in combination with bevacizumab, but the overall prognosis remains poor.There is clearly an unmet therapeutic need in patients with either platinum-resistant relapse or platinum-sensitive relapse.

Actual start date of recruitment	01 March 2019
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	France: 74
Worldwide total number of subjects	74
EEA total number of subjects	74

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)	33
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 01/03/2019 and 23/01/2020

Pre-assignment

Screening details:

93 patients were eligible in which 19 were excluded, 74 were enrolled and treated (41 in Platinum-resistant relapse cohort and 33 in Platinum-sensitive relapse cohort)

Period 1

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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	Platinum-resistant relapse (PRR) cohort

Arm description:

Platinum-resistant relapse was defined as disease progression <6 months after the last platinum dose and ≥1 line of previous platinum and taxane-containing chemotherapy.

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 300mg was administered orally twice daily

Investigational medicinal product name	FKB238
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

FKB238 (bevacizumab biosimilar; Centus Biotherapeutics, Cambridge, UK) 15mg/kg was administered once every 3 weeks (Q3W) intravenously (initially 90min, subsequently 60, then 30min if well tolerated).

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1.12g was administered Q3W, 1-h intravenous infusion, more than 1h after olaparib, starting from Cycle 1. Subsequent infusion durations could be reduced.

Arm title	Platinum-sensitive relapse (PSR) cohort

Arm description:

Platinum-sensitive relapse was defined as disease progression ≥6 months after the last platinum dose in

any prior line.

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 300mg was administered orally twice daily

Investigational medicinal product name	FKB238
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

FKB238 (bevacizumab biosimilar; Centus Biotherapeutics, Cambridge, UK) 15mg/kg was administered once every 3 weeks (Q3W) intravenously (initially 90min, subsequently 60, then 30min if well tolerated).

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1.12g was administered Q3W, 1-h intravenous infusion, more than 1h after olaparib, starting from Cycle 1. Subsequent infusion durations could be reduced.

Number of subjects in period 1	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort
Started	41	33
Completed	41	33

Baseline characteristics

Reporting groups	
Reporting group title	Platinum-resistant relapse (PRR) cohort
Reporting group description:	
Platinum-resistant relapse was defined as disease progression <6 months after the last platinum dose and ≥1 line of previous platinum and taxane-containing chemotherapy.	
Reporting group title	Platinum-sensitive relapse (PSR) cohort
Reporting group description:	
Platinum-sensitive relapse was defined as disease progression ≥6 months after the last platinum dose in any prior line.	

Reporting group values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort	Total
Number of subjects	41	33	74
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	15	34
From 65-84 years	21	18	39
85 years and over	1	0	1
Age continuous Units: years			
median	66	65	
full range (min-max)	38 to 89	43 to 81	-
Gender categorical Units: Subjects			
Female	41	33	74
ECOG performance status Units: Subjects			
ECOG 0	20	24	44
ECOG 1	21	9	30
FIGO stage Units: Subjects			
II	2	2	4
III	21	22	43
IV	14	6	20
Unknown / Missing	4	3	7
Tumor origin Units: Subjects			
Ovarian	37	29	66
Primary peritoneal	4	4	8
Adenocarcinoma type at diagnosis			

Units: Subjects			
High-grade serous	38	33	71
Endometrioid Grade 2/3	1	0	1
Undifferentiated	1	0	1
Other	1	0	1
BRCA1/2 deleterious mutation			
Units: Subjects			
Yes	4	11	15
No	37	22	59
Germline BRCA mutation			
Units: Subjects			
BRCA1	2	6	8
BRCA2	2	3	5
NA	37	24	61
Somatic BRCA mutation (isolated)			
Units: Subjects			
BRCA1	0	3	3
BRCA2	0	0	0
NA	41	30	71
Prior systematic therapy : PARP inhibitor			
Units: Subjects			
PARP inhibitor: Olaparib	4	9	13
PARP inhibitor: Niraparib	7	8	15
PARP inhibitor: Rucaparib	2	0	2
No PARP inhibitor	28	16	44
Prior systematic therapy : Bevacizumab			
Units: Subjects			
Bevacizumab	35	21	56
No Bevacizumab	6	12	18
Prior systematic therapy : Antiangiogenic agent			
Units: Subjects			
Antiangiogenic agent	36	28	64
No antiangiogenic agent	5	5	10
Prior systematic therapy : Other antiangiogenic agent			
Units: Subjects			
Other antiangiogenic agent	11	8	19
NA	30	25	55
Prior systematic therapy : N lines chemotherapy			
Units: Number			
median	3	2	
full range (min-max)	1 to 8	1 to 8	-
Exposition to Treatment : Durvalumab			
Units: Number			
median	8	10.5	
full range (min-max)	1 to 32	2 to 30	-
Exposition to Treatment : Fkb238			
Units: Number			
median	8	10	

full range (min-max)	1 to 32	1 to 30	-
Exposition to Treatment : Olaparib Units: Number			
median	7	9	
full range (min-max)	1 to 30	1 to 28	-
Time between inclusion and last follow-up (in months) Units: month			
median	14.28	15.57	
full range (min-max)	0.96 to 21.45	2.58 to 20.69	-

Subject analysis sets

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

Subject analysis set description:

The Intent-to-treat (ITT) population is defined as all patients included in the cohort considered, regardless of whether they actually received treatment.

Reporting group values	ITT population		
Number of subjects	74		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	33		
From 65-84 years	40		
85 years and over	1		
Age continuous Units: years			
median	65.5		
full range (min-max)	38 to 89		
Gender categorical Units: Subjects			
Female	74		
ECOG performance status Units: Subjects			
ECOG 0	44		
ECOG 1	30		
FIGO stage Units: Subjects			
II	4		
III	43		
IV	20		
Unknown / Missing	7		
Tumor origin			

Units: Subjects			
Ovarian	66		
Primary peritoneal	8		
Adenocarcinoma type at diagnosis Units: Subjects			
High-grade serous	71		
Endometrioid Grade 2/3	1		
Undifferentiated	1		
Other	1		
BRCA1/2 deleterious mutation Units: Subjects			
Yes	15		
No	59		
Germline BRCA mutation Units: Subjects			
BRCA1	8		
BRCA2	5		
NA	61		
Somatic BRCA mutation (isolated) Units: Subjects			
BRCA1	3		
BRCA2	0		
NA	71		
Prior systematic therapy : PARP inhibitor Units: Subjects			
PARP inhibitor: Olaparib	13		
PARP inhibitor: Niraparib	15		
PARP inhibitor: Rucaparib	2		
No PARP inhibitor	44		
Prior systematic therapy : Bevacizumab Units: Subjects			
Bevacizumab	56		
No Bevacizumab	18		
Prior systematic therapy : Antiangiogenic agent Units: Subjects			
Antiangiogenic agent	64		
No antiangiogenic agent	10		
Prior systematic therapy : Other antiangiogenic agent Units: Subjects			
Other antiangiogenic agent	19		
NA	55		
Prior systematic therapy : N lines chemotherapy Units: Number			
median	2		
full range (min-max)	1 to 8		
Exposition to Treatment : Durvalumab Units: Number			
median	9		

full range (min-max)	1 to 32		
Exposition to Treatment : Fkb238 Units: Number median full range (min-max)	 9 1 to 32		
Exposition to Treatment : Olaparib Units: Number median full range (min-max)	 8.5 1 to 30		
Time between inclusion and last follow-up (in months) Units: month median full range (min-max)	 15.44 0.96 to 21.45		

End points

End points reporting groups

Reporting group title	Platinum-resistant relapse (PRR) cohort
Reporting group description:	
Platinum-resistant relapse was defined as disease progression <6 months after the last platinum dose and ≥1 line of previous platinum and taxane-containing chemotherapy.	
Reporting group title	Platinum-sensitive relapse (PSR) cohort
Reporting group description:	
Platinum-sensitive relapse was defined as disease progression ≥6 months after the last platinum dose in any prior line.	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-treat (ITT) population is defined as all patients included in the cohort considered, regardless of whether they actually received treatment.	

Primary: Rate of clinical and radiological non-progression disease

End point title	Rate of clinical and radiological non-progression disease
End point description:	
End point type	Primary
End point timeframe:	
Overall study	

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Rate				
number (confidence interval 90%)				
Rate of non-progressive disease [90% CI] RECIST	0.698 (0.559 to 0.8)	0.438 (0.292 to 0.574)		
Rate of non-progressive disease [90% CI] irRECIST	0.775 (0.643 to 0.863)	0.561 (0.405 to 0.691)		

Statistical analyses

Statistical analysis title	Kaplan-Meier estimates
Comparison groups	Platinum-resistant relapse (PRR) cohort v Platinum-sensitive relapse (PSR) cohort

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Kaplan-Meier estimates

Primary: Rate of clinical and radiological non-progression disease : Maximum follow-up

End point title	Rate of clinical and radiological non-progression disease : Maximum follow-up

End point description:

End point type	Primary

End point timeframe:

Overall time

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: month				
Maximum Follow-up (months)	3	6		

Statistical analyses

Statistical analysis title	Kaplan-Meier estimates
Comparison groups	Platinum-resistant relapse (PRR) cohort v Platinum-sensitive relapse (PSR) cohort
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Kaplan-Meier estimates

Primary: Rate of clinical and radiological non-progression disease : Time to measure the rate according RECIST/clinical criteria

End point title	Rate of clinical and radiological non-progression disease : Time to measure the rate according RECIST/clinical criteria

End point description:

End point type	Primary

End point timeframe:
Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: month				
number (not applicable)				
Time to measure the rate according RECIST/clinical	2.744	5.653		

Statistical analyses

Statistical analysis title	Kaplan-Meier estimates
Comparison groups	Platinum-resistant relapse (PRR) cohort v Platinum-sensitive relapse (PSR) cohort
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Kaplan-Meier estimates

Secondary: CA-125 decline

End point title	CA-125 decline

End point description:

End point type	Secondary

End point timeframe:
Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	41	33	74	
Units: kU/L				
median (full range (min-max))				
CA-125 - Value (kU/L)	281.10 (10.10 to 25000.00)	42.75 (3.00 to 12000.00)	148.00 (3.00 to 25000.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Rate				
number (not applicable)				
PFS (RECIST)	0.5	0.5		
PFS (irRECIST)	0.5	0.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) : Time in months

End point title	Progression free survival (PFS) : Time in months

End point description:

Median PFS (per RECIST and/or clinical progression) was 4.1 months (95% CI 3.5–5.9) in platinum-resistant patients and 4.9 months (95% CI 2.9–7.0) in platinum-sensitive patients.
Efficacy outcomes were similar using irRECIST, with higher non-progression rates and longer median PFS in both groups: 5.4 months (95% CI 4.0–7.2) vs 7 months (95% CI 3.3– +Inf, which was published as the value 9999 in this EudraCT database), respectively.

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: month				
number (confidence interval 95%)				
Time in months RECIST	4.1322 (3.4711 to 5.9174)	4.8595 (2.8760 to 6.9752)		
Time in months irRECIST	5.3884 (4.0331 to 7.1736)	6.9752 (3.2727 to 9999)		

Attachments (see zip file)	Progression Free Survival (PFS) RECIST/Fig 3. Progression Free Progression-free survival irRECIST/Fig 4. Progression Free

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Rate				
number (confidence interval 95%)				
Time in months	18.5455 (9.6198 to 21.6860)	20.8595 (16.6612 to 36.4628)		

Attachments (see zip file)	Overall survival (OS)/Overall survival (OS).JPG

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response by RECIST

End point title	Tumor response by RECIST

End point description:

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	41	33	74	
Units: Patients				
CR	0	1	1	
PR	11	11	22	
SD	18	16	34	
PD	10	4	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response by irRECIST

End point title	Tumor response by irRECIST

End point description:

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	41	33	74	
Units: Patients				
CR	1	2	3	
PR	9	12	21	
SD	24	14	38	
PD	6	4	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity

End point title	Toxicity

End point description:

When n = 7 for PRR cohort and n = 13 for PSR cohort, treatment toxicity was analyzed. Toxicity was assessed by CTCAE V.5.0 scale.

End point type	Secondary

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	41	33	74	
Units: Adverse events				
Not graded	1	1	2	
Grade 1	515	418	933	
Grade 2	238	192	430	
Grade 3	70	35	105	
Grade 4	3	2	5	
Grade 5	3	0	3	
Unknown	23	46	69	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroups analysis according to BRCA: Rate of clinical and radiological non-progression disease

End point title	Subgroups analysis according to BRCA: Rate of clinical and radiological non-progression disease
End point description: Translational research	
End point type	Other pre-specified
End point timeframe: Overall study	

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Rate				
number (confidence interval 90%)				
Rate of non-progressive disease RECIST no BRC1/2	0.722 (0.578 to 0.824)	0.455 (0.277 to 0.616)		
Rate of non-progressive disease RECIST with BRC1/2	0.500 (0.103 to 0.809)	0.400 (0.159 to 0.633)		
Rate of non-progressive disease irRECIST no BRC1/2	0.806 (0.668 to 0.890)	0.587 (0.395 to 0.737)		
Rate of non-progressive disease irRECIST BRC1/2	0.500 (0.103 to 0.809)	0.500 (0.230 to 0.721)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroups analysis according to BRCA: Rate of clinical and radiological non-progression disease: Additional information

End point title	Subgroups analysis according to BRCA: Rate of clinical and radiological non-progression disease: Additional information
End point description:	
End point type	Other pre-specified
End point timeframe: Overall study	

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: month				
number (not applicable)				

Maximum Follow-up (months) no BCRA1/2 mutation	3	6		
Maximum Follow-up (months) BCRA1/2 mutation	3	6		
Time to measure the rate RECIST no BRCA1/2	2.744	5.653		
Time to measure the rate RECIST BRCA1/2	1.322	4.198		
Time to measure the rate irRECIST no BRCA1/2	2.744	5.653		
Time to measure the rate irRECIST BRCA1/2	1.355	4.231		
Stratum Number no BRCA1/2 mutation	1	1		
Stratum Number BRCA1/2 mutation	2	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroups analysis according to BRCA: Tumor objective response rate (ORR) according to RECIST

End point title	Subgroups analysis according to BRCA: Tumor objective response rate (ORR) according to RECIST

End point description:

End point type	Other pre-specified

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Patients				
(no BRCA1/2 mutation)	1	1		
(BRCA1/2 mutation)	1	0		
CR (no BRCA1/2 mutation)	0	0		
CR (BRCA1/2 mutation)	0	1		
PR (no BRCA1/2 mutation)	1	3		
PR (BRCA1/2 mutation)	10	8		
SD (no BRCA1/2 mutation)	0	6		
SD (BRCA1/2 mutation)	18	10		
PD (no BRCA1/2 mutation)	2	1		
PD (BRCA1/2 mutation)	8	3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroups analysis according to BRCA: Tumor objective response rate (ORR) according to irRECIST

End point title	Subgroups analysis according to BRCA: Tumor objective response rate (ORR) according to irRECIST

End point description:

End point type	Other pre-specified

End point timeframe:

Overall study

End point values	Platinum-resistant relapse (PRR) cohort	Platinum-sensitive relapse (PSR) cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: Patients				
(BRCA1/2 mutation)	1	0		
(no BRCA1/2 mutation)	0	1		
CR (BRCA1/2 mutation)	1	1		
CR (no BRCA1/2 mutation)	0	1		
PR (BRCA1/2 mutation)	8	9		
PR (no BRCA1/2 mutation)	1	3		
SD (BRCA1/2 mutation)	23	9		
SD (no BRCA1/2 mutation)	1	5		
PD (BRCA1/2 mutation)	4	3		
PD (no BRCA1/2 mutation)	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	Platinum resistant relapse (PRR)
Reporting group description: -	
Reporting group title	Platinum sensitive relapse (PSR)
Reporting group description: -	

Serious adverse events	Platinum resistant relapse (PRR)	Platinum sensitive relapse (PSR)	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 41 (39.02%)	7 / 33 (21.21%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 41 (4.88%)	5 / 33 (15.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalization			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurodesis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (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			
Performance status decreased			

subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (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	1 / 41 (2.44%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 41 (2.44%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumopathy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive pulmonary disease			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			
subjects affected / exposed	1 / 41 (2.44%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	3 / 41 (7.32%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Transaminase value increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Change in ECG			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drain site complication			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral fracture			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriospasm coronary			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anemia			
subjects affected / exposed	8 / 41 (19.51%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 41 (2.44%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subocclusive syndrome			
subjects affected / exposed	1 / 41 (2.44%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			

subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (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	1 / 41 (2.44%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteropathy NOS			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 41 (0.00%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin rash			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Proteinuria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroiditis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	7 / 41 (17.07%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 41 (0.00%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella oxytoca infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			

subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 41 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Platinum resistant relapse (PRR)	Platinum sensitive relapse (PSR)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 41 (100.00%)	32 / 33 (96.97%)	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	8 / 41 (19.51%)	14 / 33 (42.42%)	
occurrences (all)	8	14	
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	1 / 41 (2.44%)	2 / 33 (6.06%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
General disorders and administration site Conditions			
subjects affected / exposed	36 / 41 (87.80%)	32 / 33 (96.97%)	
occurrences (all)	36	32	
Immune system disorders			

Immune system disorders subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2	1 / 33 (3.03%) 1	
Reproductive system and breast disorders Reproductive system and breast disorders subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2	1 / 33 (3.03%) 1	
Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal Disorders subjects affected / exposed occurrences (all)	25 / 41 (60.98%) 25	20 / 33 (60.61%) 20	
Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all)	9 / 41 (21.95%) 9	0 / 33 (0.00%) 0	
Investigations Investigations subjects affected / exposed occurrences (all)	12 / 41 (29.27%) 12	7 / 33 (21.21%) 7	
Injury, poisoning and procedural complications Injury, poisoning and procedural Complications subjects affected / exposed occurrences (all)	6 / 41 (14.63%) 6	2 / 33 (6.06%) 2	
Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4	4 / 33 (12.12%) 4	
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	17 / 41 (41.46%) 17	18 / 33 (54.55%) 18	
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	28 / 41 (68.29%) 28	16 / 33 (48.48%) 16	

Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all)	 2 / 41 (4.88%) 2	 1 / 33 (3.03%) 1	
Eye disorders Eye disorders subjects affected / exposed occurrences (all)	 4 / 41 (9.76%) 4	 3 / 33 (9.09%) 3	
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	 38 / 41 (92.68%) 38	 31 / 33 (93.94%) 31	
Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all)	 3 / 41 (7.32%) 3	 5 / 33 (15.15%) 5	
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	 11 / 41 (26.83%) 11	 8 / 33 (24.24%) 8	
Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all)	 10 / 41 (24.39%) 10	 6 / 33 (18.18%) 6	
Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all)	 13 / 41 (31.71%) 13	 6 / 33 (18.18%) 6	
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue Disorders subjects affected / exposed occurrences (all)	 23 / 41 (56.10%) 23	 19 / 33 (57.58%) 19	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	 22 / 41 (53.66%) 22	 18 / 33 (54.55%) 18	
Metabolism and nutrition disorders			

Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	26 / 41 (63.41%) 26	18 / 33 (54.55%) 18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2019	Protocol containing amendment n°1
16 September 2019	Protocol containing amendment n°2
24 August 2020	Protocol containing amendment n°4
13 January 2021	Protocol containing amendment n°5
25 June 2021	Protocol containing amendment n°6
07 December 2021	Protocol containing amendment n°7

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.

Single-arm nature, small sample size, use of archival tissue for translational research , and a minority of patients with BRCA mutation status in both populations. The study was not powered to show statistical differences in these subgroups.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38443333