Clinical trial results:
A Phase 2, Open-Label Study of Rucaparib in Patients with Platinum-Sensitive, Relapsed, High-Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

Summary

EudraCT number	2013-000517-20
Trial protocol	GB ES FR
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	25 August 2021
First version publication date	25 August 2021

Trial information

Trial identification

Sponsor protocol code	CO-338-017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01891344
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clovis Oncology UK Ltd
Sponsor organisation address	Granta Centre, Granta Park, Great Abington, Cambridge, United Kingdom, CB21 6GP
Public contact	Dr Lindsey Rolfe, Clovis Oncology UK Ltd, +44 12233645500, lrolfe@clovisoncology.com
Scientific contact	Dr Lindsey Rolfe, Clovis Oncology UK Ltd, +44 12233645500, lrolfe@clovisoncology.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	01 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine progression-free survival (PFS) in patients with relapsed platinum-sensitive ovarian cancer classified into molecularly defined subgroups by a prospectively defined HRD signature (Part 1)
- To estimate objective response rate (ORR) in heavily pre-treated patients with relapsed ovarian cancer classified into molecularly-defined subgroups by a prospectively defined HRD signature (Part 2)

Protection of trial subjects:

A formal safety data review occurred after the first 20 patients were enrolled, then quarterly until Part 1 of the study was fully enrolled, and then every 6 months thereafter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 October 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	France: 71
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Canada: 137
Country: Number of subjects enrolled	United States: 193
Worldwide total number of subjects	491
EEA total number of subjects	134

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	271
From 65 to 84 years	217
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

491 subjects were recruited from 64 sites across 6 countries

Pre-assignment

Screening details:

Part 1 of the study enrolled patients who received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: tBRCA

Arm description:

Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor. Part 1 enrolled patients who received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 1: Non-tBRCA LOH+

Arm description:

Patients without a BRCA mutation in their tumor, but have high LOH (loss of heterozygosity). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 1: Non-tBRCA LOH-

Arm description:

Patients without a BRCA mutation in their tumor, but have low LOH. Part 1 enrolled patients received ≥ 1prior platinum-based regimen and had platinum-sensitive disease.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 1: Non-tBRCA LOH Unknown

Arm description:

Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 2: tBRCA

Arm description:

Patients with a deleterious BRCA mutation detected in their tumor. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 2: Non-tBRCA LOH+

Arm description:

Patients without a BRCA mutation in their tumor, but have high LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason

for discontinuation.

Arm title	Part 2: Non-tBRCA LOH-

Arm description:

Patients without a BRCA mutation in their tumor, but have low LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Arm title	Part 2: Non-tBRCA LOH Unknown

Arm description:

Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.

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

Dosage and administration details:

Patients took 600 mg rucaparib orally twice daily (BID) starting on Day 1. Patients took rucaparib BID for continuous 28-day cycles until disease progression as assessed by the investigator, or other reason for discontinuation.

Number of subjects in period 1	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-
Started	40	82	70
Completed	34	80	70
Not completed	6	2	0
Ongoing	6	2	-

Number of subjects in period 1	Part 1: Non-tBRCA LOH Unknown	Part 2: tBRCA	Part 2: Non-tBRCA LOH+
Started	12	84	73
Completed	11	80	72
Not completed	1	4	1
Ongoing	1	4	1

Number of subjects in period 1	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown
Started	107	23
Completed	107	23
Not completed	0	0
Ongoing	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: tBRCA
Reporting group description:	
Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor. Part 1 enrolled patients who received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH+
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have high LOH (loss of heterozygosity). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH-
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have low LOH. Part 1 enrolled patients received ≥ 1prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH Unknown
Reporting group description:	
Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 2: tBRCA
Reporting group description:	
Patients with a deleterious BRCA mutation detected in their tumor. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH+
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have high LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH-
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have low LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH Unknown
Reporting group description:	
Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	

Reporting group values	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-
Number of subjects	40	82	70
Age categorical Units: Subjects			
Adults (18-64 years)	24	39	34
From 65-84 years	16	43	35
85 years and over	0	0	1
Age continuous Units: years			
median	58.5	65	65
full range (min-max)	33 to 78	39 to 83	31 to 86

Gender categorical Units: Subjects			
Female	40	82	70
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	3	4	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	1
White	33	67	56
More than one race	0	0	0
Unknown or Not Reported	2	9	8
Platinum Sensitivity Status			
Measure Description: Refractory = Best response of progressive disease (PD) and PD occurs during or up to 2 months after regimen; Resistant = PD 0-<6 months after last platinum with best response other than PD; Sensitive = PD ≥6 months after last platinum			
Units: Subjects			
Refractory	0	0	0
Resistant	0	1	0
Sensitive	40	81	70
Number of Prior Chemotherapy Regimens Units: Subjects			
=0	0	0	0
=1	17	45	47
=2	14	21	16
=3	4	13	6
=4	4	1	0
=5	1	1	1
>5	0	1	0
Number of Prior Platinum Regimens Units: Subjects			
=0	0	0	0
=1	17	45	47
=2	15	25	16
=3	6	10	6
>3	2	2	1

Reporting group values	Part 1: Non-tBRCA LOH Unknown	Part 2: tBRCA	Part 2: Non-tBRCA LOH+
Number of subjects	12	84	73
Age categorical Units: Subjects			
Adults (18-64 years)	5	53	47
From 65-84 years	7	31	26
85 years and over	0	0	0
Age continuous Units: years			
median	69.5	60.5	61
full range (min-max)	44 to 81	41 to 82	35 to 82

Gender categorical Units: Subjects			
Female	12	84	73
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	5	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	10	59	46
More than one race	0	0	0
Unknown or Not Reported	0	19	22
Platinum Sensitivity Status			
Measure Description: Refractory = Best response of progressive disease (PD) and PD occurs during or up to 2 months after regimen; Resistant = PD 0-<6 months after last platinum with best response other than PD; Sensitive = PD ≥6 months after last platinum			
Units: Subjects			
Refractory	0	12	14
Resistant	1	41	46
Sensitive	11	31	13
Number of Prior Chemotherapy Regimens Units: Subjects			
=0	0	0	0
=1	10	0	0
=2	1	0	1
=3	1	52	44
=4	0	32	28
=5	0	0	0
>5	0	0	0
Number of Prior Platinum Regimens Units: Subjects			
=0	0	0	0
=1	10	2	4
=2	1	34	31
=3	1	40	36
>3	0	8	2

Reporting group values	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown	Total
Number of subjects	107	23	491
Age categorical Units: Subjects			
Adults (18-64 years)	56	13	271
From 65-84 years	49	10	217
85 years and over	2	0	3
Age continuous Units: years			
median	64	62	
full range (min-max)	42 to 91	43 to 81	-

Gender categorical Units: Subjects			
Female	107	23	491
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	2
Asian	5	0	27
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	0	0	6
White	82	18	371
More than one race	0	0	0
Unknown or Not Reported	19	5	84
Platinum Sensitivity Status			
Measure Description: Refractory = Best response of progressive disease (PD) and PD occurs during or up to 2 months after regimen; Resistant = PD 0-<6 months after last platinum with best response other than PD; Sensitive = PD ≥6 months after last platinum			
Units: Subjects			
Refractory	18	4	48
Resistant	56	15	160
Sensitive	33	4	283
Number of Prior Chemotherapy Regimens Units: Subjects			
=0	0	0	0
=1	0	0	119
=2	1	0	54
=3	73	17	210
=4	31	6	102
=5	2	0	5
>5	0	0	1
Number of Prior Platinum Regimens Units: Subjects			
=0	0	0	0
=1	7	3	135
=2	55	7	184
=3	44	12	155
>3	1	1	17

Subject analysis sets

Subject analysis set title	Part 1 Overall
Subject analysis set type	Per protocol
Subject analysis set description: Includes all Part 1 patients	
Subject analysis set title	Part 2 Overall
Subject analysis set type	Per protocol
Subject analysis set description: Includes all Part 2 patients	

Reporting group values	Part 1 Overall	Part 2 Overall	
Number of subjects	204	287	
Age categorical Units: Subjects			
Adults (18-64 years)	102	169	
From 65-84 years	101	116	
85 years and over	1	2	
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Platinum Sensitivity Status			
Measure Description: Refractory = Best response of progressive disease (PD) and PD occurs during or up to 2 months after regimen; Resistant = PD 0-<6 months after last platinum with best response other than PD; Sensitive = PD ≥6 months after last platinum			
Units: Subjects			
Refractory Resistant Sensitive			
Number of Prior Chemotherapy Regimens Units: Subjects			
=0 =1 =2 =3 =4 =5 >5			
Number of Prior Platinum Regimens Units: Subjects			
=0 =1 =2 =3 >3			

End points

End points reporting groups

Reporting group title	Part 1: tBRCA
Reporting group description:	
Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor. Part 1 enrolled patients who received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH+
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have high LOH (loss of heterozygosity). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH-
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have low LOH. Part 1 enrolled patients received ≥ 1prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 1: Non-tBRCA LOH Unknown
Reporting group description:	
Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 1 enrolled patients received ≥ 1 prior platinum-based regimen and had platinum-sensitive disease.	
Reporting group title	Part 2: tBRCA
Reporting group description:	
Patients with a deleterious BRCA mutation detected in their tumor. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH+
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have high LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH-
Reporting group description:	
Patients without a BRCA mutation in their tumor, but have low LOH. Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Reporting group title	Part 2: Non-tBRCA LOH Unknown
Reporting group description:	
Patients without a BRCA mutation in their tumor, and have unknown LOH due to missing results and/or failed test result(s). Part 2 enrolled patients who received at least 3, but no more than 4, prior chemotherapy regimens.	
Subject analysis set title	Part 1 Overall
Subject analysis set type	Per protocol
Subject analysis set description:	
Includes all Part 1 patients	
Subject analysis set title	Part 2 Overall
Subject analysis set type	Per protocol
Subject analysis set description:	
Includes all Part 2 patients	

Primary: Progression-free Survival (PFS) According to RECIST v1.1 in Molecularly-defined HRD (Homologous Recombination Deficiency) Subgroups (Part 1 of Study)

End point title	Progression-free Survival (PFS) According to RECIST v1.1 in Molecularly-defined HRD (Homologous Recombination Deficiency) Subgroups (Part 1 of Study)[1]

End point description:

The primary efficacy endpoint of PFS is calculated as 1+ the number of days from the first dose of study drug to disease progression by RECIST (Response Evaluation Criteria in Solid Tumors), as determined by

the investigator or death due to any cause, whichever occurs first. Progression is defined using RECIST v1.1, as at least a 20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions.

End point type	Primary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports PFS for Part 1 patients only.

End point values	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-	Part 1: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	82	70	12
Units: Days				
median (confidence interval 95%)	388 (273 to 448)	174 (158 to 231)	160 (110 to 188)	223 (55 to 499)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Part 1: tBRCA v Part 1: Non-tBRCA LOH-
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.273
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.437

Statistical analysis title	Statistical Analysis 2
Comparison groups	Part 1: Non-tBRCA LOH- v Part 1: Non-tBRCA LOH+
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.428
upper limit	0.871

Primary: Objective Response Rate (ORR) by RECIST v1.1 in Molecularly-defined HRD Subgroups (Part 2 of Study)

End point title	Objective Response Rate (ORR) by RECIST v1.1 in Molecularly-defined HRD Subgroups (Part 2 of Study)[2][3]

End point description:

The confirmed response rate by RECIST v1.1 is defined as the percentage of patients with a confirmed complete response (CR) or partial response (PR) on subsequent tumor assessment at least 28 days after first response documentation. Complete response (CR) is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Partial response (PR) is at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of longest diameter.

End point type	Primary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses was not required for this ORR primary endpoint.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports ORR for Part 2 patients only.

End point values	Part 2: tBRCA	Part 2: Non-tBRCA LOH+	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	73	107	23
Units: Days				
number (confidence interval 95%)	31.0 (21.3 to 42.0)	6.8 (2.3 to 15.3)	5.6 (2.1 to 11.8)	13.0 (2.8 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) by RECIST v1.1 (Part 1 of Study)

End point title	Objective Response Rate (ORR) by RECIST v1.1 (Part 1 of Study)[4]

End point description:

The confirmed response rate by RECIST v1.1 is defined as the percentage of patients with a confirmed CR or PR on subsequent tumor assessment at least 28 days after first response documentation. Complete response (CR) is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Partial response (PR) is at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of longest diameter.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports ORR for Part 1 patients only.

End point values	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-	Part 1: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	82	70	12
Units: Percentage of patients				
number (confidence interval 95%)	80.0 (64.4 to 90.9)	28.0 (18.7 to 39.1)	10.0 (4.1 to 19.5)	33.3 (9.9 to 65.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) by RECIST v1.1 and GCIG CA-125 Criteria

End point title	Objective Response Rate (ORR) by RECIST v1.1 and GCIG CA-125 Criteria

End point description:

The endpoint of ORR defined as the percentage of patients with a best response of CR or PR using RECIST v 1.1 or response per Gynecologic Cancer InterGroup cancer antigen 125 (GCIG CA-125) criteria. Complete response (CR) is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Partial response (PR) is at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of longest diameter. A response to CA-125 has occurred if there is at least a 50% decrease from baseline: 1. in a sample collected after initiation of study treatment AND 2. that is confirmed in a subsequent sample collected ≥21 days after the prior sample. The absolute value of this confirmatory sample must be ≤110% of the prior sample. The date when the first sample with a 50% decrease from baseline is observed is the date of the CA-125 response.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

End point values	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-	Part 1: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	82	70	12
Units: percentage of patients				
number (confidence interval 95%)	87.5 (73.2 to 95.8)	46.3 (35.3 to 57.7)	21.4 (12.5 to 32.9)	50.0 (21.1 to 78.9)

End point values	Part 2: tBRCA	Part 2: Non-tBRCA LOH+	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	73	107	23
Units: percentage of patients				
number (confidence interval 95%)	54.8 (43.5 to 65.7)	12.3 (5.8 to 22.1)	13.1 (7.3 to 21.0)	30.4 (13.2 to 52.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response Per RECIST v1.1

End point title	Duration of Response Per RECIST v1.1

End point description:

Duration of response (DOR) for any confirmed RECIST CR or PR measured from the date of the first occurrence of a response until the first occurrence of progressive disease (PD) per RECIST. For patients who continued treatment post-progression, the first date of progression was used for the analysis. Any patients with an ongoing response were censored at the date of the last post-baseline scan. Complete response(CR) is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Partial response (PR) is at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of longest diameter.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

End point values	Part 1: tBRCA	Part 1: Non-tBRCA LOH+	Part 1: Non-tBRCA LOH-	Part 1: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	23	7	4
Units: Days				
median (confidence interval 95%)	281 (194 to 393)	329 (174 to 451)	169 (141 to 260)	225 (100 to 1454)

End point values	Part 2: tBRCA	Part 2: Non-tBRCA LOH+	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	5	6	3
Units: Days				
median (confidence interval 95%)	176 (169 to 312)	282 (111 to 1012)	314 (169 to 492)	181 (169 to 224)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) According to RECIST v1.1 in Molecularly-defined HRD Subgroups (Part 2 of Study)

End point title	Progression-free Survival (PFS) According to RECIST v1.1 in Molecularly-defined HRD Subgroups (Part 2 of Study)[5]

End point description:

Progression-Free Survival (PFS) is calculated as 1+ the number of days from the first dose of study drug to disease progression by RECIST, as determined by the investigator or death due to any cause, whichever occurs first. Progression is defined using RECIST v1.1, as at least a 20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from C1D1 until disease progression, death or withdrawal of consent. After 18 months on study, assessments every 16 weeks. Total follow-up was up to approximately 3 years.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports PFS for Part 2 patients only.

End point values	Part 2: tBRCA	Part 2: Non-tBRCA LOH+	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	73	107	23
Units: Days				
median (confidence interval 95%)	223 (188 to 275)	57 (54 to 112)	113 (63 to 165)	110 (56 to 154)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Part 2 of Study)

End point title	Overall Survival (Part 2 of Study)[6]

End point description:

Overall survival (OS) is defined as the number of days from the date of first dose of study drug to the date of death (due to any cause). Patients without a known date of death will be censored on the date the patient was last known to be alive.

End point type	Secondary

End point timeframe:

All patients in Part 2 were followed for survival, subsequent therapy, and secondary malignancy every 12 weeks until death, loss to follow-up, withdrawal of consent from study or study closure, whichever happened first, up to 7 years.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports OS for Part 2 patients only.

End point values	Part 2: tBRCA	Part 2: Non-tBRCA LOH+	Part 2: Non-tBRCA LOH-	Part 2: Non-tBRCA LOH Unknown
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	73	107	23
Units: Months				
median (confidence interval 95%)	22.7 (16.7 to 28.6)	14.7 (10.8 to 19.8)	13.3 (9.1 to 16.0)	14.1 (7.4 to 20.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Trough (Cmin) Level Rucaparib Concentrations

End point title	Steady State Trough (Cmin) Level Rucaparib Concentrations

End point description:

Per protocol, the secondary PK endpoint, trough (Cmin) concentrations of rucaparib were summarized with descriptive statistics overall and by cycle in all patients with at least one PK sample collected. Blood samples for trough level PK analysis of rucaparib were drawn at the following timepoints only: on Day 15 of Cycle 1 and on Day 1 of Cycles 2, 3, and 4. Data for other timepoints is not available.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15 to Cycle 4 Day 1, or approximately 10 weeks

End point values	Part 1 Overall	Part 2 Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	196[7]	267[8]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 15	2020.76 (± 1145.164)	2276.37 (± 1587.586)		
Cycle 2 Day 1	1652.27 (± 935.503)	1689.83 (± 1039.953)		
Cycle 3 Day 1	1557.32 (± 952.903)	1552.09 (± 1054.346)		
Cycle 4 Day 1	1530.41 (± 765.940)	1629.14 (± 1026.999)		

Notes:

[7] - C1D15 = 196 patients
C2D1 = 186 patients
C3D1 = 159 patients
C4D1 = 142 patients
[8] - C1D15 = 267 patients
C2D1 = 242 patients
C3D1 = 174 patients
C4D1 = 149 patients

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the time informed consent was obtained until 28 days after last dose of study drug, approximately 5 years.

Adverse event reporting additional description:

If a subject experiences the same preferred term (system organ class) multiple times, then the subject will be counted only once for that preferred term(system organ class). Adverse Events were monitored/assessed without regard to the subgroups.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Part 1: Overall

Reporting group description:

All patients who participated in Part 1 who received at least one dose of rucaparib

Reporting group title	Part 2: Overall

Reporting group description:

All patients who participated in Part 2 who received at least one dose of rucaparib

Serious adverse events	Part 1: Overall	Part 2: Overall	
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 204 (26.47%)	92 / 287 (32.06%)	
number of deaths (all causes)	2	18	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	11 / 204 (5.39%)	10 / 287 (3.48%)	
occurrences causally related to treatment / all	0 / 13	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 8	

Metastatic neoplasm			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 204 (0.00%)	4 / 287 (1.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 204 (0.00%)	7 / 287 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 4	
Hyperthermia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 204 (0.49%)	4 / 287 (1.39%)	
occurrences causally related to treatment / all	0 / 1	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 204 (0.49%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 204 (0.98%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			

subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 204 (0.49%)	3 / 287 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood cholesterol increased			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 204 (0.49%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocyte count decreased			

subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (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	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Long QT syndrome congenital			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
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	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (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			
Amnesia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	1 / 204 (0.49%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 204 (5.39%)	12 / 287 (4.18%)	
occurrences causally related to treatment / all	12 / 17	9 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 204 (0.49%)	6 / 287 (2.09%)	
occurrences causally related to treatment / all	1 / 1	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulocytopenia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 204 (0.49%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 204 (0.98%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	1 / 204 (0.49%)	6 / 287 (2.09%)	
occurrences causally related to treatment / all	0 / 1	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	2 / 204 (0.98%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 204 (0.98%)	3 / 287 (1.05%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 204 (0.49%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 204 (0.49%)	6 / 287 (2.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal perforation			

subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 204 (0.49%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 204 (1.47%)	7 / 287 (2.44%)	
occurrences causally related to treatment / all	1 / 3	11 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	11 / 204 (5.39%)	8 / 287 (2.79%)	
occurrences causally related to treatment / all	0 / 13	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 204 (0.49%)	9 / 287 (3.14%)	
occurrences causally related to treatment / all	2 / 2	8 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic haematoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
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			
Dermatomyositis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 204 (2.94%)	3 / 287 (1.05%)	
occurrences causally related to treatment / all	2 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture pain			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Empyema			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 204 (0.98%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 204 (0.49%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	4 / 204 (1.96%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal infection			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 204 (1.47%)	4 / 287 (1.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 204 (0.49%)	5 / 287 (1.74%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			

subjects affected / exposed	0 / 204 (0.00%)	1 / 287 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 287 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 204 (0.00%)	2 / 287 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: Overall	Part 2: Overall	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	203 / 204 (99.51%)	285 / 287 (99.30%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	83 / 204 (40.69%)	85 / 287 (29.62%)	
occurrences (all)	163	161	
Aspartate aminotransferase increased			
subjects affected / exposed	74 / 204 (36.27%)	92 / 287 (32.06%)	
occurrences (all)	117	137	
Blood alkaline phosphatase increased			
subjects affected / exposed	19 / 204 (9.31%)	24 / 287 (8.36%)	
occurrences (all)	28	31	
Blood cholesterol increased			
subjects affected / exposed	14 / 204 (6.86%)	13 / 287 (4.53%)	
occurrences (all)	22	24	
Blood creatinine increased			
subjects affected / exposed	37 / 204 (18.14%)	65 / 287 (22.65%)	
occurrences (all)	74	122	
Neutrophil count decreased			

subjects affected / exposed	20 / 204 (9.80%)	12 / 287 (4.18%)	
occurrences (all)	53	23	
Platelet count decreased			
subjects affected / exposed	15 / 204 (7.35%)	36 / 287 (12.54%)	
occurrences (all)	25	98	
Weight decreased			
subjects affected / exposed	42 / 204 (20.59%)	30 / 287 (10.45%)	
occurrences (all)	64	38	
White blood cell count decreased			
subjects affected / exposed	13 / 204 (6.37%)	12 / 287 (4.18%)	
occurrences (all)	27	22	
Vascular disorders			
Hot flush			
subjects affected / exposed	15 / 204 (7.35%)	10 / 287 (3.48%)	
occurrences (all)	15	10	
Hypertension			
subjects affected / exposed	18 / 204 (8.82%)	12 / 287 (4.18%)	
occurrences (all)	28	16	
Nervous system disorders			
Dizziness			
subjects affected / exposed	42 / 204 (20.59%)	35 / 287 (12.20%)	
occurrences (all)	66	43	
Dysgeusia			
subjects affected / exposed	88 / 204 (43.14%)	93 / 287 (32.40%)	
occurrences (all)	123	121	
Headache			
subjects affected / exposed	36 / 204 (17.65%)	35 / 287 (12.20%)	
occurrences (all)	54	42	
Lethargy			
subjects affected / exposed	13 / 204 (6.37%)	5 / 287 (1.74%)	
occurrences (all)	24	7	
Neuropathy peripheral			
subjects affected / exposed	11 / 204 (5.39%)	11 / 287 (3.83%)	
occurrences (all)	14	17	
Peripheral sensory neuropathy			

subjects affected / exposed	11 / 204 (5.39%)	2 / 287 (0.70%)	
occurrences (all)	20	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	73 / 204 (35.78%)	124 / 287 (43.21%)	
occurrences (all)	306	387	
Neutropenia			
subjects affected / exposed	13 / 204 (6.37%)	18 / 287 (6.27%)	
occurrences (all)	26	40	
Thrombocytopenia			
subjects affected / exposed	24 / 204 (11.76%)	44 / 287 (15.33%)	
occurrences (all)	37	104	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	24 / 204 (11.76%)	68 / 287 (23.69%)	
occurrences (all)	45	152	
Chills			
subjects affected / exposed	16 / 204 (7.84%)	8 / 287 (2.79%)	
occurrences (all)	22	8	
Fatigue			
subjects affected / exposed	140 / 204 (68.63%)	157 / 287 (54.70%)	
occurrences (all)	336	357	
Influenza like illness			
subjects affected / exposed	11 / 204 (5.39%)	6 / 287 (2.09%)	
occurrences (all)	15	6	
Oedema peripheral			
subjects affected / exposed	21 / 204 (10.29%)	38 / 287 (13.24%)	
occurrences (all)	27	48	
Pyrexia			
subjects affected / exposed	30 / 204 (14.71%)	34 / 287 (11.85%)	
occurrences (all)	34	42	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	41 / 204 (20.10%)	32 / 287 (11.15%)	
occurrences (all)	52	40	
Abdominal pain			

subjects affected / exposed	63 / 204 (30.88%)	93 / 287 (32.40%)	
occurrences (all)	102	123	
Abdominal pain lower			
subjects affected / exposed	12 / 204 (5.88%)	12 / 287 (4.18%)	
occurrences (all)	14	14	
Abdominal pain upper			
subjects affected / exposed	31 / 204 (15.20%)	36 / 287 (12.54%)	
occurrences (all)	37	47	
Ascites			
subjects affected / exposed	13 / 204 (6.37%)	12 / 287 (4.18%)	
occurrences (all)	24	26	
Constipation			
subjects affected / exposed	95 / 204 (46.57%)	84 / 287 (29.27%)	
occurrences (all)	155	104	
Diarrhoea			
subjects affected / exposed	76 / 204 (37.25%)	84 / 287 (29.27%)	
occurrences (all)	135	142	
Dry mouth			
subjects affected / exposed	11 / 204 (5.39%)	12 / 287 (4.18%)	
occurrences (all)	12	16	
Dyspepsia			
subjects affected / exposed	24 / 204 (11.76%)	20 / 287 (6.97%)	
occurrences (all)	28	30	
Flatulence			
subjects affected / exposed	13 / 204 (6.37%)	7 / 287 (2.44%)	
occurrences (all)	13	7	
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 204 (5.39%)	15 / 287 (5.23%)	
occurrences (all)	12	19	
Nausea			
subjects affected / exposed	161 / 204 (78.92%)	219 / 287 (76.31%)	
occurrences (all)	316	377	
Small intestinal obstruction			
subjects affected / exposed	12 / 204 (5.88%)	9 / 287 (3.14%)	
occurrences (all)	18	13	
Stomatitis			

subjects affected / exposed	25 / 204 (12.25%)	15 / 287 (5.23%)	
occurrences (all)	45	19	
Vomiting			
subjects affected / exposed	92 / 204 (45.10%)	126 / 287 (43.90%)	
occurrences (all)	184	235	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	35 / 204 (17.16%)	30 / 287 (10.45%)	
occurrences (all)	57	35	
Dyspnoea			
subjects affected / exposed	46 / 204 (22.55%)	68 / 287 (23.69%)	
occurrences (all)	62	106	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	22 / 204 (10.78%)	7 / 287 (2.44%)	
occurrences (all)	24	8	
Dry skin			
subjects affected / exposed	14 / 204 (6.86%)	6 / 287 (2.09%)	
occurrences (all)	16	6	
Erythema			
subjects affected / exposed	7 / 204 (3.43%)	16 / 287 (5.57%)	
occurrences (all)	8	17	
Photosensitivity reaction			
subjects affected / exposed	30 / 204 (14.71%)	18 / 287 (6.27%)	
occurrences (all)	37	19	
Pruritus			
subjects affected / exposed	20 / 204 (9.80%)	16 / 287 (5.57%)	
occurrences (all)	25	19	
Rash			
subjects affected / exposed	21 / 204 (10.29%)	13 / 287 (4.53%)	
occurrences (all)	26	15	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	14 / 204 (6.86%)	17 / 287 (5.92%)	
occurrences (all)	17	23	
Insomnia			

subjects affected / exposed	23 / 204 (11.27%)	30 / 287 (10.45%)	
occurrences (all)	26	37	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 204 (10.29%)	20 / 287 (6.97%)	
occurrences (all)	24	24	
Back pain			
subjects affected / exposed	33 / 204 (16.18%)	25 / 287 (8.71%)	
occurrences (all)	43	30	
Myalgia			
subjects affected / exposed	17 / 204 (8.33%)	15 / 287 (5.23%)	
occurrences (all)	24	20	
Pain in extremity			
subjects affected / exposed	21 / 204 (10.29%)	21 / 287 (7.32%)	
occurrences (all)	30	36	
Malignant neoplasm progression			
subjects affected / exposed	14 / 204 (6.86%)	14 / 287 (4.88%)	
occurrences (all)	22	18	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 204 (7.35%)	13 / 287 (4.53%)	
occurrences (all)	16	24	
Upper respiratory tract infection			
subjects affected / exposed	27 / 204 (13.24%)	10 / 287 (3.48%)	
occurrences (all)	31	10	
Urinary tract infection			
subjects affected / exposed	40 / 204 (19.61%)	36 / 287 (12.54%)	
occurrences (all)	60	47	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	85 / 204 (41.67%)	112 / 287 (39.02%)	
occurrences (all)	146	176	
Dehydration			
subjects affected / exposed	17 / 204 (8.33%)	24 / 287 (8.36%)	
occurrences (all)	24	38	
Hypokalaemia			

subjects affected / exposed	17 / 204 (8.33%)	19 / 287 (6.62%)	
occurrences (all)	22	22	
Hypomagnesaemia			
subjects affected / exposed	13 / 204 (6.37%)	29 / 287 (10.10%)	
occurrences (all)	16	45	
Hyponatraemia			
subjects affected / exposed	7 / 204 (3.43%)	15 / 287 (5.23%)	
occurrences (all)	11	31	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2013	•Starting dose was established as 600 mg rucaparib BID. •Language was added to allow a reduction in starting dose if warranted by the data and to clarify dose modification criteria. •Formal safety review added. •Safety language regarding AE management and assessment was added for ALT and AST elevations, and treatment-related AEs. •Language was clarified to reflect that ORR would consist of an integrated assessment of RECIST Version 1.1 and GCIG CA 125 response. •The option of collecting and testing ascites samples was removed.
30 May 2014	•HRD subgroups were revised to include groups with tumor genomic LOH (high or low), as well as BRCA1/2 gene mutation. •The primary objective, and associated endpoint, was changed from efficacy defined by ORR to efficacy as defined by PFS. •Inclusion and exclusion criteria were modified.
19 December 2014	•Study design was revised to be a 2-part study. •Specified that the primary endpoint for the heavily pretreated patients enrolled in Part 2 of the study was ORR in molecularly-defined subgroups. •PFS and OS were to be assessed as secondary endpoints. •Inclusion and exclusion criteria were modified. •Additional analytes were added to the required safety laboratory panel to further evaluate the safety profile of rucaparib. • Guidance was added to specify that rucaparib does not have to be held for Grade 3 elevations of ALT/AST if not accompanied by other signs of liver dysfunction. •Added language to specify that patients enrolled into Part 1 and Part 2 would receive 120 and 300/200 mg tablets, respectively, when initiating treatment. •GCIG CA-125 response criteria were modified to only require 1 predose sample. •Changes to statistical analyses •Specified that IRR could be performed as a supportive analysis for all (Part 1 and Part 2) or a subset of patients.
29 June 2016	•Study population amended to include parameters to more clearly define women of childbearing potential, and more stringent contraception requirements added. •Modification of dietary restrictions to reflect updated restrictions regarding concomitant use of CYP substrates. •Management guidelines for Grade 3 or Grade 4 ALT/AST elevations provided. •Prior and concomitant therapies revised to reflect updated restrictions on concomitant use of medications that are CYP substrates. •Study procedures updated to specify requirement for serum pregnancy test at each cycle of treatment from Cycle 2 and beyond. •Adverse event management amended to include information pertaining to adverse events of special interest.
17 July 2019	•This amendment was to modify the end of study language to clarify that the sponsor could close the study and provide alternatives for patients to continue receiving rucaparib treatment, and to revise the Schedule of Assessments for patients remaining in treatment or follow-up, reducing the number of assessments required at study visits as compared to previously; however, an appropriate level of safety monitoring would remain in place. •An update to decrease the frequency of formal safety reviews to an as needed basis after all patients are enrolled and have been on study at least 6 months or had discontinued prior to 6 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported