Clinical trial results:
A Phase IIIb, Randomised, Double-blind, Placebo-controlled, Multicentre Study of Olaparib Maintenance Retreatment in Patients with Epithelial Ovarian Cancer Previously Treated with a PARPi and Responding to Repeat Platinum Chemotherapy (OReO)

Summary

EudraCT number	2016-003346-90
Trial protocol	FR PL BE DE GB ES IT
Global end of trial date	17 February 2022

Results information

Result version number	v1 (current)
This version publication date	14 October 2022
First version publication date	14 October 2022

Trial information

Trial identification

Sponsor protocol code	D0816C00014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03106987
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Södertälje, Södertälje, Sweden, 151 85
Public contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2021
Global end of trial reached?	Yes
Global end of trial date	17 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and tolerability of Olaparib retreatment, versus placebo, in non mucinous Epithelial ovarian cancer (EOC) patients

Protection of trial subjects:

The study was performed in accordance with ethical principles that had their origin in the Declaration of Helsinki and were consistent with International Council for Harmonisation Good Clinical Practices (ICH-GCP) and the AstraZeneca policy on Bioethics and Human Biological Samples. The Principal Investigator ensured that each patient was given full and adequate oral and written information about the study. Patients provided signed and dated informed consent before any procedure specific to the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 June 2017
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	Belgium: 6
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 58
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 50
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Spain: 46
Country: Number of subjects enrolled	United Kingdom: 8
Worldwide total number of subjects	220
EEA total number of subjects	206

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)	127
From 65 to 84 years	92
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at study centres in 11 countries (France, Italy, Spain, Germany, Poland, Belgium, Denmark, Israel, United Kingdom, Norway, and Canada) between 8-Jun-2017 and 15-Feb-2021.

Pre-assignment

Screening details:

Patients were randomised into 1 of 2 cohorts depending on their known BRCA1/2 status (BRCA1/2 +ve or BRCA1/2-ve). Within each cohort, patients were randomised in a 2 Olaparib:1 placebo ratio. Randomisation was stratified by prior use of bevacizumab and number of prior regimens of platinum-containing chemotherapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaparib (BRCA1/2 +ve)

Arm description:

Patients received Olaparib 300mg tablets orally twice daily (bd) continuously

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:

Patients received Olaparib 300mg tablets orally bd

Arm title	Placebo (BRCA1/2 +ve)

Arm description:

Patients received Placebo 300mg tablets orally bd continuously

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

Dosage and administration details:

Patients received Placebo 300mg tablets orally bd

Arm title	Olaparib (BRCA1/2 -ve)

Arm description:

Patients received Olaparib 300mg tablets orally bd continuously

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:
Patients received Olaparib 300mg tablets orally bd

Arm title	Placebo (BRCA1/2 -ve)

Arm description:
Patients received Placebo 300mg tablets orally bd continuously

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

Dosage and administration details:
Patients received Placebo 300mg tablets orally bd

Number of subjects in period 1	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)
Started	74	38	72
Completed	30	15	54
Not completed	44	23	18
Adverse event, serious fatal	37	22	12
Consent withdrawn by subject	5	1	4
Lost to follow-up	2	-	2

Number of subjects in period 1	Placebo (BRCA1/2 -ve)
Started	36
Completed	25
Not completed	11
Adverse event, serious fatal	8
Consent withdrawn by subject	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib (BRCA1/2 +ve)
Reporting group description: Patients received Olaparib 300mg tablets orally twice daily (bd) continuously	
Reporting group title	Placebo (BRCA1/2 +ve)
Reporting group description: Patients received Placebo 300mg tablets orally bd continuously	
Reporting group title	Olaparib (BRCA1/2 -ve)
Reporting group description: Patients received Olaparib 300mg tablets orally bd continuously	
Reporting group title	Placebo (BRCA1/2 -ve)
Reporting group description: Patients received Placebo 300mg tablets orally bd continuously	

Reporting group values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)
Number of subjects	74	38	72
Age Categorical Units: Patients			
< 50	11	3	4
≥ 50 to < 65	40	20	29
≥ 65 to < 75	20	12	30
≥ 75	3	3	9
Age Continuous Units: Years			
arithmetic mean	59.2	61.5	64.2
standard deviation	± 9.31	± 9.22	± 9.64
Sex: Female, Male Units:			
Female	74	38	72
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
White	71	35	66
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	0	1
Hawaiian Native or Other Pacific Islander	0	0	0
Other	3	3	5
Missing Data	0	0	0

Reporting group values	Placebo (BRCA1/2 -ve)	Total	
Number of subjects	36	220	
Age Categorical Units: Patients			
< 50	1	19	

≥ 50 to < 65	19	108	
≥ 65 to < 75	11	73	
≥ 75	5	20	
Age Continuous Units: Years			
arithmetic mean	63.3		
standard deviation	± 9.05	-	
Sex: Female, Male Units:			
Female	36	220	
Male	0	0	
Race/Ethnicity, Customized Units: Subjects			
White	33	205	
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	0	1	
Hawaiian Native or Other Pacific Islander	0	0	
Other	2	13	
Missing Data	1	1	

End points

End points reporting groups

Reporting group title	Olaparib (BRCA1/2 +ve)
Reporting group description:	
Patients received Olaparib 300mg tablets orally twice daily (bd) continuously	
Reporting group title	Placebo (BRCA1/2 +ve)
Reporting group description:	
Patients received Placebo 300mg tablets orally bd continuously	
Reporting group title	Olaparib (BRCA1/2 -ve)
Reporting group description:	
Patients received Olaparib 300mg tablets orally bd continuously	
Reporting group title	Placebo (BRCA1/2 -ve)
Reporting group description:	
Patients received Placebo 300mg tablets orally bd continuously	

Primary: Efficacy: Progression-free survival (PFS)

End point title	Efficacy: Progression-free survival (PFS)
End point description:	
PFS (per RECIST 1.1) was defined as the time from randomisation until the date of Investigator assessed objective radiological disease progression or death (by any cause in the absence of disease progression). Objective progression (per REC I ST 1.1) is defined as at least a 20% increase in the sum of the diameters of the target lesions and an absolute increase of >5 mm, or an overall non-target lesion assessment of progression or a new lesion. Patients who have not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment.	
End point type	Primary
End point timeframe:	
At randomization visit and at every 12 weeks (+/- 7 days) until objective radiological disease progression as determined by the investigator or other discontinuation criteria are met (assessed upto 3.8 years)	

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	4.3 (2.79 to 5.49)	2.8 (2.73 to 4.96)	5.3 (2.89 to 5.55)	2.8 (2.79 to 2.89)

Statistical analyses

Statistical analysis title	Olaparib (BRCA1/2 +ve) vs Placebo (BRCA1/2 +ve)
Comparison groups	Placebo (BRCA1/2 +ve) v Olaparib (BRCA1/2 +ve)

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.022
Method	Stratified log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.566
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.372
upper limit	0.868

Statistical analysis title	Olaparib (BRCA1/2 -ve) vs Placebo (BRCA1/2 -ve)
Comparison groups	Olaparib (BRCA1/2 -ve) v Placebo (BRCA1/2 -ve)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0023
Method	Stratified log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.264
upper limit	0.708

Secondary: Efficacy: Overall survival (OS)	
End point title	Efficacy: Overall survival (OS)
End point description:	
OS was defined as the time from the date of randomisation until death due to any cause. Patients not known to have died at the time of analysis were censored based on the last recorded date on which the patients were known to be alive. Here, arbitrary value 99.9999 represent that Upper limit was not calculated due to insufficient number of events.	
End point type	Secondary
End point timeframe:	
From randomisation till Long-term follow-up (12-weekly beyond 30 days after last dose of study treatment) assessed upto 3.8 years	

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	20.1 (16.39 to 25.43)	20.9 (15.21 to 23.92)	23.2 (15.15 to 99.9999)	30.2 (17.84 to 99.9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Time to progression by Gynecologic Cancer Intergroup (GCIG) criteria

End point title	Efficacy: Time to progression by Gynecologic Cancer Intergroup (GCIG) criteria

End point description:

Time to progression by RECIST or CA-125 or death is defined as the time from randomisation to the earlier date of RECIST progression or CA-125 progression or death by any cause. Patients without a CA-125 progression or a RECIST progression who are still alive at the time of analysis were censored at the time of their last evaluable RECIST assessment and/or their last available CA-125 measurement, whichever is the earliest at the time of analysis. Patients that do not have any evaluable RECIST assessments or any CA-125 results post-randomisation were censored at the date of randomisation.

End point type	Secondary

End point timeframe:

At screening (Visit 1) and at every 12 weeks (±7 days), until objective disease progression, based on progressive serial elevation of serum CA-125 according to the GCIG criteria, or until discontinuation for other reasons (assessed upto 3.8 years)

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	2.8 (2.76 to 5.36)	2.8 (2.73 to 3.98)	2.9 (2.79 to 5.32)	2.79 (2.63 to 2.79)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Time to first subsequent treatment commencement (TFST)

End point title	Efficacy: Time to first subsequent treatment commencement (TFST)

End point description:

TFST was assessed as time from randomisation to first subsequent treatment commencement or death if this occurs before commencement of first subsequent treatment. Patients not known to have had a further subsequent therapy or death were censored at the last known time to have not received subsequent therapy.

End point type	Secondary

End point timeframe:

From follow-up i.e. 30 days after last dose of study medication till end of study (assessed every 12 weeks upto 3.8 years)

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	5.8 (4.67 to 9.17)	5.1 (3.58 to 6.11)	7.9 (5.88 to 11.07)	4.3 (3.68 to 6.41)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Time to second subsequent treatment commencement (TSST)

End point title	Efficacy: Time to second subsequent treatment commencement (TSST)

End point description:

TSST was assessed as time from randomisation to second subsequent treatment commencement or death if this occurs before commencement of second subsequent treatment. Patients not known to have had a further second subsequent therapy or death were censored at the last known time to have not received second subsequent therapy.

End point type	Secondary

End point timeframe:

From follow-up i.e. 30 days after last dose of study medication till end of study (assessed every 12 weeks upto 3.8 years)

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	13.1 (11.10 to 15.64)	11.7 (8.61 to 13.60)	15.4 (11.60 to 23.62)	12.7 (10.35 to 16.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Time to study treatment discontinuation (TDT)

End point title	Efficacy: Time to study treatment discontinuation (TDT)

End point description:

TDT was assessed as time from randomisation to study treatment discontinuation or death if this occurs before discontinuation of study treatment. Patients not known to have died at the time of analysis and not known to have discontinued study treatment were censored based on the last recorded date on which the patients were known to be alive.

End point type	Secondary

End point timeframe:

From follow-up 30 days after last dose of study medication till long-term follow-up i.e. 12-weekly beyond 30 days after last dose of study treatment

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Months				
median (confidence interval 95%)	4.5 (3.35 to 5.59)	3.4 (2.86 to 5.49)	5.6 (3.42 to 5.78)	3.1 (2.79 to 3.91)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Change from baseline in Health-related quality of life (HRQoL)

End point title	Efficacy: Change from baseline in Health-related quality of life (HRQoL)

End point description:

Health related quality of life (HRQoL) of Olaparib maintenance retreatment compared to placebo as measured by the Functional Assessment of Cancer Therapy – Ovarian (FACT-O) Trial Outcome Index (TOI) was determined. HRQoL was analysed using the FACT-O tool by mixed model for repeated measures (MMRM) analysis of the change from baseline in TOI score. FACT-O TOI is scored from O to 100 with higher scores denoting better quality of life. The higher the score, the better the HRQoL.

End point type	Secondary

End point timeframe:

At Baseline, and from Day 1 until objective disease progression (assessed upto 2 years)

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	35	55	35
Units: Change in scores				
least squares mean (standard error)	-1.27 (± 0.55)	1.67 (± 0.89)	-2.08 (± 0.60)	0.58 (± 0.90)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with Adverse Events (AEs), and Serious Adverse Events (SAEs)

End point title	Number of patients with Adverse Events (AEs), and Serious Adverse Events (SAEs)

End point description:

All AEs/serious adverse events (SAEs) reported during the study were recorded.

End point type	Secondary

End point timeframe:

At Baseline and from Day 1 till follow-up i.e. 30 days after last dose of study medication (assessed upto 3.8 years)

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Patients				
Treatment emergent adverse event (TEAE)	64	33	66	31
TEAE causally related to treatment (CRT)	50	23	53	14
TEAE of CTCAE grade 3 or higher	11	2	15	3
TEAE of CTCAE ≥ grade 3 CRT	5	1	5	1
TEAE with outcome = death	0	0	0	0
TEAE with outcome = death, CRT	0	0	0	0
TESAE (including events with outcome = death)	5	0	11	2
TESAE (including events with outcome = death), CRT	1	0	3	0
TEAE = discontinuation of study medication	2	0	1	0
TEAE = discontinuation of study medication, CRT	1	0	0	0
TEAE leading to dose modification	18	6	28	2
TEAE leading to dose modification, CRT	14	5	21	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with Adverse Event of Special Interest (AESI)

End point title	Number of patients with Adverse Event of Special Interest (AESI)

End point description:

All AESIs reported during the study were recorded.

End point type	Secondary

End point timeframe:

At Baseline and from Day 1 till long-term follow-up i.e. 12-weekly beyond 30 days after last dose of

End point values	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)	Placebo (BRCA1/2 -ve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	38	72	36
Units: Patients	1	1	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Screening (Day -27 to Day 0) up to 12-weekly beyond 30 days after the last dose of study treatment (assessed up to 3.8 years)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Olaparib (BRCA1/2 +ve)
Reporting group description:	
Patients received olaparib 300mg tablets orally twice daily (bd) continuously	
Reporting group title	Placebo (BRCA1/2 +ve)
Reporting group description:	
Patients received placebo 300mg tablets administered orally twice daily (bd) continuously	
Reporting group title	Olaparib (BRCA1/2 -ve)
Reporting group description:	
Patients received olaparib 300mg tablets orally twice daily (bd) continuously	
Reporting group title	Placebo (BRCA1/2 -ve)
Reporting group description:	
Patients received placebo 300mg tablets administered orally twice daily (bd) continuously	

Serious adverse events	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 74 (6.76%)	0 / 38 (0.00%)	11 / 72 (15.28%)
number of deaths (all causes)	39	22	15
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated hernia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal perforation			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic haematoma			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo (BRCA1/2 -ve)		
Total subjects affected by serious adverse events			

subjects affected / exposed	2 / 36 (5.56%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Incarcerated hernia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileal perforation			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic haematoma			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Olaparib (BRCA1/2 +ve)	Placebo (BRCA1/2 +ve)	Olaparib (BRCA1/2 -ve)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 74 (86.49%)	33 / 38 (86.84%)	65 / 72 (90.28%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast neoplasm			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Oesophageal squamous cell carcinoma			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Basal cell carcinoma			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 74 (2.70%)	2 / 38 (5.26%)	0 / 72 (0.00%)
occurrences (all)	2	2	0
Hypertension			
subjects affected / exposed	2 / 74 (2.70%)	1 / 38 (2.63%)	1 / 72 (1.39%)
occurrences (all)	2	2	1

Hypotension			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	1
Cyanosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	18 / 74 (24.32%)	3 / 38 (7.89%)	15 / 72 (20.83%)
occurrences (all)	21	3	20
Axillary pain			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	13 / 74 (17.57%)	5 / 38 (13.16%)	13 / 72 (18.06%)
occurrences (all)	15	5	18
Illness			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	1 / 74 (1.35%)	1 / 38 (2.63%)	1 / 72 (1.39%)
occurrences (all)	1	1	1
Pyrexia			

subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	3 / 72 (4.17%)
occurrences (all)	1	0	4
Sluggishness			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Complication associated with device			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Xerosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Transplant rejection			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Ovarian vein thrombosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			

subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 74 (6.76%)	1 / 38 (2.63%)	5 / 72 (6.94%)
occurrences (all)	5	1	6
Dysphonia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	7 / 74 (9.46%)	2 / 38 (5.26%)	7 / 72 (9.72%)
occurrences (all)	8	2	7
Oropharyngeal pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 74 (2.70%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	3	1	0
Dyssomnia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Emotional disorder			

subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Mental disorder			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Mood swings			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 74 (4.05%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	4	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	1
Blood albumin decreased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 74 (1.35%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	4 / 74 (5.41%)	1 / 38 (2.63%)	4 / 72 (5.56%)
occurrences (all)	8	1	5
Blood urea increased			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	3 / 72 (4.17%)
occurrences (all)	5	0	6
Weight decreased			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Rib fracture			

subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Eye contusion			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Angina pectoris			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	4 / 74 (5.41%)	1 / 38 (2.63%)	3 / 72 (4.17%)
occurrences (all)	7	1	3
Dysgeusia			
subjects affected / exposed	3 / 74 (4.05%)	1 / 38 (2.63%)	1 / 72 (1.39%)
occurrences (all)	3	1	1
Headache			

subjects affected / exposed	6 / 74 (8.11%)	1 / 38 (2.63%)	3 / 72 (4.17%)
occurrences (all)	8	1	3
Neuropathy peripheral			
subjects affected / exposed	1 / 74 (1.35%)	2 / 38 (5.26%)	2 / 72 (2.78%)
occurrences (all)	1	3	2
Neurotoxicity			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	2 / 72 (2.78%)
occurrences (all)	1	0	2
Syncope			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Anosmia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Taste disorder			

subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 74 (17.57%)	2 / 38 (5.26%)	15 / 72 (20.83%)
occurrences (all)	18	3	21
Leukopenia			
subjects affected / exposed	4 / 74 (5.41%)	0 / 38 (0.00%)	3 / 72 (4.17%)
occurrences (all)	5	0	4
Neutropenia			
subjects affected / exposed	4 / 74 (5.41%)	4 / 38 (10.53%)	8 / 72 (11.11%)
occurrences (all)	5	5	13
Lymphopenia			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	6 / 72 (8.33%)
occurrences (all)	2	0	6
Thrombocytopenia			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	4 / 72 (5.56%)
occurrences (all)	2	0	5
Anaemia macrocytic			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Microcytic anaemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Vertigo			

subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	4 / 72 (5.56%)
occurrences (all)	1	0	4
Sudden hearing loss			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Eye irritation			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	3 / 72 (4.17%)
occurrences (all)	0	1	3
Abdominal pain			
subjects affected / exposed	8 / 74 (10.81%)	11 / 38 (28.95%)	6 / 72 (8.33%)
occurrences (all)	9	14	8
Abdominal pain upper			
subjects affected / exposed	7 / 74 (9.46%)	0 / 38 (0.00%)	4 / 72 (5.56%)
occurrences (all)	8	0	6
Aphthous ulcer			
subjects affected / exposed	1 / 74 (1.35%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	9 / 74 (12.16%)	6 / 38 (15.79%)	9 / 72 (12.50%)
occurrences (all)	9	9	9
Diarrhoea			
subjects affected / exposed	10 / 74 (13.51%)	5 / 38 (13.16%)	12 / 72 (16.67%)
occurrences (all)	14	6	13
Dry mouth			
subjects affected / exposed	4 / 74 (5.41%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	4	0	0
Dyspepsia			

subjects affected / exposed	2 / 74 (2.70%)	2 / 38 (5.26%)	2 / 72 (2.78%)
occurrences (all)	2	3	3
Dysphagia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	2 / 74 (2.70%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	2	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	29 / 74 (39.19%)	4 / 38 (10.53%)	30 / 72 (41.67%)
occurrences (all)	34	5	37
Odynophagia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	8 / 74 (10.81%)	4 / 38 (10.53%)	6 / 72 (8.33%)
occurrences (all)	11	4	10
Abdominal discomfort			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	2 / 72 (2.78%)
occurrences (all)	0	0	2
Abnormal faeces			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Frequent bowel movements			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Oesophagitis			

subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Oesophageal pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 74 (1.35%)	3 / 38 (7.89%)	2 / 72 (2.78%)
occurrences (all)	1	3	2
Dry skin			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	2 / 72 (2.78%)
occurrences (all)	2	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 74 (1.35%)	2 / 38 (5.26%)	0 / 72 (0.00%)
occurrences (all)	1	2	0
Rash			
subjects affected / exposed	1 / 74 (1.35%)	1 / 38 (2.63%)	2 / 72 (2.78%)
occurrences (all)	1	1	5
Rash maculo-papular			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0

Blister			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Nail disorder			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Renal Failure			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 74 (0.00%)	3 / 38 (7.89%)	2 / 72 (2.78%)
occurrences (all)	0	3	2

Arthritis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	2 / 74 (2.70%)	1 / 38 (2.63%)	2 / 72 (2.78%)
occurrences (all)	2	1	2
Bone pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Hypercreatinaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	4 / 74 (5.41%)	1 / 38 (2.63%)	2 / 72 (2.78%)
occurrences (all)	4	1	2
Muscular weakness			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Osteoporosis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 74 (0.00%)	2 / 38 (5.26%)	2 / 72 (2.78%)
occurrences (all)	0	2	2

Intervertebral disc protrusion			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis cryptosporidial			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Genital herpes			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	0 / 74 (0.00%)	2 / 38 (5.26%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
Hordeolum			

subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	4	0	0
Oral herpes			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Pleural infection			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	2 / 74 (2.70%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
Tooth abscess			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	2 / 74 (2.70%)	4 / 38 (10.53%)	3 / 72 (4.17%)
occurrences (all)	2	4	3
Abscess jaw			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Otitis media			

subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	2 / 72 (2.78%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 74 (2.70%)	1 / 38 (2.63%)	7 / 72 (9.72%)
occurrences (all)	2	1	8
Hypercholesterolaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 38 (2.63%)	1 / 72 (1.39%)
occurrences (all)	0	1	1
Hypermagnesaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 74 (1.35%)	1 / 38 (2.63%)	0 / 72 (0.00%)
occurrences (all)	1	1	0
Hyponatraemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 38 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
Folate deficiency			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1

Hyperchloraemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Hypernatraemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 38 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1

Non-serious adverse events	Placebo (BRCA1/2 -ve)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 36 (83.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast neoplasm			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Basal cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Cyanosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		

Varicose vein			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Axillary pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	3		
Illness			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	2		
Sluggishness			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Complication associated with device			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gait disturbance			

subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Xerosis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Immune system disorders			
Transplant rejection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Ovarian vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Vulvovaginal dryness			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dyspnoea			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Nasal dryness			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Respiratory tract congestion			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dyssomnia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Emotional disorder			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Mental disorder			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Mood swings			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Blood albumin decreased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Platelet count decreased			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Eye contusion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hand fracture			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Angina pectoris			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Neuropathy peripheral			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Neurotoxicity			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Paraesthesia			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Polyneuropathy			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Anosmia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Post herpetic neuralgia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Taste disorder			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Neutropenia			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Lymphopenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Anaemia macrocytic			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Microcytic anaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Neutrophilia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Sudden hearing loss			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Eye irritation			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Aphthous ulcer			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Dry mouth			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Nausea			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Odynophagia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Abnormal faeces			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oesophagitis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Oesophageal pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Paraesthesia oral			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	2		
Hyperhidrosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Nail disorder			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia			

syndrome			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Skin reaction			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Renal Failure			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	4		
Arthritis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Flank pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypercreatinaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

Spinal pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gastroenteritis cryptosporidial			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Genital herpes			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pleural infection			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Abscess jaw			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		

Hypercholesterolaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Folate deficiency			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hyperchloraemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Hypernatraemia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2017	Study Design, Rationale for Study Design, Doses, and Control Groups sections updated to limit enrolment for patients with documented prior exposure to PARPi. Inclusion Criteria updated to: a) Specify eligible histopathology by excluding carcinosarcoma, clear cell carcinoma and discussion for patients with mixed tumours. b) Limit enrolment for patients with documented prior exposure to PARPi. c) Clarify partial or complete radiological response is due to most recent chemotherapy. d) Allow calculation of CrCl estimate by using the Cockcroft-Gault equation of ≥51 mL/min or 24-hour urine test. Exclusion Criteria updated to: a) Allow eligibility of Neuropathy Grade 2. b) Remove: "Previous allogeneic bone marrow transplant or double umbilical cord blood transplantation". c) Restrict eligibility for patients who had received a whole blood transfusion within 30 days prior to screening tests instead of 90 days prior to randomisation. Screen failure section clarified re-screening was permitted and the process to perform re-screening. Scheduled Assessments updated to: a) Add pregnancy testing for females of childbearing potential during each on site treatment visit. b) Remove requirements to complete additional eCRF when an AE of nausea or vomiting occurred. c) Clarify that if a patient discontinued treatment (and/or received a subsequent cancer therapy) prior to progression, then the patient should be followed until objective disease progression as defined by RECIST 1.1. Interim Analysis updated to include a pre-specified interim analysis for futility, ensuring that exposure of patients to an ineffective treatment was excluded. IDMC unblinded interim (or ongoing) efficacy and safety review to pick out a major risk:benefit discrepancy.
04 January 2019	Sample size estimate updated to 228 (assumptions on sample size were to be reviewed at the time of the interim analysis). Amended assumptions for expected median PFS in placebo treated patients (4.5 months) based on prior data; calculations of sample size adjusted to support detection of a 0.5 HR in both cohorts. Oxaliplatin added as an acceptable platinum chemotherapy. Inclusion criterion related to continued platinum sensitivity modified to allow patients who had no measurable disease following debulking surgery and a CA 125 which was not rising.
15 October 2020	Acceptable birth control methods updated so that women of childbearing potential and their partners, who were sexually active, must have agreed to use 1 highly effective form of contraception and their partners had to use a male condom. New section to detail assessments required for patients still on study treatment after primary PFS analysis. Data cut-off and subsequent database lock and timing for the primary analysis was clarified: after the later of the 2 cohorts reached the defined number of progression or death events. Updated timing of OS analysis to the time of the primary analysis for PFS, and again after 50% death events in either cohort or 60 months after FPI, whichever was earlier.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported