Clinical trial results:
OPINION - A Phase IIIb, Single-arm, Open-label Multicentre Study of Olaparib Maintenance Monotherapy in Platinum Sensitive Relapsed non-Germline BRCA Mutated Ovarian Cancer Patients who are in Complete or Partial Response Following Platinum-based Chemotherapy

Summary

EudraCT number	2017-002767-17
Trial protocol	CZ SI BG GB NL ES BE AT SE PT NO DK FI PL IT RO
Global end of trial date	10 March 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	D0816C00020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03402841
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, 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	10 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy by progression-free survival (PFS) (investigator-recorded assessments according to modified Response Evaluation Criteria In Solid Tumours version 1.1 (RECIST v1.1) of olaparib maintenance monotherapy in non-germline breast cancer susceptibility gene mutated (non-gBRCAm) platinum-sensitive relapsed (PSR) ovarian cancer.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	Czechia: 22
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Finland: 13
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Slovenia: 17
Country: Number of subjects enrolled	Spain: 52
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	Switzerland: 12
Country: Number of subjects enrolled	United Kingdom: 15
Worldwide total number of subjects	279
EEA total number of subjects	203

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)	132
From 65 to 84 years	146
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This was a Phase IIIb, single-arm, open-label multicentre study to assess the efficacy and safety of single-agent olaparib as a maintenance treatment in eligible patients. A total of 279 patients were enrolled in this study.

Pre-assignment

Screening details:

Olaparib was administered to all patients at a starting dose of 300 milligrams (mg) twice daily. Dose reductions were required in patients experiencing toxicities or due to concomitant medication (CM).

Period 1

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

Arms

Arm title	Olaparib

Arm description:

Olaparib was administered to all patients at a starting dose of 300 mg twice daily. Dose reductions were required in patients
experiencing toxicities or due to CM. Patients continued with olaparib until documented disease progression as assessed by the Investigator or unacceptable toxicity or for as long as they did not meet any other discontinuation criteria.

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	AZD2281, KU-0059436
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 2*150 mg olaparib tablets (i.e. total 300 mg) twice daily at the same time each day, approximately 12 hours apart with one glass of water. Olaparib tablets taken with or without food.

Number of subjects in period 1	Olaparib
Started	279
Completed	128
Not completed	151
Consent withdrawn by subject	3
Death	146
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib
Reporting group description:	
Olaparib was administered to all patients at a starting dose of 300 mg twice daily. Dose reductions were required in patients experiencing toxicities or due to CM. Patients continued with olaparib until documented disease progression as assessed by the Investigator or unacceptable toxicity or for as long as they did not meet any other discontinuation criteria.	

Reporting group values	Olaparib	Total	
Number of subjects	279	279	
Age Categorical			
Units:			
Age Continuous			
Units: years			
arithmetic mean	64.0		
standard deviation	± 9.19	-	
Gender Categorical			
Units: Patients			
Female	279	279	
Male	0	0	
Race			
Units: Subjects			
White	273	273	
Black or African American	1	1	
Asian	2	2	
Unspecified	2	2	
Missing	1	1	
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	271	271	
Missing	1	1	

End points

End points reporting groups

Reporting group title	Olaparib

Reporting group description:

Olaparib was administered to all patients at a starting dose of 300 mg twice daily. Dose reductions were required in patients
experiencing toxicities or due to CM. Patients continued with olaparib until documented disease progression as assessed by the Investigator or unacceptable toxicity or for as long as they did not meet any other discontinuation criteria.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[1]

End point description:

PFS is defined as the time from date of first dose until the date of objective radiological disease progression; assessed according to modified RECIST 1.1 or death (by any cause in the absence of progression). Progression was determined by investigator assessment, RECIST 1.1. Calculated using the Kaplan-Meier technique. Confidence intervals (CI) for median PFS was derived based on Brookmeyer-Crowley method. The Full Analysis Set (FAS) included all enrolled patients assigned to olaparib.

End point type	Primary

End point timeframe:

Up to maximum of 32 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single arm study, the comparison analysis cannot be performed for this end point.

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: months				
median (confidence interval 95%)	9.2 (7.6 to 10.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Subsequent Therapy or Death (TFST)

End point title	Time to First Subsequent Therapy or Death (TFST)

End point description:

TFST is defined as the time from date of first dose to date of first subsequent treatment commencement or death due to any cause if this occurs before commencement of first subsequent treatment. Calculated using the Kaplan-Meier technique. CI for median TFST was derived based on Brookmeyer-Crowley method. The FAS included all enrolled patients assigned to olaparib.

End point type	Secondary

End point timeframe:

Up to a maximum of 43 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: months				
median (confidence interval 95%)	13.9 (11.5 to 16.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Discontinuation or Death (TDT)

End point title	Time to Treatment Discontinuation or Death (TDT)

End point description:

TDT is defined as the time from date of first dose to date of study drug discontinuation or death due to any cause if this occurs before study drug discontinuation. Calculated using the Kaplan-Meier technique. CI for median TDT was derived based on Brookmeyer-Crowley method. The FAS included all enrolled patients assigned to olaparib.

End point type	Secondary

End point timeframe:

Up to a maximum of 43 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: months				
median (confidence interval 95%)	9.6 (7.8 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by Homologous Recombination Deficiency (HRD)/ Breast Cancer Susceptibility Gene Mutation (Mutated) (BRCAm) Status

End point title	PFS by Homologous Recombination Deficiency (HRD)/ Breast Cancer Susceptibility Gene Mutation (Mutated) (BRCAm) Status

End point description:

HRD/BRCAm status was based on the central blood and tumour assessments. Assessed according to modified RECIST 1.1 or death (by any cause in the absence of progression). Progression was determined by investigator assessment, RECIST 1.1. Calculated using the Kaplan-Meier technique. CI for median PFS was derived based on Brookmeyer-Crowley method. The FAS included all enrolled patients assigned

to Olaparib. Only FAS patients with available central assessment are reported. Here, 99999=the upper CI was not calculable due to insufficient progression events.

End point type	Secondary

End point timeframe:

Up to maximum of 32 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	242			
Units: months				
median (confidence interval 95%)				
HRD status positive and/or sBRCAm subgroup (n=121)	11.1 (9.2 to 14.6)			
HRD status positive, non-BRCAm subgroup (n=94)	9.7 (8.1 to 13.6)			
HRD status negative subgroup (n=115)	7.3 (5.5 to 9.0)			
sBRCAm subgroup (n=27)	16.4 (12.8 to 99999)			
gBRCAm subgroup (n=6)	12.1 (3.7 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Chemotherapy-free Interval (CT-FI)

End point title	Chemotherapy-free Interval (CT-FI)

End point description:

CT-FI is defined as the time from the date of the last dose of platinum chemotherapy prior to olaparib maintenance therapy until the date of initiation of the next anticancer therapy. Calculated using the Kaplan-Meier technique. CI for median CT-FI was derived based on Brookmeyer-Crowley method. The FAS included all enrolled patients assigned to olaparib.

End point type	Secondary

End point timeframe:

Up to a maximum of 43 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: months				
median (confidence interval 95%)	17.9 (13.8 to 23.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from the date of first dose of olaparib to the date of death from any cause. Calculated using the Kaplan-Meier technique. CI for median OS was derived based on Brookmeyer-Crowley method. The FAS included all enrolled patients assigned to olaparib.

End point type	Secondary

End point timeframe:

Up to a maximum of 43 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: months				
median (confidence interval 95%)	32.7 (29.5 to 35.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With any Improvement From Baseline in Trial Outcome Index (TOI) Score at any Point During the Treatment Period

End point title	Percentage of Patients With any Improvement From Baseline in Trial Outcome Index (TOI) Score at any Point During the Treatment Period

End point description:

Improvement was defined as a functional assessment of cancer therapy - ovarian (FACT-O) TOI response of "any improvement" at any time point over the course of treatment. The TOI is an established single targeted index composed of the following scales of the FACT-O: physical and functional well-being and additional concerns. The range of possible scores for the FACT-O TOI is 0-100, with a higher score indicating better health related quality of life (HRQoL). An increase in score from baseline indicates an improvement in HRQoL. The FACT-O set consisted of all FAS patients with at least a baseline and a post-baseline assessment (excluding the end of treatment and 30-day follow up assessments).

End point type	Secondary

End point timeframe:

Baseline up to a maximum of 32 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	249			
Units: percentage of patients				
number (confidence interval 95%)	64.3 (58.0 to 70.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients With a 10-Point Deterioration From Baseline in TOI Score at any Point During the Treatment Period

End point title	Percentage of Patients With a 10-Point Deterioration From Baseline in TOI Score at any Point During the Treatment Period

End point description:

10-point deterioration was defined as a FACT-O TOI response of "10-point deterioration" at any time point over the course of treatment. The TOI is an established single targeted index composed of the following scales of the FACT-O: physical and functional well-being and additional concerns. The range of possible scores for the FACT-O TOI is 0-100, with a higher score indicating better HRQoL. A decrease in score of at least 10 points from baseline was defined as a clinically meaningful deterioration. The FACT-O set consisted of all FAS patients with at least a baseline and a post-baseline assessment (excluding the end of treatment and 30-day follow up assessments).

End point type	Secondary

End point timeframe:

Baseline up to a maximum of 32 months

End point values	Olaparib			
Subject group type	Reporting group			
Number of subjects analysed	249			
Units: percentage of patients				
number (confidence interval 95%)	42.6 (36.3 to 49.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Includes adverse events with an onset date on or after the date of first dose and up to and including 30 days following the date of last dose of olaparib, up to a maximum of 43 months

Adverse event reporting additional description:

Safety Analysis set consisted of all patients in the FAS who received at least 1 dose of olaparib.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Olaparib 300mg BID

Reporting group description:

Olaparib was administered to all patients at a starting dose of 300 mg twice daily. Dose reductions were required in patients experiencing toxicities or due to CM.
Patients continued with olaparib until documented disease progression as assessed by the Investigator or unacceptable toxicity or for as long as they did not meet any other discontinuation criteria.

Serious adverse events	Olaparib 300mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	58 / 279 (20.79%)		
number of deaths (all causes)	146		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Pelvic venous thrombosis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic embolus				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic respiratory disease				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	22 / 279 (7.89%)		
occurrences causally related to treatment / all	29 / 31		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal wall thickening			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Dyspepsia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mechanical ileus			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumoperitoneum			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestinal obstruction			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			

subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia aspiration			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Appendicitis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Metabolism and nutrition disorders				
Dehydration				

subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Olaparib 300mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	268 / 279 (96.06%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Seborrhoeic keratosis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Embolism			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Flushing			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	5		
Hot flush			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	4		
Haematoma			

subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	7 / 279 (2.51%)		
occurrences (all)	7		
Hypotension			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	4		
Lymphoedema			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Peripheral coldness			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Thrombosis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
General disorders and administration site conditions			
Adhesion			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	46 / 279 (16.49%)		
occurrences (all)	57		
Face oedema			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Early satiety			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Chills			

subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Chest pain				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Fatigue				
subjects affected / exposed	82 / 279 (29.39%)			
occurrences (all)	103			
Influenza like illness				
subjects affected / exposed	5 / 279 (1.79%)			
occurrences (all)	5			
Infusion site extravasation				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Localised oedema				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Malaise				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oedema				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Non-cardiac chest pain				
subjects affected / exposed	5 / 279 (1.79%)			
occurrences (all)	5			
Mucosal inflammation				
subjects affected / exposed	9 / 279 (3.23%)			
occurrences (all)	10			
Mass				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oedema peripheral				
subjects affected / exposed	13 / 279 (4.66%)			
occurrences (all)	15			
Peripheral swelling				

subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	16 / 279 (5.73%)		
occurrences (all)	23		
Swelling			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	5 / 279 (1.79%)		
occurrences (all)	5		
Pelvic discomfort			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Vaginal discharge			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Vaginal haemorrhage			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Vulvovaginal pain			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Heavy menstrual bleeding			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			

Cough				
subjects affected / exposed	31 / 279 (11.11%)			
occurrences (all)	36			
Chronic respiratory disease				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	2			
Asthma				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Haemoptysis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Dyspnoea				
subjects affected / exposed	14 / 279 (5.02%)			
occurrences (all)	15			
Dysphonia				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Hiccups				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Dry throat				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Hypoxia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Nasal disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Nasal congestion				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	2			
Lung infiltration				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			

Laryngeal pain			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Pharyngeal inflammation			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	6 / 279 (2.15%)		
occurrences (all)	8		
Organising pneumonia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	5 / 279 (1.79%)		
occurrences (all)	6		
Pulmonary embolism			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	4		
Dyspnoea exertional			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Psychiatric disorders			
Affect lability			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Agitation			

subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Anxiety				
subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	6			
Bradyphrenia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Depression				
subjects affected / exposed	7 / 279 (2.51%)			
occurrences (all)	7			
Genito-pelvic pain/penetration disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Panic attack				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Irritability				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Insomnia				
subjects affected / exposed	14 / 279 (5.02%)			
occurrences (all)	14			
Hallucination, visual				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Tension				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Sleep disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Restlessness				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			

Mood swings			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Product issues			
Device breakage			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 279 (2.51%)		
occurrences (all)	9		
Amylase increased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	6 / 279 (2.15%)		
occurrences (all)	8		
Blood potassium decreased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	2		
Blood creatinine increased			
subjects affected / exposed	29 / 279 (10.39%)		
occurrences (all)	46		
Blood creatine increased			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	4		
Blood potassium increased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	6		
Blood urea increased			

subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Creatinine renal clearance decreased				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Blood sodium decreased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Blood pressure decreased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Glomerular filtration rate decreased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Lipase increased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	6			
Mean cell volume increased				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Neutrophil count decreased				
subjects affected / exposed	14 / 279 (5.02%)			
occurrences (all)	32			
Monocyte count increased				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	2			

Occult blood			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Troponin I increased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	16 / 279 (5.73%)		
occurrences (all)	33		
Urine analysis abnormal			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Vitamin B12 decreased			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	6 / 279 (2.15%)		
occurrences (all)	6		
Weight increased			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	3		
White blood cell count decreased			
subjects affected / exposed	13 / 279 (4.66%)		
occurrences (all)	29		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Arthropod sting			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Contusion			

subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Bone fissure				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Fall				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Head injury				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Hand fracture				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	3			
Humerus fracture				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Procedural pain				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Joint injury				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Rib fracture				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Soft tissue injury				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Tooth fracture				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Stoma site haemorrhage				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Wound complication				

subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Arrhythmia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	3		
Tachycardia			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	2		
Ageusia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Balance disorder			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	3		
Carpal tunnel syndrome			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Disturbance in attention			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	17 / 279 (6.09%)		
occurrences (all)	22		
Dysgeusia			

subjects affected / exposed	40 / 279 (14.34%)			
occurrences (all)	44			
Epilepsy				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	2			
Nerve compression				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Migraine				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Hypoaesthesia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	24 / 279 (8.60%)			
occurrences (all)	27			
Neuropathy peripheral				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Peripheral sensory neuropathy				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Paraesthesia				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Neurotoxicity				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Polyneuropathy				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Taste disorder				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	4			
Syncope				

subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Somnolence			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Transient ischaemic attack			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Trigeminal nerve disorder			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Dyskinesia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Hypotonia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	102 / 279 (36.56%)		
occurrences (all)	197		
Anaemia macrocytic			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	6 / 279 (2.15%)		
occurrences (all)	9		
Lymphadenopathy			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		

Leukopenia subjects affected / exposed occurrences (all)	15 / 279 (5.38%) 25		
Erythropenia subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Macrocytosis subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Thrombocytopenia subjects affected / exposed occurrences (all)	20 / 279 (7.17%) 31		
Neutropenia subjects affected / exposed occurrences (all)	31 / 279 (11.11%) 62		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Deafness subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Ear haemorrhage subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Meniere's disease subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Vertigo subjects affected / exposed occurrences (all)	4 / 279 (1.43%) 5		
Eye disorders Amaurosis fugax subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Cataract			

subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Dry eye			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Eye disorder			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Visual impairment			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	4		
Abdominal distension			
subjects affected / exposed	13 / 279 (4.66%)		
occurrences (all)	13		
Abdominal hernia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	43 / 279 (15.41%)		
occurrences (all)	52		
Abdominal pain lower			
subjects affected / exposed	6 / 279 (2.15%)		
occurrences (all)	7		
Abdominal pain upper			
subjects affected / exposed	16 / 279 (5.73%)		
occurrences (all)	18		
Abnormal faeces			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		

Angular cheilitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Aerophagia				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	3			
Aphthous ulcer				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Chronic gastritis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Ascites				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	23 / 279 (8.24%)			
occurrences (all)	28			
Defaecation urgency				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Diarrhoea				
subjects affected / exposed	40 / 279 (14.34%)			
occurrences (all)	55			
Dry mouth				
subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	6			
Dyspepsia				
subjects affected / exposed	16 / 279 (5.73%)			
occurrences (all)	18			
Dysphagia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Enteritis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			

Eructation				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Epigastric discomfort				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Faeces soft				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Gastrooesophageal reflux disease				
subjects affected / exposed	5 / 279 (1.79%)			
occurrences (all)	5			
Gastritis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Gastric ulcer				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Flatulence				
subjects affected / exposed	8 / 279 (2.87%)			
occurrences (all)	8			
Gingival pain				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Lip dry				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Intestinal obstruction				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	4			
Haemorrhoids				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Haemorrhoidal haemorrhage				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			

Mouth ulceration				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Nausea				
subjects affected / exposed	136 / 279 (48.75%)			
occurrences (all)	187			
Odynophagia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oesophagitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oral mucosal exfoliation				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Palatal disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Toothache				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Tooth disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Stomatitis				
subjects affected / exposed	13 / 279 (4.66%)			
occurrences (all)	13			
Regurgitation				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Vomiting				
subjects affected / exposed	45 / 279 (16.13%)			
occurrences (all)	68			
Tooth development disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			

Irritable bowel syndrome subjects affected / exposed occurrences (all) Faecal vomiting subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1 1 / 279 (0.36%) 1		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all) Hepatotoxicity subjects affected / exposed occurrences (all) Liver disorder subjects affected / exposed occurrences (all) Bile duct stenosis subjects affected / exposed occurrences (all) Hepatic cytolysis subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 3 1 / 279 (0.36%) 1 1 / 279 (0.36%) 1 1 / 279 (0.36%) 1 1 / 279 (0.36%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Cold sweat subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) Hyperkeratosis subjects affected / exposed occurrences (all) Dry skin	16 / 279 (5.73%) 16 1 / 279 (0.36%) 1 2 / 279 (0.72%) 2 1 / 279 (0.36%) 1		

subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	7			
Ecchymosis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Eczema				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Erythema				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Nail disorder				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Lichen sclerosus				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Night sweats				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Onychoclasis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Pruritus				
subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	7			
Rash erythematous				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	10 / 279 (3.58%)			
occurrences (all)	13			
Rash macular				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	2			
Rosacea				

subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Rash maculo-papular			
subjects affected / exposed	4 / 279 (1.43%)		
occurrences (all)	4		
Sensitive skin			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	4		
Urticaria			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Hair texture abnormal			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Nail ridging			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Nail discolouration			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	9 / 279 (3.23%)		
occurrences (all)	10		
Chronic kidney disease			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	3		
Haematuria			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		

Hydronephrosis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Nocturia				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Micturition urgency				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Pollakiuria				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Proteinuria				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Polyuria				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Renal disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Renal failure				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Renal impairment				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	4			
Nephrolithiasis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Urinary tract obstruction				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Urinary tract disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 279 (9.32%)		
occurrences (all)	30		
Arthritis			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	27 / 279 (9.68%)		
occurrences (all)	30		
Bone pain			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	8		
Coccydynia			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	2		
Groin pain			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Joint effusion			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Muscle contracture			

subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Muscle spasms				
subjects affected / exposed	16 / 279 (5.73%)			
occurrences (all)	16			
Neck pain				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Myalgia				
subjects affected / exposed	10 / 279 (3.58%)			
occurrences (all)	11			
Musculoskeletal pain				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Musculoskeletal chest pain				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Osteoarthritis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Muscular weakness				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Osteopenia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Osteoporosis				
subjects affected / exposed	4 / 279 (1.43%)			
occurrences (all)	4			
Rheumatic disorder				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Pubic pain				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Pain in extremity				

subjects affected / exposed	7 / 279 (2.51%)		
occurrences (all)	8		
Rotator cuff syndrome			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Spinal osteoarthritis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Tenosynovitis stenosans			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Atypical mycobacterial lower respiratory tract infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Bacterial infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	3 / 279 (1.08%)		
occurrences (all)	4		
Candida infection			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Cellulitis			

subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Diverticulitis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Cystitis				
subjects affected / exposed	10 / 279 (3.58%)			
occurrences (all)	15			
Conjunctivitis viral				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Clostridium difficile infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Enteritis infectious				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Erysipelas				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Eye infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Fungal infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Gastroenteritis norovirus				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Gingivitis				

subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Herpes simplex				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	7			
Infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Laryngitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Lower respiratory tract infection				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Nasopharyngitis				
subjects affected / exposed	15 / 279 (5.38%)			
occurrences (all)	17			
Nail infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oral candidiasis				
subjects affected / exposed	3 / 279 (1.08%)			
occurrences (all)	3			
Pharyngitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Pharyngitis streptococcal				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	3			
Otitis media				

subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Paronychia				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Pneumonia viral				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	6 / 279 (2.15%)			
occurrences (all)	6			
Respiratory tract infection				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Rhinitis				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Respiratory tract infection viral				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Tooth abscess				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Skin infection				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Tooth infection				
subjects affected / exposed	2 / 279 (0.72%)			
occurrences (all)	2			
Urethritis				
subjects affected / exposed	1 / 279 (0.36%)			
occurrences (all)	1			
Upper respiratory tract infection				

subjects affected / exposed	12 / 279 (4.30%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	27 / 279 (9.68%)		
occurrences (all)	36		
Wound infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Device related infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Salmonellosis			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	2 / 279 (0.72%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	1 / 279 (0.36%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	32 / 279 (11.47%)		
occurrences (all)	34		

Hypercholesterolaemia subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 2		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 2		
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Hyperkalaemia subjects affected / exposed occurrences (all)	3 / 279 (1.08%) 4		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Hypochloraemia subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1		
Vitamin D deficiency subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 2		
Hyponatraemia subjects affected / exposed occurrences (all)	4 / 279 (1.43%) 6		
Hypomagnesaemia subjects affected / exposed occurrences (all)	6 / 279 (2.15%) 8		
Hypokalaemia subjects affected / exposed occurrences (all)	13 / 279 (4.66%) 20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2017	To improve clarity on study conduct, maintain consistency of information across protocol sections in line with revised AstraZeneca standard guidance. Details of retrospective Germline breast cancer susceptibility gene (gBRCA) testing added for sample collection. Details updated for biomarker analysis.
26 October 2018	To improve clarity on study conduct, maintain consistency of information across protocol sections in line with revised AstraZeneca standard guidance. New study countries added (Norway and Finland), Japan deleted, number of planned patients updated. Modification of objectives. Addition of an acceptable chemotherapeutic. Summaries of previous studies updated. Addition of alternative creatinine clearance measure. Addition of excluded therapy. Updated to specify events and time required before final analysis. Definition of "lost to follow-up" revised. Updated details for biomarker testing. Revised management of anaemia section. Potential drug-drug interactions updated. Definition of "Time to treatment discontinuation (TDT)" revised. Updated information on primary analysis/study end date. Appendices updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported