



Clinical trial results:

A Study of Durvalumab Alone and Durvalumab+Olaparib in Advanced, Platinum-Ineligible Bladder Cancer (BAYOU)

Summary

EudraCT number	2017-004556-27
Trial protocol	ES
Global end of trial date	15 October 2020

Results information

Result version number	v1 (current)
This version publication date	05 May 2022
First version publication date	05 May 2022

Trial information

Trial identification

Sponsor protocol code	D933IC00003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03459846
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, 1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, 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	15 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 October 2020
Global end of trial reached?	Yes
Global end of trial date	15 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of durvalumab + olaparib combination therapy compared with durvalumab + placebo in terms of PFS

Protection of trial subjects:

Patients given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2018
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	Russian Federation: 40
Country: Number of subjects enrolled	Taiwan: 26
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Vietnam: 20
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Korea, Republic of: 30
Worldwide total number of subjects	154
EEA total number of subjects	20

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)	40
From 65 to 84 years	104
85 years and over	10

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was performed no more than 28 days before the date of randomization and, ideally, was performed as close as possible to and prior to the date of randomization

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Durva + Olaparib

Arm description:

Durva + Olaparib

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

Dosage and administration details:

100 and 150 mg tablets

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500-mg vial solution for infusion after dilution. 50 mg/mL solution

Arm title	Durva + Placebo
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Arm description:

Durva + Placebo

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

Dosage and administration details:

100 and 150 mg matching tablets

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use
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Dosage and administration details:

500-mg vial solution for infusion after dilution. 50 mg/mL solution

Number of subjects in period 1	Durva + Olaparib	Durva + Placebo
Started	78	76
Completed	0	0
Not completed	78	76
Adverse event, serious fatal	52	46
Consent withdrawn by subject	2	2
Study terminated by sponsor	24	28

Baseline characteristics

Reporting groups

Reporting group title	Durva + Olaparib
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Reporting group description:

Durva + Olaparib

Reporting group title	Durva + Placebo
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Reporting group description:

Durva + Placebo

Reporting group values	Durva + Olaparib	Durva + Placebo	Total
Number of subjects	78	76	154
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	21	40
From 65-84 years	52	52	104
85 years and over	7	3	10
Age Continuous			
Units: Years			
arithmetic mean	73.4	70.2	
standard deviation	± 10.8	± 10.26	-
Sex: Female, Male			
Units: Participants			
Female	22	21	43
Male	56	55	111
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	3	3	6
Not Hispanic or Latino	75	73	148

End points

End points reporting groups

Reporting group title	Durva + Olaparib
Reporting group description:	
Durva + Olaparib	
Reporting group title	Durva + Placebo
Reporting group description:	
Durva + Placebo	

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
End point description:	
Progression-free survival based on investigator assessments according to RECIST 1.1	
End point type	Primary
End point timeframe:	
Tumor assessments every 8 weeks after randomization for the first 48 weeks and then every 12 weeks thereafter until clinical progression with or without RECIST 1.1-defined radiological progression	

End point values	Durva + Olaparib	Durva + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	76		
Units: Months				
median (confidence interval 95%)	4.2 (3.6 to 5.6)	3.5 (1.9 to 5.1)		

Statistical analyses

Statistical analysis title	Progression-free survival (PFS)
Comparison groups	Durva + Olaparib v Durva + Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.789
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.641
upper limit	1.387

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

Number of Participants with Overall Survival (OS)

End point type	Secondary
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End point timeframe:

Approximately 31 months after the first patient was randomised.

End point values	Durva + Olaparib	Durva + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	76		
Units: Participants				
Died	52	46		
Censored	26	30		

Statistical analyses

Statistical analysis title	Overall Survival (OS)
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Comparison groups	Durva + Olaparib v Durva + Placebo
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Number of subjects included in analysis	154
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.728
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Method	Regression, Cox
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Parameter estimate	Hazard ratio (HR)
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Point estimate	1.07
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	0.719
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upper limit	1.606
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Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
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End point description:

ORR is the number (%) of patients with at least one visit response of Complete response (CR) or Partial response (PR)

End point type	Secondary
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End point timeframe:

Up until progression, or last evaluable assessment in the absence in progression

End point values	Durva + Olaparib	Durva + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	76		
Units: Participants				
Response	22	14		
No Response	56	62		

Statistical analyses

Statistical analysis title	Objective Response Rate (ORR)
Comparison groups	Durva + Olaparib v Durva + Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.142
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	3.778

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
End point description:	Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): $\geq 30\%$ decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. DoR is the time from the date of first documented response until the date of documented progression or death in the absence of disease progression
End point type	Secondary
End point timeframe:	Tumor assessments every 8 weeks after randomization for the first 48 weeks and then every 12 weeks thereafter until clinical progression with or without RECIST 1.1-defined radiological progression

End point values	Durva + Olaparib	Durva + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	14		
Units: Months				
median (inter-quartile range (Q1-Q3))	8.9 (4.7 to 12.1)	14.8 (7.5 to 17.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of the patient signing the informed consent form until the follow-up period is completed (90 days after the last dose of the Investigational Product)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Durva + Placebo
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Reporting group description:

Durva + Placebo

Reporting group title	Durva + Olaparib
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Reporting group description:

Durva + Olaparib

Serious adverse events	Durva + Placebo	Durva + Olaparib	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 76 (34.21%)	37 / 76 (48.68%)	
number of deaths (all causes)	46	52	
number of deaths resulting from adverse events	5	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of prostate			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 76 (1.32%)	2 / 76 (2.63%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 76 (1.32%)	2 / 76 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			

subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Genital haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balanoposthitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Immune-mediated pneumonitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			

subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Myasthenia gravis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 76 (1.32%)	5 / 76 (6.58%)	
occurrences causally related to treatment / all	1 / 1	3 / 5	
deaths causally related to treatment / all	1 / 1	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 76 (1.32%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 76 (0.00%)	4 / 76 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	

Haematuria			
subjects affected / exposed	1 / 76 (1.32%)	3 / 76 (3.95%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 76 (1.32%)	3 / 76 (3.95%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	3 / 76 (3.95%)	2 / 76 (2.63%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 76 (1.32%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	6 / 76 (7.89%)	6 / 76 (7.89%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	2 / 76 (2.63%)	3 / 76 (3.95%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Kidney infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia bacteraemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			

subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Durva + Placebo	Durva + Olaparib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 76 (82.89%)	65 / 76 (85.53%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 76 (7.89%)	1 / 76 (1.32%)	
occurrences (all)	6	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 76 (17.11%)	22 / 76 (28.95%)	
occurrences (all)	13	25	
Asthenia			
subjects affected / exposed	2 / 76 (2.63%)	10 / 76 (13.16%)	
occurrences (all)	2	11	
Pyrexia			
subjects affected / exposed	7 / 76 (9.21%)	7 / 76 (9.21%)	
occurrences (all)	9	7	
Oedema peripheral			
subjects affected / exposed	4 / 76 (5.26%)	3 / 76 (3.95%)	
occurrences (all)	5	3	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	4 / 76 (5.26%)	0 / 76 (0.00%)	
occurrences (all)	5	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 76 (3.95%)	7 / 76 (9.21%)	
occurrences (all)	3	7	
Cough			
subjects affected / exposed	6 / 76 (7.89%)	6 / 76 (7.89%)	
occurrences (all)	6	6	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 76 (5.26%)	3 / 76 (3.95%)	
occurrences (all)	4	3	
Investigations			

Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	8 / 76 (10.53%) 9	
Amylase increased subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	4 / 76 (5.26%) 5	
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	1 / 76 (1.32%) 1	
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3	7 / 76 (9.21%) 7	
Headache subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 7	3 / 76 (3.95%) 3	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	21 / 76 (27.63%) 22	34 / 76 (44.74%) 50	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	6 / 76 (7.89%) 6	20 / 76 (26.32%) 23	
Constipation subjects affected / exposed occurrences (all)	12 / 76 (15.79%) 15	13 / 76 (17.11%) 14	
Diarrhoea subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 7	10 / 76 (13.16%) 12	
Vomiting subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 3	7 / 76 (9.21%) 8	
Abdominal pain subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	6 / 76 (7.89%) 6	

Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	4 / 76 (5.26%) 4	
Dyspepsia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	2 / 76 (2.63%) 2	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	6 / 76 (7.89%) 6	7 / 76 (9.21%) 9	
Pruritus subjects affected / exposed occurrences (all)	8 / 76 (10.53%) 8	6 / 76 (7.89%) 6	
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	6 / 76 (7.89%) 6	7 / 76 (9.21%) 8	
Endocrine disorders			
Hypothyroidism subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 5	7 / 76 (9.21%) 7	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	7 / 76 (9.21%) 7	8 / 76 (10.53%) 8	
Arthralgia subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	5 / 76 (6.58%) 7	
Pain in extremity subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 6	1 / 76 (1.32%) 1	
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	9 / 76 (11.84%) 11	
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	10 / 76 (13.16%) 10	19 / 76 (25.00%) 22	
Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	4 / 76 (5.26%) 4	
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	3 / 76 (3.95%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2018	Sections updated to reflect the change in the number of patients randomized from approximately 256 to 150 patients and the change in the stratification factors to include the patient's homologous recombination repair (HRR) status (mutant versus wildtype). Section 3 (Objectives and Endpoints) was updated to reflect the revised study objectives and endpoints in light of the change in the analysis plan to analyse the Full Analysis Set as the primary analysis population rather than the HRR mutant subgroup population.
15 November 2019	Updated throughout the protocol: PFS will not be updated at the time of the final OS analysis for the HRRm subgroup.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported