Clinical trial results:
A Phase 2 Study to Evaluate Safety and Anti-tumor Activity of Avelumab in Combination With Talazoparib in Subjects With BRCA or ATM Mutant Tumors

Summary

EudraCT number	2018-000345-39
Trial protocol	GB NL FR BE DK ES IT
Global end of trial date	03 February 2023

Results information

Result version number	v1 (current)
This version publication date	16 September 2023
First version publication date	16 September 2023

Trial information

Trial identification

Sponsor protocol code	B9991032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03565991
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	03 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate objective response rate (ORR) of avelumab in combination with talazoparib, in subjects with locally advanced or metastatic solid tumors harboring BRCA1, BRCA2 or ATM defect.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	52 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 126
Worldwide total number of subjects	200
EEA total number of subjects	61

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)	135
From 65 to 84 years	63
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 270 subjects were screened for this study, 202 subjects were enrolled and assigned to study treatment but 2 subjects never started the treatment. In total 200 subjects were treated (159 in Cohort 1 and 41 in Cohort 2).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)

Arm description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the BRCA1 or BRCA2 genes were enrolled in Cohort 1. Talazoparib was self-administered orally at a starting dose of 1 mg Once Daily (QD) for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour Intravenous (IV) infusion Every 2 Weeks (Q2W) on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Arm type	Experimental
Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab was administered as a 1-hour IV infusion Q2W at a dose of 800 mg.

Investigational medicinal product name	Talazoparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Talazoparib was administered orally at 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Talazoparib was administered orally at 0.75 mg QD for subjects with moderate renal impairment.

Arm title	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)

Arm description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the ATM gene without concurrent BRCA1/2 defect were enrolled in Cohort 2. Talazoparib was self-administered orally at a starting dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Arm type	Experimental

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

Dosage and administration details:

Avelumab was administered as a 1-hour IV infusion Q2W at a dose of 800 mg.

Investigational medicinal product name	Talazoparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Talazoparib was administered orally at 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Talazoparib was administered orally at 0.75 mg QD for subjects with moderate renal impairment.

Number of subjects in period 1	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)
Started	159	41
Completed	1	0
Not completed	158	41
Adverse event, serious fatal	1	-
Adverse event, not serious	4	1
Consent withdrawn by subject	2	6
Global deterioration of health status	14	4
Death	3	-
Adverse event, serious non-fatal	2	1
Unspecified	11	-
Progressive disease	121	29

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)
Reporting group description:	
Subjects with locally advanced or metastatic solid tumors with one or more defects in the BRCA1 or BRCA2 genes were enrolled in Cohort 1. Talazoparib was self-administered orally at a starting dose of 1 mg Once Daily (QD) for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour Intravenous (IV) infusion Every 2 Weeks (Q2W) on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.	
Reporting group title	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)
Reporting group description:	
Subjects with locally advanced or metastatic solid tumors with one or more defects in the ATM gene without concurrent BRCA1/2 defect were enrolled in Cohort 2. Talazoparib was self-administered orally at a starting dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.	

Reporting group values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)	Total
Number of subjects	159	41	200
Age Categorical Units: Subjects			
< 65 years	110	25	135
65 - <75 years	34	11	45
75 - <85 years	15	3	18
>=85 years	0	2	2
Age Continuous Units: Years			
arithmetic mean	57.35	61.76	
standard deviation	± 12.88	± 12.47	-
Sex: Female, Male Units: Subjects			
Female	108	24	132
Male	51	17	68
Race/Ethnicity, Customized Units: Subjects			
Black or African American	8	3	11
American Indian or Alaska Native	1	0	1
Asian	15	0	15
White	117	37	154
Not reported	18	1	19
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11	2	13
Not Hispanic or Latino	131	39	170
Unknown or Not Reported	17	0	17

Subject analysis sets

Subject analysis set title	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib
Subject analysis set type	Full analysis

Subject analysis set description:

Talazoparib was self-administered orally QD at a dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Reporting group values	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib		
Number of subjects	200		
Age Categorical Units: Subjects			
< 65 years	135		
65 - <75 years	45		
75 - <85 years	18		
>=85 years	2		
Age Continuous Units: Years			
arithmetic mean	58.25		
standard deviation	± 12.89		
Sex: Female, Male Units: Subjects			
Female	132		
Male	68		
Race/Ethnicity, Customized Units: Subjects			
Black or African American	11		
American Indian or Alaska Native	1		
Asian	15		
White	154		
Not reported	19		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13		
Not Hispanic or Latino	170		
Unknown or Not Reported	17		

End points

End points reporting groups

Reporting group title	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)

Reporting group description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the BRCA1 or BRCA2 genes were enrolled in Cohort 1. Talazoparib was self-administered orally at a starting dose of 1 mg Once Daily (QD) for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour Intravenous (IV) infusion Every 2 Weeks (Q2W) on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Reporting group title	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)

Reporting group description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the ATM gene without concurrent BRCA1/2 defect were enrolled in Cohort 2. Talazoparib was self-administered orally at a starting dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Subject analysis set title	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib
Subject analysis set type	Full analysis

Subject analysis set description:

Talazoparib was self-administered orally QD at a dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Primary: Percentage of Subjects With Confirmed Objective Response (OR) as Assessed by Blinded Independent Central Review (BICR)

End point title	Percentage of Subjects With Confirmed Objective Response (OR) as Assessed by Blinded Independent Central Review (BICR)[1]

End point description:

For subjects with solid tumors except metastatic Castration Resistant Prostate Cancer (mCRPC),OR was defined as a complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors version 1.1(RECIST v1.1),both confirmed by repeat assessments performed >=4 weeks after the criteria for response were first met.For subjects with mCRPC, OR was defined as the percentage of subjects with a best overall soft tissue response of CR or PR per RECIST v1.1 with no evidence of confirmed bone disease progression per Prostate Cancer Working Group3(PCWG3) criteria.CR was defined as complete disappearance of all target&non-target lesions with the exception of nodal disease.PR was defined as >=30% decrease under baseline of the sum of diameters of all target measurable lesions.Non-target PR lesions must be non-Progressive Disease (PD),which was unequivocal progression of pre-existing lesions.The analysis set included all enrolled subjects with >=1 dose of study

End point type	Primary

End point timeframe:

From the first dose of study treatment until the date of first documented disease progression or date of death from any cause, whichever came first, assessed up to approximately 24 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: No statistical analysis was planned for this endpoint

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Percentage of subjects				
number (confidence interval 95%)	27.7 (20.9 to 35.3)	7.3 (1.5 to 19.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation where subjects administered a product. TEAEs were those events with onset dates occurring during the on-treatment period. A Serious Adverse Event (SAE) was any untoward medical occurrence at any dose that: resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or resulted in congenital anomaly/birth defect. A treatment-related AE was any untoward medical occurrence attributed to the study drug in a subject who received study drug. TEAEs were graded using National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTCAE) v4.03 as Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE. The safety analysis set included all enrolled subjects who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From baseline up to 30 days after last dose of study treatment, maximum up to 4.3 years approximately

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Subjects				
TEAEs	156	40		
treatment-related TEAEs	148	34		
grade >=3 TEAEs	114	22		
grade >=3 treatment-related TEAEs	85	17		
SAEs	50	7		
treatment-related SAEs	12	4		
TEAEs leading to all study drugs' discontinuation	5	2		
treatment-related TEAEs (study drugs discontinue)	0	1		
TEAEs leading to death	14	2		

treatment-related TEAEs leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With New or Worsening Hematology Laboratory Test Results During the On-Treatment Period

End point title	Number of Subjects With New or Worsening Hematology Laboratory Test Results During the On-Treatment Period

End point description:

The laboratory results were graded according to the CTCAE v4.03. The number and percentage of subjects with newly occurring or worsening hematology abnormalities to Grade>=1 during the on-treatment period were summarized. Per NCI CTCAE toxicity grading v4.03, Grade 1(G1) = mild; Grade 2(G2) = moderate; Grade 3(G3) = severe; Grade 4(G4) = life-threatening; Grade 5(G5) = death related to AE. On-treatment period was defined as the time from the first dose of study treatment through minimum (30 days + last dose of study treatment, start day of new anti-cancer drug therapy -1 day). The safety analysis set included all enrolled subjects who received at least 1 dose of study treatment. Abbreviations: APTTP=activated partial thromboplastin time prolonged; HI=hemoglobin increased; INR=International Normalized Ratio; LCD=lymphocyte count decreased; LCI=lymphocyte count increased; NCD=neutrophil count decreased; N/W=new or worsened; PCD=platelet count decreased; WBCD=white blood cell decreased.

End point type	Secondary

End point timeframe:

From baseline up to 30 days after last dose of study treatment, maximum up to 4.3 years approximately

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[2]	41[3]		
Units: Subjects				
N/W to G1 (Parameter: APTTP) (n=5,1)	0	0		
N/W to G2 (Parameter: APTTP) (n=5,1)	0	0		
N/W to G3 (Parameter: APTTP) (n=5,1)	0	0		
N/W to G4 (Parameter: APTTP) (n=5,1)	0	0		
N/W to G1 (Parameter: anemia) (n=151,40)	27	9		
N/W to G2 (Parameter: anemia) (n=151,40)	33	6		
N/W to G3 (Parameter: anemia) (n=151,40)	61	12		
N/W to G4 (Parameter: anemia) (n=151,40)	0	0		
N/W to G1 (Parameter: HI) (n=157,41)	1	0		
N/W to G2 (Parameter: HI) (n=157,41)	0	0		
N/W to G3 (Parameter: HI) (n=157,41)	0	0		
N/W to G4 (Parameter: HI) (n=157,41)	0	0		

N/W to G1 (Parameter: INR) (n=6,0)	1	0		
N/W to G2 (Parameter: INR) (n=6,0)	0	0		
N/W to G3 (Parameter: INR) (n=6,0)	0	0		
N/W to G4 (Parameter: INR) (n=6,0)	0	0		
N/W to G1 (Parameter: LCD) (n=154,40)	15	6		
N/W to G2 (Parameter: LCD) (n=154,40)	58	15		
N/W to G3 (Parameter: LCD) (n=154,40)	34	7		
N/W to G4 (Parameter: LCD) (n=154,40)	3	0		
N/W to G1 (Parameter: LCI) (n=156,41)	0	0		
N/W to G2 (Parameter: LCI) (n=156,41)	3	0		
N/W to G3 (Parameter: LCI) (n=156,41)	1	0		
N/W to G4 (Parameter: LCI) (n=156,41)	0	0		
N/W to G1 (Parameter: NCD) (n=154,40)	15	2		
N/W to G2 (Parameter: NCD) (n=154,40)	42	8		
N/W to G3 (Parameter: NCD) (n=154,40)	16	4		
N/W to G4 (Parameter: NCD) (n=154,40)	3	1		
N/W to G1 (Parameter: PCD) (n=152,41)	59	16		
N/W to G2 (Parameter: PCD) (n=152,41)	16	3		
N/W to G3 (Parameter: PCD) (n=152,41)	14	4		
N/W to G4 (Parameter: PCD) (n=152,41)	11	1		
N/W to G1 (Parameter: WBCD) (n=156,41)	45	14		
N/W to G2 (Parameter: WBCD) (n=156,41)	52	11		
N/W to G3 (Parameter: WBCD) (n=156,41)	15	5		
N/W to G4 (Parameter: WBCD) (n=156,41)	2	0		

Notes:

[2] - Subjects with available data (n=X, X in category titles) were analyzed.

[3] - Subjects with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With New or Worsening Chemistry Laboratory Test Results During the On-Treatment Period

End point title	Number of Subjects With New or Worsening Chemistry Laboratory Test Results During the On-Treatment Period

End point description:

The laboratory results were graded according to the CTCAE v4.03. The number and percentage of subjects with newly occurring or worsening chemistry abnormalities to Grade >=1 during the on-treatment period were summarized. As per NCI CTCAE toxicity grading v4.03, Grade1(G1)=mild; Grade2(G2)=moderate; Grade3(G3)=severe; Grade4(G4)=life-threatening; Grade5(G5)=death related to AE. On-treatment period was defined as the time from the first dose of study treatment through minimum (30days + last dose of study treatment, start day of new anti-cancer drug therapy -1day).

The safety analysis set included all enrolled subjects who received at least 1 dose of study treatment.
Abbreviations: ALTI=alanine aminotransferase increased; ALPI=alkaline phosphatase increased; ASTI=aspartate aminotransferase increased; BBI=blood bilirubin increased; CPKI=creatine phosphokinase increased; CI=creatinine increased; GGTI=gamma glutamyl transferase increased; LI=lipase increased; SAI=serum amylase increased.

End point type	Secondary

End point timeframe:

From baseline up to 30 days after last dose of study treatment, maximum up to 4.3 years approximately

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[4]	41[5]		
Units: Subjects				
N/W to G1 (Parameter: ALTI) (n=152,41)	30	10		
N/W to G2 (Parameter: ALTI) (n=152,41)	6	0		
N/W to G3 (Parameter: ALTI) (n=152,41)	3	3		
N/W to G4 (Parameter: ALTI) (n=152,41)	1	0		
N/W to G1 (Parameter: ALPI) (n=153,41)	25	12		
N/W to G2 (Parameter: ALPI) (n=153,41)	21	5		
N/W to G3 (Parameter: ALPI) (n=153,41)	7	1		
N/W to G4 (Parameter: ALPI) (n=153,41)	1	0		
N/W to G1 (Parameter: ASTI) (n=150,40)	35	5		
N/W to G2 (Parameter: ASTI) (n=150,40)	13	2		
N/W to G3 (Parameter: ASTI) (n=150,40)	2	4		
N/W to G4 (Parameter: ASTI) (n=150,40)	1	0		
N/W to G1 (Parameter: BBI) (n=154,40)	7	2		
N/W to G2 (Parameter: BBI) (n=154,40)	7	2		
N/W to G3 (Parameter: BBI) (n=154,40)	2	1		
N/W to G4 (Parameter: BBI) (n=154,40)	0	0		
N/W to G1 (Parameter: CPKI) (n=151,41)	22	3		
N/W to G2 (Parameter: CPKI) (n=151,41)	8	1		
N/W to G3 (Parameter: CPKI) (n=151,41)	2	3		
N/W to G4 (Parameter: CPKI) (n=151,41)	0	1		
N/W to G1 (Parameter: CI) (n=153,40)	87	24		

N/W to G2 (Parameter: CI) (n=153,40)	12	4		
N/W to G3 (Parameter: CI) (n=153,40)	1	0		
N/W to G4 (Parameter: CI) (n=153,40)	1	0		
N/W to G1 (Parameter: GGTI) (n=147,40)	23	8		
N/W to G2 (Parameter: GGTI) (n=147,40)	16	5		
N/W to G3 (Parameter: GGTI) (n=147,40)	26	7		
N/W to G4 (Parameter: GGTI) (n=147,40)	1	1		
N/W to G1 (Parameter: hypercalcemia) (n=156,41)	11	4		
N/W to G2 (Parameter: hypercalcemia) (n=156,41)	0	0		
N/W to G3 (Parameter: hypercalcemia) (n=156,41)	1	0		
N/W to G4 (Parameter: hypercalcemia) (n=156,41)	0	0		
N/W to G1 (Parameter: hyperglycemia) (n=155,41)	23	5		
N/W to G2 (Parameter: hyperglycemia) (n=155,41)	2	0		
N/W to G3 (Parameter: hyperglycemia) (n=155,41)	3	2		
N/W to G4 (Parameter: hyperglycemia) (n=155,41)	1	0		
N/W to G1 (Parameter: hyperkalemia) (n=156,40)	13	3		
N/W to G2 (Parameter: hyperkalemia) (n=156,40)	6	0		
N/W to G3 (Parameter: hyperkalemia) (n=156,40)	1	0		
N/W to G4 (Parameter: hyperkalemia) (n=156,40)	1	0		
N/W to G1 (Parameter: hypermagnesemia) (n=155,41)	9	4		
N/W to G2 (Parameter: hypermagnesemia) (n=155,41)	0	0		
N/W to G3 (Parameter: hypermagnesemia) (n=155,41)	3	0		
N/W to G4 (Parameter: hypermagnesemia) (n=155,41)	0	0		
N/W to G1 (Parameter: hypernatremia) (n=156,41)	8	1		
N/W to G2 (Parameter: hypernatremia) (n=156,41)	0	0		
N/W to G3 (Parameter: hypernatremia) (n=156,41)	0	0		
N/W to G4 (Parameter: hypernatremia) (n=156,41)	0	0		
N/W to G1 (Parameter: hypoalbuminemia) (n=150,39)	21	6		
N/W to G2 (Parameter: hypoalbuminemia) (n=150,39)	10	2		
N/W to G3 (Parameter: hypoalbuminemia) (n=150,39)	2	1		
N/W to G4 (Parameter: hypoalbuminemia) (n=150,39)	0	0		
N/W to G1 (Parameter: hypocalcemia) (n=153,41)	27	2		

N/W to G2 (Parameter: hypocalcemia) (n=153,41)	6	1		
N/W to G3 (Parameter: hypocalcemia) (n=153,41)	3	0		
N/W to G4 (Parameter: hypocalcemia) (n=153,41)	0	0		
N/W to G1 (Parameter: hypoglycemia) (n=155,41)	10	4		
N/W to G2 (Parameter: hypoglycemia) (n=155,41)	1	0		
N/W to G3 (Parameter: hypoglycemia) (n=155,41)	0	0		
N/W to G4 (Parameter: hypoglycemia) (n=155,41)	0	0		
N/W to G1 (Parameter: hypokalemia) (n=155,41)	0	0		
N/W to G2 (Parameter: hypokalemia) (n=155,41)	24	8		
N/W to G3 (Parameter: hypokalemia) (n=155,41)	4	1		
N/W to G4 (Parameter: hypokalemia) (n=155,41)	0	0		
N/W to G1 (Parameter: hypomagnesemia) (n=156,41)	24	5		
N/W to G2 (Parameter: hypomagnesemia) (n=156,41)	2	0		
N/W to G3 (Parameter: hypomagnesemia) (n=156,41)	1	0		
N/W to G4 (Parameter: hypomagnesemia) (n=156,41)	1	0		
N/W to G1 (Parameter: hyponatremia) (n=153,40)	29	10		
N/W to G2 (Parameter: hyponatremia) (n=153,40)	0	0		
N/W to G3 (Parameter: hyponatremia) (n=153,40)	11	2		
N/W to G4 (Parameter: hyponatremia) (n=153,40)	0	0		
N/W to G1 (Parameter: hypophosphatemia) (n=153,41)	0	0		
N/W to G2 (Parameter: hypophosphatemia) (n=153,41)	18	4		
N/W to G3 (Parameter: hypophosphatemia) (n=153,41)	2	1		
N/W to G4 (Parameter: hypophosphatemia) (n=153,41)	0	0		
N/W to G1 (Parameter: LI) (n=157,41)	13	4		
N/W to G2 (Parameter: LI) (n=157,41)	9	3		
N/W to G3 (Parameter: LI) (n=157,41)	7	2		
N/W to G4 (Parameter: LI) (n=157,41)	2	1		
N/W to G1 (Parameter: SAI) (n=156,41)	16	3		
N/W to G2 (Parameter: SAI) (n=156,41)	1	2		
N/W to G3 (Parameter: SAI) (n=156,41)	2	2		
N/W to G4 (Parameter: SAI) (n=156,41)	1	1		

Notes:

[4] - Subjects with available data (n=X, X in category titles) were analyzed.

[5] - Subjects with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Lowest (Trough) Concentration (Ctrough) of Avelumab

End point title	Serum Lowest (Trough) Concentration (Ctrough) of Avelumab

End point description:

Ctrough was defined as predose concentration during multiple dosing. The determination method of Ctrough was observing directly from data.
The lower limit of quantification (LLQ) was 0.2 mcg/mL.
For Cycle 1 Day 1, as the number of observations above lower limit of quantification (NALQ) = 0, summary statistics were not presented.
The avelumab PK concentration analysis set included all subjects (Cohort 1 and Cohort 2 combined) who received at least 1 dose of study intervention and had at least one concentration measurement for avelumab. Number of subjects analyzed = number of subjects evaluable for this OM. Number analyzed = subjects evaluable at the specific time point.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 3, 6, 12, 18, 24 and Day 15 of Cycle 1

End point values	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib			
Subject group type	Subject analysis set			
Number of subjects analysed	199[6]			
Units: microgram(mcg)/milliliter(mL)				
geometric mean (geometric coefficient of variation)				
CYCLE1DAY1 (n=180)	99999 (± 99999)			
CYCLE1DAY15 (n=164)	21.06 (± 58)			
CYCLE3DAY1 (n=110)	32.65 (± 63)			
CYCLE6DAY1 (n=83)	36.23 (± 60)			
CYCLE12DAY1 (n=35)	41.80 (± 60)			
CYCLE18DAY1 (n=16)	35.19 (± 54)			
CYCLE24DAY1 (n=10)	37.21 (± 54)			

Notes:

[6] - 99999 is entered for data not presented.
n=subjects analyzed with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Maximum Concentration (Cmax) for Avelumab

End point title	Serum Maximum Concentration (Cmax) for Avelumab

End point description:

Cmax was defined as maximum observed plasma concentration. The determination method of Cmax was observing directly from data. The avelumab PK concentration analysis set included all subjects (Cohort 1 and Cohort 2 combined) who received at least 1 dose of study intervention and had at least one concentration measurement for avelumab. Number of subjects analyzed = number of subjects evaluable for this OM. Number analyzed = subjects evaluable at the specific time point.

End point type	Secondary

End point timeframe:

One hour post-dose on Day 1 of Cycles 1, 3, 6, 12, 18, 24 and Day 15 of Cycle 1

End point values	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib			
Subject group type	Subject analysis set			
Number of subjects analysed	199[7]			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)				
CYCLE1DAY1 (n=161)	223.0 (± 39)			
CYCLE1DAY15 (n=146)	221.6 (± 38)			
CYCLE3DAY1 (n=114)	225.6 (± 34)			
CYCLE6DAY1 (n=79)	222.3 (± 37)			
CYCLE12DAY1 (n=35)	248.2 (± 25)			
CYCLE18DAY1 (n=17)	265.9 (± 20)			
CYCLE24DAY1 (n=9)	286.1 (± 21)			

Notes:

[7] - Subjects with available data (n=X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Ctrough for Talazoparib

End point title	Plasma Ctrough for Talazoparib

End point description:

Ctrough was defined as predose concentration during multiple dosing. The determination method of Ctrough was observing directly from data. For Cycle 1 Day 1, as the number of observations above lower limit of quantification (NALQ) = 0, summary statistics were not presented.
Evaluable subjects were subjects with non-missing Ctrough concentrations at each specific time point and meeting 2 conditions: subjects received 14 consecutive days of talazoparib dose without dosing interruption prior to sample collection (except on Cycle 1 Day 1) and sample collection within 24 hours ± 10% (2 hours and 24 minutes) after the previous day's dose and no more than 5 minutes (0.083 hours) after the administration of the dose on the day of PK sample collection. Predose PK samples on Cycle 1 Day 1 must have been collected prior to dose.
The analysis set included all subjects who received at least 1 dose of study intervention and had at least one Ctrough concentration measurement for talazoparib.

End point type	Secondary

End point timeframe:

Predose on Cycle 1 Days 1, 15 and Cycle 3 Day 1

End point values	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib			
Subject group type	Subject analysis set			
Number of subjects analysed	199[8]			
Units: picogram(pg)/mL				
geometric mean (geometric coefficient of variation)				
CYCLE1DAY1 (Starting Dose: 1 mg QD) (n=170)	99999 (± 99999)			
CYCLE1DAY15 (Starting Dose: 1 mg QD) (n=62)	4649 (± 61)			
CYCLE3DAY1 (Starting Dose: 1 mg QD) (n=30)	3313 (± 113)			
CYCLE1DAY1 (Starting Dose: 0.75 mg QD) (n=16)	99999 (± 99999)			
CYCLE1DAY15 (Starting Dose: 0.75 mg QD) (n=2)	7612 (± 99999)			
CYCLE3DAY1 (Starting Dose: 0.75 mg QD) (n=4)	4314 (± 42)			

Notes:

[8] - 99999 is entered for data not presented or not estimable.
n=subjects analyzed with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Post-dose Concentrations for Talazoparib

End point title	Plasma Post-dose Concentrations for Talazoparib

End point description:

In this OM, the post-dose concentrations for talazoparib in plasma were reported.
The Analysis Population included all subjects (Cohort 1 and Cohort 2 combined) who received at least 1 dose of talazoparib, had at least one non-missing concentration measurement at any collection scheduled time point, received 14 consecutive days of talazoparib dose without dosing interruption prior to sample collection (except on Cycle 1 Day 1) and sample collection was performed within ± 10% (12 minutes) of nominal time post-dose.

End point type	Secondary

End point timeframe:

Postdose (samples collected within 2 hours post dose plus/minus 12 minutes) on Days 1,15 of Cycle 1, and Day 1 of Cycle 3

End point values	Avelumab 800 mg Intravenous (IV) Q2W plus talazoparib			
Subject group type	Subject analysis set			
Number of subjects analysed	106[9]			
Units: pg/mL				

geometric mean (geometric coefficient of variation)				
CYCLE1DAY1 (Starting Dose: 1 mg QD) (n=76)	1833 (± 275)			
CYCLE1DAY15 (Starting Dose: 1 mg QD) (n=51)	7985 (± 79)			
CYCLE3DAY1 (Starting Dose: 1 mg QD) (n=22)	7800 (± 69)			
CYCLE1DAY1 (Starting Dose: 0.75 mg QD) (n=6)	1663 (± 100)			
CYCLE1DAY15 (Starting Dose: 0.75 mg QD) (n=6)	12590 (± 47)			
CYCLE3DAY1 (Starting Dose: 0.75 mg QD) (n=3)	8366 (± 53)			

Notes:

[9] - Subjects with available data (n=X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects by Avelumab Anti-drug Antibody (ADA) Categories

End point title	Number of Subjects by Avelumab Anti-drug Antibody (ADA) Categories

End point description:

Blood samples were assayed for ADA. ADA never-positive=no positive ADA results at any time point. ADA ever-positive=at least one positive ADA result at any time point. Baseline ADA positive=a positive ADA result at baseline. Treatment-boosted ADA=a positive ADA result at baseline and the titer >=8×baseline titer at least once after treatment with avelumab. Treatment-induced ADA=subject was ADA-negative at baseline and had at least one positive post-baseline ADA result; or had at least one positive post-baseline ADA result if no baseline sample. Transient ADA response=subjects with treatment-induced ADA had (a single positive ADA result or duration between first and last positive result <16weeks) and ADA result at the last assessment was not positive. Persistent ADA response=subjects with treatment-induced ADA had duration between first & last positive ADA result >=16weeks or a positive ADA result at the last assessment. Analysis population=subjects with >=1 ADA sample for avelumab.

End point type	Secondary

End point timeframe:

Predose (within 2 hours before start of avelumab infusion) on Day 1 of Cycles 1, 3, 6, 12, 18, 24 and Day 15 of Cycle 1

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[10]	40[11]		
Units: Subjects				
ADA never-positive (n=159,40)	153	39		
ADA ever-positive (n=159,40)	6	1		
Baseline ADA positive (n=150,38)	5	1		
Treatment-boosted ADA (n=143,37)	0	0		
Treatment-induced ADA (n=147,38)	1	0		
Transient ADA response (n=147,38)	1	0		

Persistent ADA response (n=147,38)	0	0		

Notes:

[10] - Subjects with available data (n=X, X in category titles) were analyzed.

[11] - Subjects with available data (n=X, X in category titles) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Neutralizing Antibodies (Nab) Levels Against Avelumab Ever-Positive

End point title	Number of Subjects With Neutralizing Antibodies (Nab) Levels Against Avelumab Ever-Positive

End point description:

Nab ever-positive was defined as at least one positive Nab result at any time point. Samples positive for ADA with persistent treatment-induced ADA response could be analyzed for Nab. The immunogenicity analysis set included subjects who had at least 1 Nab sample collected for avelumab. Nabs data were not collected due to insufficient number of subjects with persistent treatment-induced ADA response. Therefore, the number of subjects analyzed for this OM was 0.

End point type	Secondary

End point timeframe:

Predose (within 2 hours before start of avelumab infusion) on Day 1 of Cycles 1, 3, 6, 12, 18, 24 and Day 15 of Cycle 1

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Subjects				

Notes:

[12] - Data were not collected due to insufficient subjects with persistent treatment-induced ADA response.

[13] - Data were not collected due to insufficient subjects with persistent treatment-induced ADA response.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Confirmed OR as Assessed by The Investigator

End point title	Percentage of Subjects With Confirmed OR as Assessed by The Investigator

End point description:

For subjects with solid tumors, except mCRPC, OR was defined as a CR or PR per RECIST v1.1, both confirmed by repeat assessments performed no less than 4 weeks after the criteria for response were first met. For subjects with mCRPC, OR was defined as the percentage of subjects with a best overall soft tissue response of CR or PR per RECIST v1.1 with no evidence of confirmed bone disease progression per PCWG3 criteria. Per RECIST v1.1, CR was defined as complete disappearance of all target and non-target lesions with the exception of nodal disease. PR was defined as greater than or equal to 30% decrease under baseline of the sum of diameters of all target measurable lesions. Non-

target PR lesions must be non-PD, where PD was unequivocal progression of pre-existing lesions.

End point type	Secondary

End point timeframe:

From the first dose of study treatment until the date of first documented disease progression or date of death from any cause, whichever comes first, assessed up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Percentage of subjects				
number (confidence interval 95%)	34.6 (27.2 to 42.5)	14.6 (5.6 to 29.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR) as Assessed by BICR

End point title	Time to Tumor Response (TTR) as Assessed by BICR

End point description:

For subjects with solid tumors, except mCRPC: TTR was defined for subjects with confirmed objective response (CR or PR) as the time from the first dose of study treatment to the first documentation of objective tumor response.
For subjects with mCRPC: TTR was defined as the time from the first dose of study treatment to the first objective evidence of soft tissue response with no evidence of confirmed bone disease progression on bone scan per PCWG3. Soft tissue response was defined as a Best Overall Response (BOR) of CR or PR per RECIST v1.1. The analysis population included all enrolled subjects who received at least 1 dose of study treatment and with confirmed CR or PR as assessed by BICR.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	3		
Units: Months				
median (full range (min-max))	1.82 (1.5 to 12.1)	5.52 (1.6 to 16.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: TTR as Assessed by Investigator

End point title	TTR as Assessed by Investigator

End point description:

For subjects with solid tumors, except mCRPC: TTR was defined for subjects with confirmed objective response (CR or PR) as the time from the first dose of study treatment to the first documentation of objective tumor response.
For subjects with mCRPC: TTR was defined as the time from the first dose of study treatment to the first objective evidence of soft tissue response with no evidence of confirmed bone disease progression on bone scan per PCWG3. Soft tissue response was defined as a BOR of CR or PR per RECIST v1.1. The analysis population included all enrolled subjects who received at least 1 dose of study treatment and with confirmed CR or PR as assessed by investigator.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	6		
Units: Months				
median (full range (min-max))	1.84 (1.5 to 18.4)	3.99 (1.9 to 14.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: DoR as Assessed by Investigator

End point title	DoR as Assessed by Investigator

End point description:

For subjects with solid tumors, except mCRPC: DoR was defined for subjects with confirmed objective response (CR or PR) as the time from the first documentation of objective tumor response to the first documentation of objective tumor progression or to death due to any cause, whichever occurred first.
For subjects with mCRPC:DoR was defined for subjects with confirmed objective response (CR or PR) as the time from the first objective evidence of soft tissue response (subsequently confirmed) per RECIST v1.1 and no evidence of confirmed bone disease progression by PCWG3 to the first subsequent objective evidence of radiographic progression or death due to any cause, whichever occurred first. Radiographic progression was defined as soft tissue progression evaluated per RECIST v1.1 or bone disease

progression evaluated per PCWG3.
The analysis population included all enrolled subjects who received at least 1 dose of study treatment and with confirmed CR or PR as assessed by investigator.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	6		
Units: Months				
median (confidence interval 95%)	8.8 (7.5 to 10.7)	7.1 (5.5 to 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) as Assessed by BICR

End point title	Duration of Response (DoR) as Assessed by BICR

End point description:

For subjects with solid tumors, except mCRPC: DoR was defined for subjects with confirmed objective response (CR or PR) as the time from the first documentation of objective tumor response to the first documentation of objective tumor progression or to death due to any cause, whichever occured first.
For subjects with mCRPC: DoR was defined for subjects with confirmed objective response (CR or PR) as the time from the first objective evidence of soft tissue response (subsequently confirmed) per RECIST v1.1 and no evidence of confirmed bone disease progression by PCWG3 to the first subsequent objective evidence of radiographic progression or death due to any cause, whichever occured first. Radiographic progression was defined as soft tissue progression evaluated per RECIST v1.1 or bone disease progression evaluated per PCWG3.
The analysis population included all enrolled subjects who received at least 1 dose of study treatment and with confirmed CR or PR as assessed by BICR.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[14]	3[15]		
Units: Months				
median (confidence interval 95%)	12.5 (7.5 to 99999)	99999 (6.7 to 99999)		

Notes:

[14] - Reason for 99999: the upper limit of the confidence interval (CI) is not crossing the 50% bound.

[15] - Reason for 99999: the median and upper limit of the CI are not crossing the 50% bound.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) as Assessed by BICR

End point title	Progression Free Survival (PFS) as Assessed by BICR

End point description:

For subjects with solid tumors, except mCRPC: PFS was defined as the time from the first dose of study treatment to the date of disease progression by RECIST v1.1 or death due to any cause, whichever occurred first.
For subjects with mCRPC: PFS was defined as the time from the first dose of study treatment to documentation of radiographic progression in soft tissue evaluated per RECIST v1.1, in bone evaluated per PCWG3, or death, whichever occurred first.
All efficacy analyses were performed based on the full analysis set. The full analysis set included all enrolled subjects who received at least 1 dose of study treatment. Subjects were classified according to the cohort assigned at enrollment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Months				
median (confidence interval 95%)	3.7 (3.1 to 5.4)	3.5 (1.8 to 5.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by Investigator

End point title	PFS as Assessed by Investigator

End point description:

For subjects with solid tumors, except mCRPC: PFS was defined as the time from the first dose of study treatment to the date of disease progression by RECIST v1.1 or death due to any cause, whichever occurred first.
For subjects with mCRPC: PFS was defined as the time from the first dose of study treatment to documentation of radiographic progression in soft tissue evaluated per RECIST v1.1, in bone evaluated per PCWG3, or death, whichever occurred first.
All efficacy analyses were performed based on the full analysis set. The full analysis set included all enrolled subjects who received at least 1 dose of study treatment. Subjects were classified according to

the cohort assigned at enrollment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Months				
median (confidence interval 95%)	5.3 (3.7 to 5.6)	3.7 (2.1 to 7.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) for All Subjects

End point title	Overall Survival (OS) for All Subjects

End point description:

OS was defined as the time from the first dose of study treatment to the date of death. Subjects without an event (death) were censored at the date of last contact. All efficacy analyses were performed based on the full analysis set. The full analysis set included all enrolled subjects who received at least 1 dose of study treatment. Subjects were classified according to the cohort assigned at enrollment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Months				
median (confidence interval 95%)	11.9 (10.1 to 13.7)	16.4 (12.8 to 21.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Prostate-Specific Antigen (PSA) Progression for Subjects With mCRPC

End point title	Time to Prostate-Specific Antigen (PSA) Progression for Subjects With mCRPC

End point description:

For subjects with mCRPC, time to PSA progression was defined as the time from the first dose to the date that a >=25% increase in PSA with an absolute increase of >=2 µg/L (2 ng/mL) above the nadir (or baseline for subjects with no PSA decline) was documented, confirmed by a second consecutive PSA value obtained >=3 weeks (21 days) later. The analysis population included all subjects with mCRPC who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	5[16]		
Units: Months				
median (confidence interval 95%)	6.5 (3.7 to 12.7)	11.3 (3.7 to 99999)		

Notes:

[16] - The upper limit of the CI is not crossing the 50% bound, thus 99999 is entered.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed PSA Response

End point title	Number of Subjects With Confirmed PSA Response

End point description:

For subjects with mCRPC, PSA response was defined as confirmed PSA decline >=50% compared to baseline. PSA response was calculated as a decline from baseline PSA (ng/mL) to the maximal PSA response with a threshold of 50%. A PSA response must have been confirmed by a second consecutive value at least 3 weeks later. The analysis population included all subjects with mCRPC who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline up to approximately 24 months

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	5		

Units: Subjects	17	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Circulating Tumor Cell (CTC) Count Conversion

End point title	Number of Subjects With Circulating Tumor Cell (CTC) Count Conversion

End point description:

For subjects with mCRPC, CTC count conversion was defined as a decrease in CTC count from >=5 CTC per 7.5 mL of blood at baseline to <5 CTC per 7.5 mL of blood anytime on study. The analysis population included all enrolled subjects with mCRPC who received at least 1 dose of study treatment, and with CTC count >=5 CTC per 7.5 mL of blood at baseline.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1 to Cycle 4

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	2		
Units: Subjects	11	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Cancer Antigen 125 (CA-125) Response

End point title	Number of Subjects With Cancer Antigen 125 (CA-125) Response

End point description:

For subjects with ovarian cancer, CA-125 response was defined as at least a 50% reduction in CA-125 levels from baseline. The response must have been confirmed and maintained for at least 28 days. The analysis population included all subjects with ovarian cancer who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each treatment Cycle, maximum up to 4.3 years approximately

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	3		
Units: Subjects	9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Different Status for Defects in BRCA1, BRCA2 and ATM

End point title	Number of Subjects With Different Status for Defects in BRCA1, BRCA2 and ATM

End point description:

Subjects were enrolled in the two cohorts based on BRCA 1/2 and ATM defect status assessed by the local laboratory. The subject BRCA and ATM status was assessed retrospectively by central laboratory, that may differ from the status assessed by the local laboratory. The ATM subjects with a negative ATM status per the central laboratory were reported to have a positive ATM status per the local laboratory. Therefore, subjects with negative ATM status might have been included in the ATM defect cohort. For defects in BRCA1, BRCA2 and ATM by central laboratory analysis, subjects were classified as positive, negative, not analyzable or missing. The number of subjects in each category of BRCA 1 defect, BRCA 2 defect, BRCA 1 or BRCA 2 defect and ATM defect were presented. The biomarker analysis set included all subjects who received at least 1 dose of study treatment and had at least 1 screening biomarker assessment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Subjects				
BRCA1 status positive	52	0		
BRCA1 status negative	65	29		
BRCA1 status not analyzable	21	4		
BRCA1 status missing	21	8		
BRCA2 status positive	53	1		
BRCA2 status negative	64	28		
BRCA2 status not analyzable	21	4		
BRCA2 status missing	21	8		

BRCA status positive	105	1		
BRCA status negative	12	28		
BRCA status not analyzable	21	4		
BRCA status missing	21	8		
ATM status positive	2	26		
ATM status negative	115	3		
ATM status not analyzable	21	4		
ATM status missing	21	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Programmed Death Ligand 1 (PD-L1) Expression in Baseline Tumor Tissue

End point title	Number of Subjects With Positive Programmed Death Ligand 1 (PD-L1) Expression in Baseline Tumor Tissue

End point description:

PD-L1 expression on tumor and infiltrating immune cells was measured by immunohistochemistry (IHC). PD-L1 expression level was defined as the number of PD-L1 positive cells and/or qualitative assessment of PD-L1 staining on tumor and inflammatory cells in regions of interest. This OM reported the number of subjects classified as positive according to scoring algorithms and cut-offs established from external sources. The biomarker analysis set included all subjects who received at least 1 dose of study treatment and had at least 1 screening biomarker assessment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Subjects	27	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects by Status of Tumor Mutational Burden (TMB) at Baseline

End point title	Number of Subjects by Status of Tumor Mutational Burden (TMB) at Baseline

End point description:

TMB was defined as the total number of mutations in the tumor genome, or number of mutations per megabase of DNA if derived from targeted sequencing. TMB categories were defined as high, low for a

number of mutations per megabase >=10 and <10, respectively. The TMB category 'Not analyzable' included subjects with available samples but not evaluable. The TMB category 'Missing' included subjects with no sample available. The number of subjects in each category at only baseline were tabulated. The biomarker analysis set included all subjects who received at least 1 dose of study treatment and had at least 1 screening biomarker assessment.

End point type	Secondary

End point timeframe:

Baseline

End point values	Cohort 1 (BReast CAncer Gene [BRCA] 1/2 defect)	Cohort 2 (Ataxia Telangiectasia Mutated [ATM] defect)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	41		
Units: Subjects				
TMB status high	9	2		
TMB status low	95	23		
TMB status not analyzable	34	8		
TMB status missing	21	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 30 days after last dose of study treatment, maximum up to 4.3 years approximately.

Adverse event reporting additional description:

The same event may appear as both an AE and an SAE. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and nonserious event during the study. Total number at risk below refers to the number of subjects evaluable for SAEs or AEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Cohort 2 (ATM defect)

Reporting group description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the ATM gene without concurrent BRCA1/2 defect were enrolled in Cohort 2. Talazoparib was self-administered orally at a starting dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Reporting group title	Cohort 1 (BRCA 1/2 defect)

Reporting group description:

Subjects with locally advanced or metastatic solid tumors with one or more defects in the BRCA1 or BRCA2 genes were enrolled in Cohort 1. Talazoparib was self-administered orally at a starting dose of 1 mg QD for subjects with normal renal function or mild renal impairment until End of Treatment. Subjects with moderate renal impairment received starting dose of 0.75 mg QD. Avelumab was administered as a 1-hour IV infusion Q2W on Days 1 and 15 of each 28-day cycle at a dose of 800 mg after administration of talazoparib and the premedication.

Serious adverse events	Cohort 2 (ATM defect)	Cohort 1 (BRCA 1/2 defect)	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 41 (17.07%)	50 / 159 (31.45%)	
number of deaths (all causes)	3	15	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			

subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant neoplasm progression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 41 (4.88%)	8 / 159 (5.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
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 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	0 / 41 (0.00%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 41 (0.00%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 41 (4.88%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 41 (4.88%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	5 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Weight decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin T increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infusion related reaction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 41 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 41 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Depressed level of consciousness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone marrow disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 41 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 41 (0.00%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine polyp			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 41 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral obstruction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
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	1 / 41 (2.44%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Osteitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacterial abdominal infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clostridial infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 41 (2.44%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	Cohort 2 (ATM defect)	Cohort 1 (BRCA 1/2 defect)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 41 (97.56%)	153 / 159 (96.23%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 41 (7.32%)	2 / 159 (1.26%)	
occurrences (all)	4	4	
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 41 (7.32%)	1 / 159 (0.63%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 41 (4.88%)	27 / 159 (16.98%)	
occurrences (all)	2	57	
Chills			
subjects affected / exposed	5 / 41 (12.20%)	17 / 159 (10.69%)	
occurrences (all)	6	22	
Fatigue			
subjects affected / exposed	19 / 41 (46.34%)	50 / 159 (31.45%)	
occurrences (all)	23	89	
Influenza like illness			
subjects affected / exposed	2 / 41 (4.88%)	10 / 159 (6.29%)	
occurrences (all)	2	12	
Oedema peripheral			
subjects affected / exposed	4 / 41 (9.76%)	12 / 159 (7.55%)	
occurrences (all)	4	13	
Pyrexia			

subjects affected / exposed	3 / 41 (7.32%)	28 / 159 (17.61%)	
occurrences (all)	4	35	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 41 (12.20%)	19 / 159 (11.95%)	
occurrences (all)	6	23	
Dyspnoea			
subjects affected / exposed	8 / 41 (19.51%)	34 / 159 (21.38%)	
occurrences (all)	9	53	
Nasal congestion			
subjects affected / exposed	1 / 41 (2.44%)	10 / 159 (6.29%)	
occurrences (all)	1	11	
Productive cough			
subjects affected / exposed	3 / 41 (7.32%)	8 / 159 (5.03%)	
occurrences (all)	3	10	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 41 (12.20%)	21 / 159 (13.21%)	
occurrences (all)	6	22	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 41 (17.07%)	16 / 159 (10.06%)	
occurrences (all)	11	27	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 41 (14.63%)	18 / 159 (11.32%)	
occurrences (all)	13	31	
Blood bilirubin increased			
subjects affected / exposed	3 / 41 (7.32%)	8 / 159 (5.03%)	
occurrences (all)	5	12	
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 41 (9.76%)	7 / 159 (4.40%)	
occurrences (all)	12	8	
Blood creatinine increased			
subjects affected / exposed	5 / 41 (12.20%)	3 / 159 (1.89%)	
occurrences (all)	10	5	

Lymphocyte count decreased			
subjects affected / exposed	3 / 41 (7.32%)	2 / 159 (1.26%)	
occurrences (all)	4	21	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 41 (7.32%)	9 / 159 (5.66%)	
occurrences (all)	3	21	
Neutrophil count decreased			
subjects affected / exposed	5 / 41 (12.20%)	21 / 159 (13.21%)	
occurrences (all)	10	55	
Weight decreased			
subjects affected / exposed	2 / 41 (4.88%)	10 / 159 (6.29%)	
occurrences (all)	3	13	
White blood cell count decreased			
subjects affected / exposed	4 / 41 (9.76%)	12 / 159 (7.55%)	
occurrences (all)	9	24	
Platelet count decreased			
subjects affected / exposed	11 / 41 (26.83%)	25 / 159 (15.72%)	
occurrences (all)	19	71	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	3 / 41 (7.32%)	22 / 159 (13.84%)	
occurrences (all)	3	23	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 41 (2.44%)	19 / 159 (11.95%)	
occurrences (all)	1	24	
Headache			
subjects affected / exposed	6 / 41 (14.63%)	35 / 159 (22.01%)	
occurrences (all)	6	48	
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 41 (7.32%)	5 / 159 (3.14%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 41 (9.76%)	20 / 159 (12.58%)	
occurrences (all)	6	57	

Anaemia			
subjects affected / exposed	18 / 41 (43.90%)	81 / 159 (50.94%)	
occurrences (all)	52	269	
Thrombocytopenia			
subjects affected / exposed	5 / 41 (12.20%)	27 / 159 (16.98%)	
occurrences (all)	8	62	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	6 / 41 (14.63%)	5 / 159 (3.14%)	
occurrences (all)	6	5	
Abdominal pain			
subjects affected / exposed	6 / 41 (14.63%)	30 / 159 (18.87%)	
occurrences (all)	8	42	
Ascites			
subjects affected / exposed	3 / 41 (7.32%)	1 / 159 (0.63%)	
occurrences (all)	3	2	
Constipation			
subjects affected / exposed	8 / 41 (19.51%)	39 / 159 (24.53%)	
occurrences (all)	10	52	
Diarrhoea			
subjects affected / exposed	10 / 41 (24.39%)	36 / 159 (22.64%)	
occurrences (all)	16	75	
Dyspepsia			
subjects affected / exposed	3 / 41 (7.32%)	10 / 159 (6.29%)	
occurrences (all)	3	11	
Nausea			
subjects affected / exposed	21 / 41 (51.22%)	73 / 159 (45.91%)	
occurrences (all)	27	102	
Vomiting			
subjects affected / exposed	11 / 41 (26.83%)	39 / 159 (24.53%)	
occurrences (all)	16	48	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 41 (7.32%)	19 / 159 (11.95%)	
occurrences (all)	3	20	
Pruritus			

subjects affected / exposed	1 / 41 (2.44%)	10 / 159 (6.29%)	
occurrences (all)	1	13	
Dry skin			
subjects affected / exposed	4 / 41 (9.76%)	5 / 159 (3.14%)	
occurrences (all)	5	5	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	5 / 41 (12.20%)	10 / 159 (6.29%)	
occurrences (all)	8	11	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 41 (26.83%)	30 / 159 (18.87%)	
occurrences (all)	13	37	
Back pain			
subjects affected / exposed	10 / 41 (24.39%)	21 / 159 (13.21%)	
occurrences (all)	16	23	
Myalgia			
subjects affected / exposed	2 / 41 (4.88%)	16 / 159 (10.06%)	
occurrences (all)	2	18	
Neck pain			
subjects affected / exposed	2 / 41 (4.88%)	9 / 159 (5.66%)	
occurrences (all)	3	12	
Pain in extremity			
subjects affected / exposed	5 / 41 (12.20%)	7 / 159 (4.40%)	
occurrences (all)	5	11	
Infections and infestations			
Sinusitis			
subjects affected / exposed	3 / 41 (7.32%)	1 / 159 (0.63%)	
occurrences (all)	3	1	
Upper respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)	12 / 159 (7.55%)	
occurrences (all)	3	13	
Urinary tract infection			
subjects affected / exposed	7 / 41 (17.07%)	11 / 159 (6.92%)	
occurrences (all)	8	14	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	12 / 41 (29.27%)	33 / 159 (20.75%)	
occurrences (all)	19	41	
Hypokalaemia			
subjects affected / exposed	5 / 41 (12.20%)	8 / 159 (5.03%)	
occurrences (all)	11	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2018	1. Based on limitations in utility of this and/or complexity to collect this exploratory endpoint, irRECIST assessments and any associated elements were removed or revised accordingly. 2. To help facilitate study conduct, the Schedule of Activities has been modified with a -1 day window for the baseline physical examination and a +/ 3 day window (formerly +/- 2 day) for treatment visits. 3. To help facilitate study conduct, the Schedule of Activities and Section 7.8 has been modified to clarify that Patient Reported Outcome assessments are not required when not available in a language understood by the patient, and to provide a window for shipment of pre-treatment tumor tissue. 4. The background section has been updated with health authority approvals for Avelumab and Talazoparib. 5. Consistent with the updated Avelumab Investigator's Brochure (version 8, 16 May 2018), the protocol was revised to update background information and recommendation for management of Grade 1 to 2 immune-related rash was updated. 6. Consistent with the updated Talazoparib Investigator's Brochure (dated August 2018), the protocol was revised to provide updated background information on clinical experience and pharmacokinetic information, to increase the duration of contraception use, and to simplify language regarding prohibited medication P-gp inhibitors. 7. Preliminary safety information and the recommended phase 2 dose from the B9991025 study has been added to the Background, Allocation to Treatment and Talazoparib administration sections. 8. Use of a Patient Enrollment Verification Form has been added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported