# 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<br>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<br>Units: Years | | | |
| arithmetic mean | 57.35 | 61.76 | |
| standard deviation | ± 12.88 | ± 12.47 | - |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 108 | 24 | 132 |
| Male | 51 | 17 | 68 |
| Race/Ethnicity, Customized<br>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)<br>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<br>Units: Subjects | | | |
| < 65 years | 135 | | |
| 65 - <75 years | 45 | | |
| 75 - <85 years | 18 | | |
| >=85 years | 2 | | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 58.25 | | |
| standard deviation | ± 12.89 | | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 132 | | |
| Male | 68 | | |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Black or African American | 11 | | |
| American Indian or Alaska Native | 1 | | |
| Asian | 15 | | |
| White | 154 | | |
| Not reported | 19 | | |
| Ethnicity (NIH/OMB)<br>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 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[6] | | | |
| 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:

[6] - Subjects with available data (n=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[7] | | | |
| 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:

[7] - 99999 is entered for data not presented.
n=subjects analyzed with available data.

## 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: 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[9] | 40[10] | | |
| 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:

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

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

### 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[11] | | | |
| 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:

[11] - Subjects with available data (n=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: 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: 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: 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: 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: 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: 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: 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: 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 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 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 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 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