Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Definitions of Select Terms and End Points

For patients with solid tumors, except metastatic castration-resistant prostate cancer (mCRPC)

- **Objective response (OR)** was defined as a complete response (CR) or partial response (PR) per RECIST v1.1 from the first dose of study treatment until disease progression or death due to any cause. Both CR and PR must have been confirmed by repeat assessments performed ≥4 weeks after initial documentation
- **OR rate (ORR)** was defined as the proportion of patients with a confirmed CR or PR according to RECIST v1.1. Confirmed responses were those that persisted on repeat tumor assessments for ≥4 weeks after initial documentation or response. Otherwise, the patient was counted as a nonresponder in the assessment of ORR. Additionally, patients with inadequate data for tumor assessment (eg, no baseline assessment or no follow-up assessments) were considered as nonresponders in the assessment of ORR
- **Time to response (TTR)** was defined for patients with confirmed OR (CR or PR) as the time from the first dose of study treatment to the first documentation of objective tumor response
- **Duration of response (DOR)** was defined for patients with confirmed OR (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
- **Progression-free survival (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
- **Overall survival (OS)** was defined as the time from the first dose of study treatment to the date of death

For patients with mCRPC

- **OR** was defined as the proportion of patients with a best overall soft tissue response of CR or PR per RECIST v1.1 from the first dose of study treatment until disease progression or death due to any cause. Soft tissue responses were confirmed by a follow-up radiographic assessment ≥4 weeks later with a repeated computed tomography (CT) or magnetic resonance imaging (MRI) scan with no evidence of confirmed bone disease progression per Prostate Cancer Working Group 3 (PCWG3) criteria. The radiographic assessment of soft tissue disease used RECIST v1.1, and bone disease was evaluated per PCWG3
- **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 is defined as a CR or PR per RECIST v1.1. The response must have been confirmed ≥4 weeks later with a repeated CT or MRI scan
- **DOR** was defined for patients with confirmed OR (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 v1.1or bone disease progression per PCWG3
- **PFS** was defined as the time from the first dose of study treatment to documentation of radiographic progression in soft tissue per RECIST v1.1 or in bone per PCWG3 or death, whichever occurred first

- **Prostate-specific antigen (PSA) response** was defined as the proportion of patients with confirmed PSA decline ≥50% compared with baseline. PSA response will be 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 ≥3 weeks later
- **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 patients with no PSA decline) was documented, confirmed by a second consecutive PSA value obtained ≥3 weeks (21 days) later
- **OS** was defined as the time from the first dose of study treatment to the date of death

For patients with ovarian cancer

- **Cancer antigen 125 (CA-125) response** was defined as a ≥50% reduction in CA-125 level from baseline. The response must have been confirmed and maintained for ≥28 days

eAppendix 2. Supplementary Methods

Biomarker Analyses

Archival or de novo baseline tumor tissue (from a diagnostic biopsy/surgery or a metastatic tumor biopsy obtained within 24 months prior to study enrollment) was centrally tested using FoundationOne CDx for known or likely pathogenic variants in *BRCA1*, *BRCA2*, and *ATM.* This hybrid capture-based next-generation sequencing (NGS) assay includes all exons of a panel of 324 genes, including *BRCA1*, *BRCA2*, and *ATM* and detects select genomic rearrangements (F1CDx_Technical_Specifications, Nov 2020). As FoundationOne CDx sequences tumor tissue without matched normal tissue, somatic-germline-zygosity analysis was used to predict germline vs somatic origin and zygosity (homozygous/hemizygous, hereafter termed homozygous, vs heterozygous) of the qualifying alterations.[1] A panel of 31 additional genes implicated directly or indirectly in DNA damage response was assessed using Foundation One CDx for exploratory analyses: *ATR*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *ERCC4*, *FANCA*, *FANCC*, *FANCG*, *FANCL*, *MLH1*, *MRE11*, *MSH2*, *MSH6*, *MUTYH*, *NBN*, *PALB2*, *PARP1*, *PARP2*, *PARP3*, *PMS2*, *POLD1*, *POLE*, *RAD51*, *RAD51B*, *RAD51C*, *RAD51D*, *RAD52*, *RAD54L*, *XRCC2*, and *XRCC3*.

Tumor mutational burden (TMB) was estimated using FoundationOne CDx with high, medium, or low TMB status defined as ≥20, ≥10 to <20, or <10 mutations per 1 Mb of DNA, respectively. The Foundation Medicine pipeline uses a default medium threshold of ≥6 mut/Mb, but ≥10 mut/Mb was used as the threshold for our main analysis based on the June 2020 approval by the US Food and Drug Administration of the anti–PD-1 antagonist pembrolizumab for patients with malignant solid tumors of any histological type with high TMB (≥10 mut/Mb).

Genomic loss of heterozygosity (gLOH) was assessed as a phenotypic output of homologous recombination deficiency (HRD) using genomic analytics at Foundation Medicine. gLOH-high or -low status was based on a threshold of 16%, reflecting the broad utility of this exploratory threshold across multiple tumor types.[2] PD-L1 expression on archival or de novo baseline tumor

tissue was assessed centrally using the Ventana SP263 immunohistochemistry (IHC) assay and scored using the Ventana SP142 IHC assay algorithm at HistoGeneX (Naperville, IL). Tumor samples with PD-L1 expression in ≥5% of immune cells or ≥1% of tumor cells, or ≥50% of tumor cells in non-small cell lung cancer (NSCLC), were positive. Blood samples for PSA analysis for patients with mCRPC and CA-125 levels for patients with ovarian cancer were taken on day 1 of each cycle.

The subset of patients treated at Memorial Sloan Kettering Cancer Center (MSKCC) underwent additional genomic analyses, including targeted NGS, whole-exome sequencing (WES), and/or whole-genome sequencing (WGS). MSKCC was responsible for validation and storage of these data. Targeted NGS was performed to identify and/or confirm the qualifying *BRCA1*, *BRCA2*, or *ATM* mutation(s) using a clinically validated, hybrid capture-based assay, MSK-IMPACT, which sequences tumor and matched normal tissue to identify mutations, copy number changes, and select structural rearrangements.[3,4] WES and WGS were performed on tumors from 20 and 16 patients, respectively. Frozen tumor tissue was weighed, and 20 to 30 mg was homogenized in RLT. DNA was extracted using the AllPrep DNA/RNA Mini Kit (QIAGEN 80204) and then eluted in 0.5× elution buffer. Peripheral blood mononuclear cells were brought up to 15 mL in cold phosphate-buffered saline, isolated with the DNeasy Blood & Tissue Kit (QIAGEN 69504) according to the manufacturer's instructions, and then eluted in 0.5× Buffer AE. For WES, 100 ng of libraries were captured by hybridization using the xGen Exome Research Panel v1.0 (Integrated DNA Technologies) according to the manufacturer's protocol with 8 cycles of polymerase chain reaction (PCR). For WGS, DNA was first quantified with PicoGreen and quality controlled by Agilent BioAnalyzer. In total, 347 to 500 ng of DNA was used to prepare libraries using the KAPA Hyper Prep Kit (Kapa Biosystems KK8504) without PCR amplification. Samples were run on either a HiSeq 4000 in a PE100 run, using the HiSeq 3000/4000 SBS kit (Illumina), or on a NovaSeq 6000 in PE150 runs, using the NovaSeq 6000 SBS v1 kit and an

S1, S2, or S4 flow cell (Illumina) for WES and WGS, respectively. For WES, normal and tumor samples were covered to an average of 260× (range, 196×-555×) and 117× (range, 93×-132×), respectively. Normal samples were covered at an average coverage of 96× (range, 85×-192×) for tumor samples and 46× (range, 39×-192×) for normal samples for WGS.

WES and WGS data were processed and analysed using the TEMPO pipeline (v1.3; https://ccstempo.netlify.app/). In brief, demultiplexed FASTQ files were aligned to the b37 assembly of the human reference genome from the GATK bundle using BWA-MEM (v0.7.17). Aligned reads were converted and sorted into BAM files using samtools (v1.9) and marked for PCR duplicates using GATK MarkDuplicates (v3.8-1). Somatic mutations (single-nucleotide variants [SNVs] and small insertions and deletions) were detected in tumor-normal pairs using MuTect2 (v4.1.0.0) and Strelka2 (v2.9.10), and structural variants were detected using Delly (v0.8.2) and Manta (v1.5.0). Variants were annotated and filtered for recurrent artifacts and false positives using methods as previously described.[5]

TMB, microsatellite instability (MSI) score, mutational signatures, zygosity, allele-specific copy number, cancer cell fractions (CCFs), and neoantigen burden were determined using TEMPO. TMB was defined as the number of nonsynonymous mutations in canonical exons per Mb. MSI score was calculated using MSI sensor, as previously described (v0.5).[6] Mutational signatures were determined via maximum likelihood-based extraction of mutational signature proportions of a set of mutation count data under a known set of inputs signature lists (“refitting”; https://github.com/mskcc/tempoSig). For zygosity determination, genome-wide total and allele-specific DNA copy number, purity, and ploidy were calculated via FACETS v0.5.6.[7] The expected number of copies for each mutation was generated based on observed variant allele fraction and local ploidy.[8] Cancer cell fractions were calculated using a binomial distribution and maximum likelihood estimation normalized to produce posterior probabilities.[9] Putative neoantigens were identified using HLA class 1 alleles identified via Polysolver[10] and considered

"high-affinity binders" by NetMHC 4.0[11] and clonal via CCF estimates described above. The Wilcoxon signed-rank test was used to compare TMB and neoantigen burden in patients with and without a response to treatment.

eAppendix 3. Supplementary Results

Biomarker Analyses

In total, 52/66 tumors (78.8%) evaluable for zygosity in the *BRCA1/2* cohort harbored *BRCA1/2* alterations with allele-specific loss of heterozygosity (LOH; *BRCA1/2* mutations under LOH), and 14/66 tumors (21.2%) did not have allele-specific LOH (**Supplemental Table 4**). The *ATM* cohort included 9/22 patients (40.9%) with tumors harboring *ATM* mutations under LOH. Of the 2 patients with *ATM* alterations who responded to therapy, 1 mutation was germline and under LOH and the other was somatic and heterozygous. Finally, we assessed whether genome-wide LOH (gLOH) predicted response to PARP inhibitors. Of patients with tumors evaluable for gLOH in the *BRCA1/2* and *ATM* cohorts, respectively, 49/76 (64.5%) and 1/18 (5.6%) were gLOH high (**Supplemental Table 4**). In the *BRCA1/2* cohort, responses occurred in 16/49 patients (32.7%) with gLOH-high tumors and 8/27 patients (29.6%) with gLOH-low tumors; 69.8% of *BRCA1/2*-dependent tumors (44/63) were gLOH high and (19/63) patients (30.2%) were gLOH low, and responses occurred in 16/44 (36.4%) and 6/19 (31.6%), respectively. In patients with non–*BRCA1/2*-dependent tumors, gLOH-high was observed in 5/13 patients (38.5%) with no responses.

In patients with TMB ≥10 mut/Mb or TMB <10 mut/Mb in the *BRCA1/2* cohort (**Supplemental Table 4**), responses occurred in 5/8 (ORR, 62.5%; 95% CI, 24.5%-91.5%) and 22/92 (ORR, 23.9%; 95% CI, 15.6%-33.9%), respectively. When this analysis was confined to patients with measurable disease, this difference was more pronounced and CIs no longer overlapped, with responses in all 5 (ORR, 100%; 95%

CI, 47.8%-100.0%) and 21/71 patients (ORR, 29.6%; 95% CI, 19.3%-41.6%), respectively. In patients with PD-L1+ or PD-L1− tumors, the ORR was 30.8% (95% CI, 14.3%-51.8%) and 26.7% (95% CI, 12.3%-45.9%), respectively.

To determine whether broader DNA sequencing with whole-exome sequencing (WES) and whole-genome sequencing (WGS) could predict response to treatment in a tumor-agnostic fashion, 34 patients underwent further genomic testing at MSKCC (**Supplementary Figure 2 and 3**).

Biomarker Analyses of Patients Treated at MSKCC

The 34 patients who were treated at MSKCC were analyzed using a previously described composite homologous recombination deficiency score[5] that combines orthogonal measures of HRD (large-scale transitions[12] and somatic SNV mutational signature 3[13]) biallelic loss of either *BRCA1* or *BRCA2* was associated with a significantly higher HRD score (*BRCA1*: median, 0.76; range, −0.70 to 2.09; *BRCA2*: median, 0.57; range, −0.83 to 1.25) compared with monoallelic inactivation (*BRCA1*: median, −1.11; range, −1.31 to 0.33; *BRCA2*: median, −0.76; range, −1.04 to 0.41). In contrast, *ATM*-mutant tumors displayed no significant difference in HRD scores between mono- and biallelically inactivated tumors (**Supplementary Figure 3**). Tumors of all 34 patients who underwent further genomic testing had low TMB (median, 2.24; range, 0.31-6.94 mut/Mb) and were microsatellite stable (MSIsensor score, 0-4), including the patients with uLMS who had durable antitumor responses. There was no significant difference between TMB levels in responders and nonresponders (median, 2.65; range, 0.99-5.11 vs median, 2.17; range, 0.31-6.94, respectively; Wilcoxon test $P>.05$). Similarly, baseline neoantigen burden was not significantly different between responders and nonresponders (median, 1.71; range, 1.20-1.80 vs median, 1.12; range, 0.11-2.97, respectively; Wilcoxon test $P>.05$).

Of the 34 patients that underwent further genomic testing: 11 had *BRCA1*-mutated tumors, 15 had *BRCA2*-mutated tumors, and 8 had *ATM*-mutated tumors. WES and WGS were successfully performed in 16 and 20 tumors, respectively, including both WES and WGS in 2 tumors. Seven of 26 patients (27%) with *BRCA1/2*-mutated tumors had confirmed responses, consistent with the response rate in the full *BRCA1/2* cohort (**Supplementary Figure 3**). No patients with *ATM*-altered tumors responded. All responses occurred in patients with *BRCA2* biallelic inactivation, including 4 with homozygous deletions and 3 with germline-truncating mutations with somatic gLOH eliminating the wild-type allele. In the 7 responding patients, 4 had *BRCA1/2*-associated tumor types (2 with HR+/HER2– breast cancer and 2 with mCRPC). The other 3 patients had uLMS; all had somatic loss of *BRCA2* through LOH deletion and continued receiving treatment at the data cutoff with ongoing responses of up to 24 months. All patients with *BRCA1/2* heterozygous mutations that retained the wild-type allele had disease progression at the first tumor assessment.

eTable 1. Patient Disposition and Treatment Exposure

	***BRCA1/2* cohort (n=159)**		***ATM* cohort (n=41)**	
	Avelumab	**Talazoparib**	**Avelumab**	**Talazoparib**
Ongoing treatment, n (%)	26 (16.4)	27 (17.0)	1 (2.4)	1 (2.4)
Discontinued treatment, n (%)	133 (83.6)	132 (83.0)	40 (97.6)	40 (97.6)
Death	3 (1.9)	3 (1.9)	0	0
Progressive disease	102 (64.2)	104 (65.4)	26 (63.4)	26 (63.4)
Adverse event	6 (3.8)	3 (1.9)	3 (7.3)	4 (9.8)
Physician's decision	2 (1.3)	1 (0.6)	0	0
Global deterioration of health status	15 (9.4)	15 (9.4)	5 (12.2)	4 (9.8)
Withdrawal by participant	2 (1.3)	2 (1.3)	6 (14.6)	6 (14.6)
Other	3 (1.9)	4 (2.5)	0	0
Duration of treatment, months				
Median	5.3	5.3	3.7	3.8
Range (minimum-maximum)	(0.5-26.7)	(0.2-26.2)	(0.5-18.6)	(0.5-18.6)

eTable 2. Best Overall Response and Confirmed Objective Response by Investigator

Best overall response, n (%)	***BRCA1/2* cohort (n=159)**	***ATM* cohort (n=41)**
CR	7 (4.4)	0
PR	46 (28.9)	6 (14.6)
SD	47 (29.6)	20 (48.8)
Non-CR/non-PD	3 (1.9)	0
PD	43 (27.0)	12 (29.3)
NE	13 (8.2)	3 (7.3)
ORR, n (%) [95% CI]	53 (33.3) [26.1-42.1]	6 (14.6) [5.6-29.2]

CR, complete response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

eTable 3. Best Overall Response and Confirmed Objective Response by BICR With Measurable Disease in *BRCA*-Dependent Tumors and in the *BRCA1/2* Cohort in Tumor Types With at Least 5 Patients

Best overall response, n (%)		***BRCA1/2* cohort**											***ATM* cohort**
	BICR	***BRCA*-dependent tumor types[a]**		***BRCA1/2* by tumor types with ≥5 patients**									**BICR**
	(N=126)	***BRCA*-dependent tumor (n=95)**	**Non–*BRCA*-dependent tumor (n=31)**	**Breast cancer (n=40)**	**HR+/HER2− breast cancer (n=20)**	**TNBC (n=20)**	**mCRPC (n=19) [a]**	**Ovarian cancer (n=18)**	**Pancreatic cancer (n=15)**	**Colorectal cancer (n=8)**	**Cholangio-carcinoma/ gallbladder cancer (n=8)**	**Other tumors (n=18)**	**(N=30)**
CR	8 (6.3)	8 (8.4)	0	2 (5.0)	2 (10.0)	0	4 (21.1)	1 (5.6)	0	0	0	1 (5.6)	0
PR	33 (26.2)	30 (31.6)	3 (9.7)	21 (52.5)	12 (60.0)	9 (45.0)	1 (5.3)	4 (22.2)	2 (13.3)	0	0	5 (27.8)	2 (6.7)
SD	32 (25.4)	26 (27.4)	6 (19.4)	9 (22.5)	3 (15.0)	6 (30.0)	11 (57.9)	4 (22.2)	2 (13.3)	1 (12.5)	3 (37.5)	2 (11.1)	18 (60.0)
Non-CR/ non-PD	0	0	0	0	0	0	0	0	0	0	0	0	0
PD	47 (37.3)	27 (28.4)	20 (64.5)	8 (20.0)	3 (15.0)	5 (25.0)	2 (10.5)	7 (38.9)	10 (66.7)	7 (87.5)	4 (50.0)	9 (50.0)	10 (33.3)
NE	6 (4.8)	4 (4.2)	2 (6.5)	0	0	0	1 (5.3)	2 (11.1)	1 (6.7)	0	1 (12.5)	1 (5.6)	0
ORR, n (%) [95% CI]	41 (32.5) [24.5-41.5]	38 (40.0) [30.1-50.6]	3 (9.7) [2.0-25.8]	23 (57.5), [40.9-73.0]	14 (70.0) [45.7-88.1]	9 (45.0) [23.1-68.5]	5 (26.3) [9.1-51.2]	5 (27.8) [9.7-53.5]	2 (13.3) [1.7-40.5]	0 [0.0-36.9]	0 [0.0-36.9]	6 (33.3) [13.3-59.0]	2 (6.7) [0.8-22.1]

[a] ORR in patients with mCRPC and measurable disease by investigator was 44.4%.

BICR, blinded independent central review; CR, complete response; HER2, human epidermal growth factor 2; HR, hormone receptor; mCRPC, metastatic castration-resistant prostate cancer; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TNBC, triple-negative breast cancer.

eTable 4. Summary of Genetic/Genomic Biomarker Status (Central Laboratory Testing)

Biomarker status, n (%)	*BRCA1/2* cohort			*ATM* cohort
	FAS (n=159)	***BRCA* dependent (n=122)**	**Non-*BRCA* dependent (n=37)**	**FAS (n=41)**
BRCA1 status				
Positive	101 (63.5)	84 (68.9)	17 (45.9)	1 (2.4)
Negative	12 (7.5)	5 (4.1)	7 (18.9)	27 (65.9)
Not analyzable	21 (13.2)	15 (12.3)	6 (16.2)	4 (9.8)
Missing	25 (15.7)	18 (14.8)	7 (18.9)	9 (22.0)
BRCA2 status				
Positive	50 (31.4)	40 (32.8)	10 (27.0)	1 (2.4)
Negative	63 (39.6)	49 (40.2)	14 (37.8)	27 (65.9)
Not analyzable	21 (13.2)	15 (12.3)	6 (16.2)	4 (9.8)
Missing	25 (15.7)	18 (14.8)	7 (18.9)	9 (22.0)
ATM				
Positive	2 (1.3)	2 (1.6)	0	26 (63.4)
Negative	111 (69.8)	87 (71.3)	24 (64.9)	2 (4.9)
Not analyzable	21 (13.2)	15 (12.3)	6 (16.2)	4 (9.8)
Missing	25 (15.7)	18 (14.8)	7 (18.9)	9 (22.0)
TMB				
≥10 mut/Mb	8 (5.0)	4 (3.3)	4 (10.8)	10 (5.0)
<10 mut/Mb	92 (57.9)	75 (61.5)	17 (45.9)	114 (57.0)
Not analyzable	34 (21.4)	25 (20.5)	9 (24.3)	42 (21.0)
Missing	25 (15.7)	18 (14.8)	7 (18.9)	34 (17.0)
Genomic LOH				
High	49 (30.8)	44 (36.1)	5 (13.5)	1 (2.4)
Low	27 (17.0)	19 (15.6)	8 (21.6)	17 (41.5)
Not analyzable	58 (36.5)	41 (33.6)	17 (45.9)	14 (34.1)
Missing	25 (15.7)	18 (14.8)	7 (18.9)	9 (22.0)
PD-L1 expression level[a]				
Positive	26 (16.4)	18 (14.8)	8 (21.6)	0
Negative	30 (18.9)	22 (18.0)	8 (21.6)	3 (7.3)
Not analyzable	4 (2.5)	2 (1.6)	2 (5.4)	1 (2.4)
Missing results	99 (62.3)	80 (65.6)	19 (51.4)	37 (90.2)
BRCA/ATM alteration origin, n	71	61	10	23
Germline	58 (81.7)	52 (85.2)	6 (60.0)	11 (47.8)
Somatic	13 (18.3)	9 (14.8)	4 (40.0)	12 (52.2)
BRCA/ATM alteration zygosity, n	66	56	10	22
Under LOH	52 (78.8)	47 (83.9)	5 (50.0)	9 (40.9)
Heterozygous	14 (21.2)	9 (16.1)	5 (50.0)	13 (59.1)

n indicates the number of patients in the FAS with evaluable alteration for origin/zygosity of *BRCA1*, *BRCA2*, or *ATM* within each cohort.

Evaluable patients are those with value of positive or negative or high, medium, or low.

FAS, full analysis set; LOH, loss of heterozygosity; PD-L1, programmed cell death-ligand 1; TMB, tumor mutational burden.

[a] PD-L1 data are relatively sparse, reflecting prioritization of limited tumor tissue for FoundationOne.

eTable 5. Summary of TEAEs (Any Grade Occurring in ≥10% of Patients or Grade ≥3 Occurring in ≥5% of Patients)

n (%)	All patients (N=200)	
	Any grade	Grade ≥3
Anemia[a]	99 (49.5)	72 (36.0)
Nausea	93 (46.5)	3 (1.5)
Fatigue	66 (33.0)	10 (5.0)
Thrombocytopenia[b]	63 (31.5)	31 (15.5)
Vomiting	49 (24.5)	2 (1.0)
Constipation	47 (23.5)	0
Diarrhea	46 (23.0)	0
Decreased appetite	44 (22.0)	2 (1.0)
Dyspnea	44 (22.0)	3 (1.5)
Neutropenia[c]	40 (20.0)	23 (11.5)
Headache	39 (19.5)	1 (0.5)
Arthralgia	38 (19.0)	2 (1.0)
Abdominal pain	32 (16.0)	6 (3.0)
Pyrexia	31 (15.5)	0
Back pain	31 (15.5)	2 (1.0)
Asthenia	29 (14.5)	3 (1.5)
Insomnia	25 (12.5)	0
Infusion-related reaction	25 (12.5)	1 (0.5)
Aspartate aminotransferase increased	24 (12.0)	5 (2.5)
Alanine aminotransferase increased	23 (11.5)	5 (2.5)
Alopecia	22 (11.0)	0
Chills	22 (11.0)	0
Cough	21 (10.5)	0

TEAE, treatment-emergent adverse event.

[a] Composite term that includes anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased, and iron deficiency anemia.

[b] Composite term that includes thrombocytopenia, platelet count decreased, and immune thrombocytopenia.

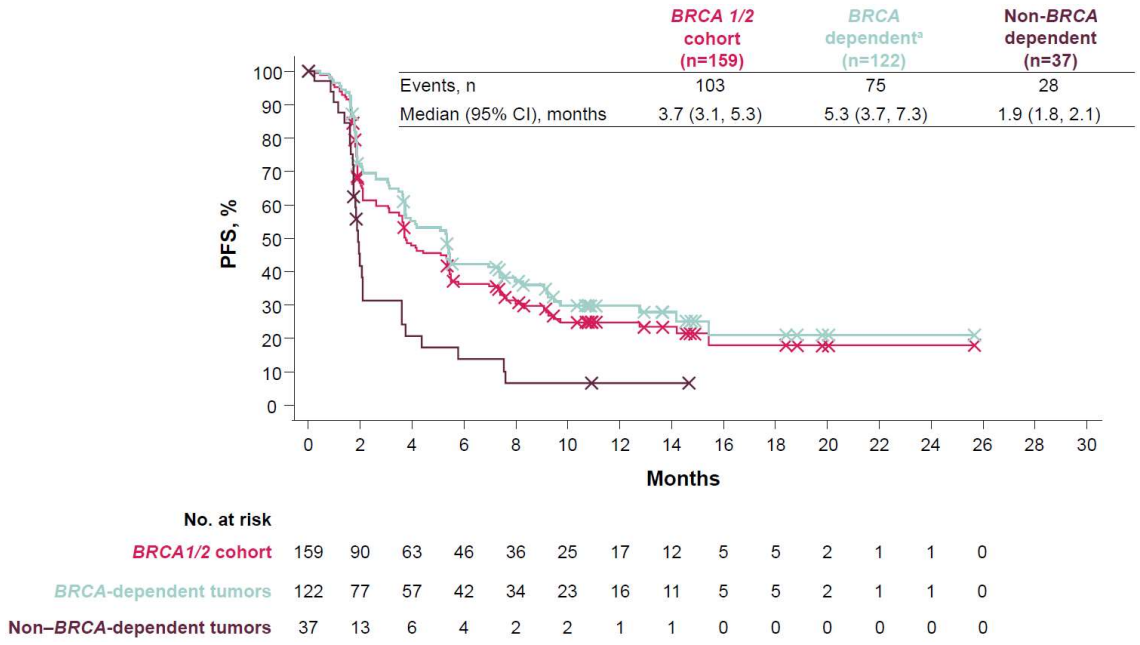
[c] Composite term that includes neutropenia, febrile neutropenia, neutrophil count decreased, and autoimmune neutropenia.

eTable 6. Treatment-Related AEs, IRRs, and irAEs

n (%)	All patients (N=200)
Treatment-related AEs leading to the discontinuation of avelumab	7 (3.5)
Treatment-related AEs leading to the discontinuation of talazoparib	5 (2.5)
Treatment-related AEs leading to dose reductions of talazoparib	67 (33.5)
Patients with any IRR	
Grade 1	17 (8.5)
Grade 2	23 (11.5)
Grade ≥3	1 (0.5)
Any irAE	
Grade 1	7 (3.5)
Grade 2	13 (6.5)
Grade ≥3	5 (2.5)

AE, adverse event; irAE, immune-related adverse event; IRR, infusion-related reaction.

eFigure 1. PFS for All Patients in the *BRCA1/2* Cohort and in *BRCA*-Dependent and non–*BRCA*-Dependent Tumor Types

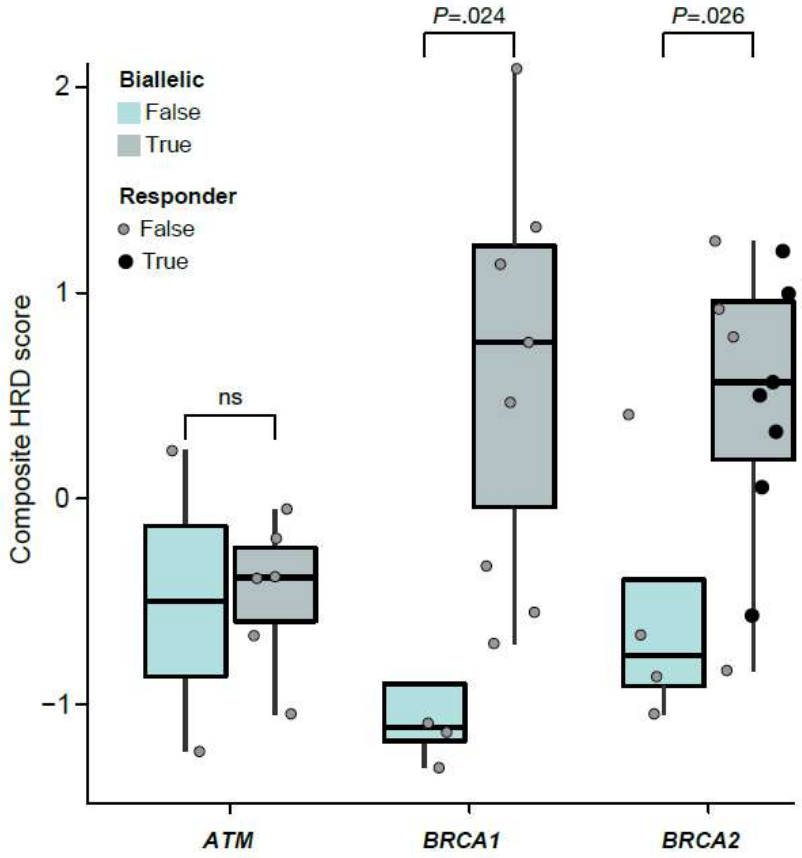


PFS, progression-free survival.

[a] Defined as breast, ovarian, prostate, and pancreatic cancers and uterine leiomyosarcoma.

eFigure 2. Molecular Analysis of a Subset of Patients Treated at Memorial Sloan Kettering Cancer Center

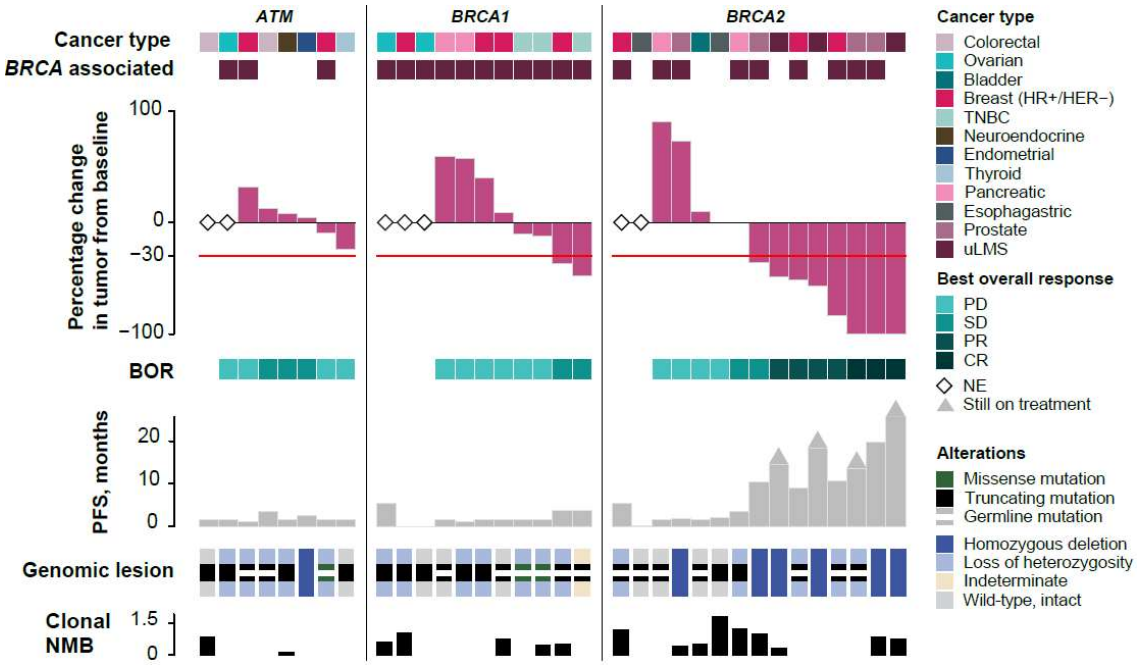
Composite HRD score in *BRCA1*-, *BRCA2*-, and *ATM*-mutant tumors separated by zygosity. Patients with a complete or partial response are highlighted.



HRD, homologous recombination deficiency; ns, nonsignificant.

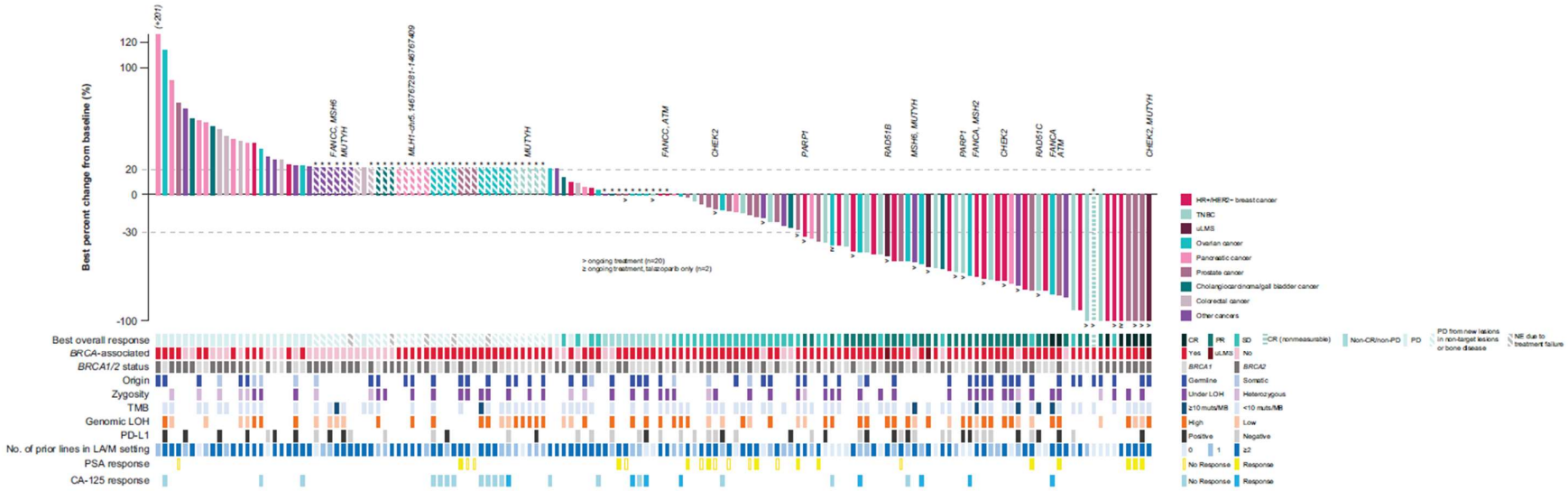
eFigure 3. Additional Molecular Analysis of a Subset of Patients

Clinicogenomic data; columns represent individual patients.



CR, complete response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; NE, not evaluable; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TNBC, triple-negative breast cancer; uLMS, uterine leiomyosarcoma.

eFigure 4. Best Percentage Change from Baseline per BICR



Eighteen patients had tumors with mutations in ≥1 of 32 additional, non-*BRCA1/2* genes implicated directly or indirectly in DNA damage response pathways (eMethods in the Supplement); mutations were more common in tumors with TMB≥10 mut/Mb. ; non–*BRCA1/2*-dependent tumors, responses occurred in 0/5 patients with *BRCA1/2* mutations under LOH vs 1/5 (20.0%) with heterozygous mutations (this tumor also had a high tumor mutational burden [TMB]). To account for all patients, including those without measurable disease at baseline and those who did not have a postbaseline assessment, the plot includes patients with target lesions at baseline and at least one postbaseline target lesion assessment and also[12]:

• A patient with no measurable disease at baseline and CR of the nontarget lesions (best percent change set to −100).

• Patients with no measurable disease at baseline and best response of non-CR/non-PD (best percent change set to 0).

• Patients with a best response of progression because of new lesions according to RECIST 1.1 or Prostate Cancer Clinical Trials Working Group 3 in patients with mCRPC or unequivocal worsening of nontarget lesions (best percent change set to +21).

• Patients with a best response of nonevaluable because of no postbaseline assessments due to early death, global deterioration of health status, or start of new anticancer therapy (best percent change set to +21).

Molecular analysis was based on results from central laboratories and supplemented by local laboratories when central results were not available.

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