Supplementary Online Content

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

eMethods. Inclusion/Exclusion Criteria and Further Information

Inclusion/exclusion criteria

Eligible patients were aged ≥18 years with advanced or metastatic breast cancer that was estrogen receptor–negative, progesterone receptor–negative, and HER2–negative, as per American Society of Clinical Oncology/College of American Pathologists guidelines[1,2]; had measurable lesions by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1; Eastern Cooperative Oncology Group performance status of 0–1; had adequate organ function; and may have received ≤2 lines of cytotoxic therapy, not counting adjuvant or neoadjuvant therapies, targeted small molecules, hormonal agents, or bevacizumab. Patients could have received platinum chemotherapy in the metastatic setting. However, the protocol was amended such that patients who progressed within 8 weeks from the day of last platinum administration were excluded. Patients were eligible regardless of their t*BRCA*mut status. Patients with previously treated brain metastases were eligible, provided that they were stable for at least 4 weeks prior to the first dose of the study treatment. Patients were excluded if they had undergone prior treatment with an anti-PD-1, anti-PD-L1, or anti PD-L2 agent, or known PARPi; if they had known active central nervous system metastases or carcinomatous meningitis; known additional malignancies that progressed or required active treatment in the past 2 years (except basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy, or *in situ* cervical cancer); were considered poor medical risks; or had participated in a study of an investigational agent within 4 weeks of the first dose of treatment.

Race

Information about race was collected given the proclivity of TNBC in the African-American population. Race was determined by the investigator.

Radiographic assessments

The same modality (CT or MRI) was used throughout the study for a given patient. After 1 year of radiographic assessments, patients had imaging performed every 12 weeks (84 ± 7 days) until disease progression. Tumor imaging for confirmation of response was performed ≥4 weeks after the first indication of response or at the next scheduled scan (ie, 9 weeks later), whichever was clinically indicated. If a patient discontinued treatment for a reason other than progression or death, withdrawal of consent, or loss to follow-up, scans continued at the specified intervals (ie, every 9 weeks for the first year and every 12 weeks thereafter).

Clinical outcomes

Duration of response was defined as the time from the first assessment of complete response or partial response until the earlier assessment of progression or death by any cause in the absence of progression. Progression-free survival was defined as the time from first dose of study treatment to the earlier of assessment of progression or death by any cause in the absence of progression. Overall survival was defined as the time from first dose of study treatment to the date of death by any cause.

Exploratory objectives

Exploratory objectives were determining clinical activity in biomarker-defined subpopulations and exploring biomarkers that may predict sensitivity or resistance to combination therapy.

Safety parameters

Safety was assessed based on adverse events (AEs), clinical laboratory values, vital signs, electrocardiograms, physical examination findings, and use of concomitant medications.

Biomarker testing

t*BRCA*mut and HRR gene mutational status were evaluated using the Myriad Genetics (Salt Lake City, UT, USA) research assay. g*BRCA* results from local testing performed by individual sites were collected when available. PD-L1 expression was evaluated by Merck & Co., Inc., Kenilworth, NJ, USA; PD-L1 status was determined using a combined proportion score (CPS) provision cutoff of 1 by immunohistochemistry (IHC) using an investigational version of the PD-L1 IHC 22C3 pharmDx (Agilent, Carpinteria, CA, USA). The CPS is the number of positively stained tumor and immune cells relative to the total number of tumor cells.

The following is a list of all participating trial sites:

Site Name	Location
Dana Farber Cancer Institute	Boston, MA
Massachusetts General Hospital	Boston, MA
Beth Israel Deaconess Medical Center	Boston, MA
HonorHealth	Scottsdale, AZ
University of Oklahoma Health Sciences Center	Oklahoma City, OK
Cedars-Sinai Medical Group	Los Angeles, CA
University Hospitals Case Medical Center	Cleveland, OH
Karmanos Cancer Institute	Detroit, MI
West Cancer Center	Memphis, TN
Women's Cancer Care	Covington, LA
Mayo Clinic - Rochester	Rochester, MN
Florida Hospital Cancer Institute	Orlando, FL
University of Alabama at Birmingham	Birmingham, AL
University of Virginia Cancer Center	Charlottesville, VA
University of California San Francisco	San Francisco, CA
Mayo Clinic - Jacksonville	Jacksonville, FL
Lahey Hospital & Medical Center	Burlington, MA
Monter Cancer Center	Lake Success, NY
Stanford University Medical School	Palo Alto, CA

Tennessee Oncology - Centennial Clinic	Nashville, TN
Levine Cancer Institute	Charlotte, NC
University of North Carolina - Chapel Hill	Chapel Hill, NC
Weill Cornell Medical College of Cornell University	New York
Tufts Medical Center	Boston, NY
Sylvester Comprehensive Cancer Center	Miami, FL
Sylvester Comprehensive Cancer Center – Deerfield Beach	Miami, FL
Sylvester Comprehensive Cancer Center – Plantation	Miami, FL
University of Chicago Medical Center	Chicago, IL
Northside Hospital Cancer Center	Atlanta, GA
University of Texas Health Science Center at San Antonio	San Antonio, TX
Morristown Memorial Hospital	Morristown, NJ
Mayo Clinic – Scottsdale	Scottsdale, AZ
University of Washington	Seattle, WA
Georgetown University Medical Center	Washington, DC

eTable 1. Patient Demographics and Baseline Characteristics

Characteristic	Full Analysis (N=55)	Efficacy-Evaluable (N=47)
Age, median (range), years	54 (32-90)	53 (32-90)
Race, n (%)		
White	43 (78)	36 (77)
Black	8 (15)	7 (15)
Asian	2 (4)	2 (4)
Not Reported	2 (4)	2 (4)
ECOG performance status, n (%)		
0	30 (55)	27 (57)
1	25 (45)	20 (43)
Prior lines of therapy in advanced/metastatic setting, median (range)[a], n (%)	1 (0-3)	1 (0-3)
0	18 (33)	17 (36)
1	22 (40)	16 (34)
2	14 (25)	13 (28)
3[b]	1 (2)	1 (2)
Previous neoadjuvant or adjuvant therapy[c], n (%)	43 (78)	37 (79)
Previous chemotherapy in advanced/metastatic setting, n (%)		
Platinum	21 (38)	17 (36)
Taxane	15 (27)	11 (23)
Gemcitabine	14 (25)	12 (26)
Capecitabine	12 (22)	10 (21)
Eribulin	7 (13)	7 (15)
Anthracycline	4 (7)	4 (9)
Cyclophosphamide	3 (5)	3 (6)
Ixabepilone	1 (2)	1 (2)
Lactate dehydrogenase, median (range), units/L	221 (106-4047)	214 (106-4047)

Abbreviations: ECOG, Eastern Cooperative Oncology Group.

[a] Not including small molecules, hormonal agents, monoclonal antibodies, or investigational agents.

[b] Patient was retrospectively determined to have received 3 prior regimens.

[c] Any type of anti-cancer therapy including but not limited to chemotherapy, biologics or hormones.

eTable 2. Biomarker Status

Biomarker Status	Full Analysis (N=55)	Efficacy Evaluable (N=47)
***BRCA* status, n (%)**		
t*BRCA*mut	15 (27)	15 (32)
g*BRCA*mut	8 (15)	8 (17)
s*BRCA*mut (g*BRCA*wt/t*BRCA*mut)	2 (4)	2 (4)
g*BRCA*unk/t*BRCA*mut	5 (9)	5 (11)
t*BRCA*wt	34 (62)	27 (57)
t*BRCA* Unknown	6 (11)	5 (11)
HRR status, n (%)		
HRRmut	21 (38)	20 (43)
HRRwt	28 (51)	22 (47)
HRR Unknown	6 (11)	5 (11)
PD-L1 status, n (%)		
Positive	36 (65)	28 (60)
Negative	13 (24)	13 (28)
Unknown	6 (11)	6 (13)

Abbreviations: g*BRCA*, germline *BRCA;* HRR, homologous recombination repair; mut, mutation; PD-L1, programmed death-ligand 1; s*BRCA*, somatic *BRCA*; t*BRCA*, tumor *BRCA*; unk; unknown; wt, wild-type.

eTable 3. Disease Control in t*BRCA*wt/Unknown Patients[a]

HRR/DDR Mutations[b]	PD-L1 Status	Best Response	PFS (Months)
CHEK1	+	CR	18.0[c]
ATR	+	CR	6.4
BLM	-	SD	8.1
NBN & RAD51C	+	SD	4.9
PALB-2[d]	UNK	SD	3.6
None detected	-	CR	10.3
None detected	-	SD	8.2
None detected	-	SD	4.2
None detected	-	SD	3.9
None detected	+	SD	1.4

Abbreviations: CR, complete response; DDR, DNA damage response; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; t*BRCA*, tumor *BRCA*; wt, wild type.

[a] Disease control defined as the proportion of patients achieving CR, PR, or SD as per RECIST v1.1. One patient with no tumor sample is not shown.

[b] HRR mutations: *ATR, BLM, NBN, RAD51C,* and *PALB-2*; DDR mutation: *CHEK1*

[c] Treatment is ongoing.

[d] g*BRCA*wt, t*BRCA* status unknown. The other 9 patients were all t*BRCA*wt.

eTable 4. ORR Subgroup Analysis in Efficacy Evaluable Population

Patient Population	n/N	ORR[a] (90% CI)
All patients	10/47	21% (12–33)
Lines of previous treatment		
0-1	9/33	27% (15–43)
≥2	1/14	7% (0.4–30)
t*BRCA* status		
t*BRCA*mut	7/15	47% (24–70)
t*BRCA*wt	3/27	11% (3–26)
Unknown	0/5	0% (0–45)
Prior platinum status		
None	7/21	33% (17–54)
Yes	3/26	12% (3–27)
PFI ≤56 days	1/14	7% (0.4–30)
PFI >56 days	2/12	17% (3–44)
PD-L1 status		
Positive	9/28	32% (18–49)
Negative	1/13	8% (0.4– 32)
Unknown	0/6	0% (0.0–39)

[a] ORR includes only confirmed responses using RECIST v1.1

Abbreviations: CI, confidence interval; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFI, platinum-free interval; mut, mutation; t, tumor; wt, wild type.

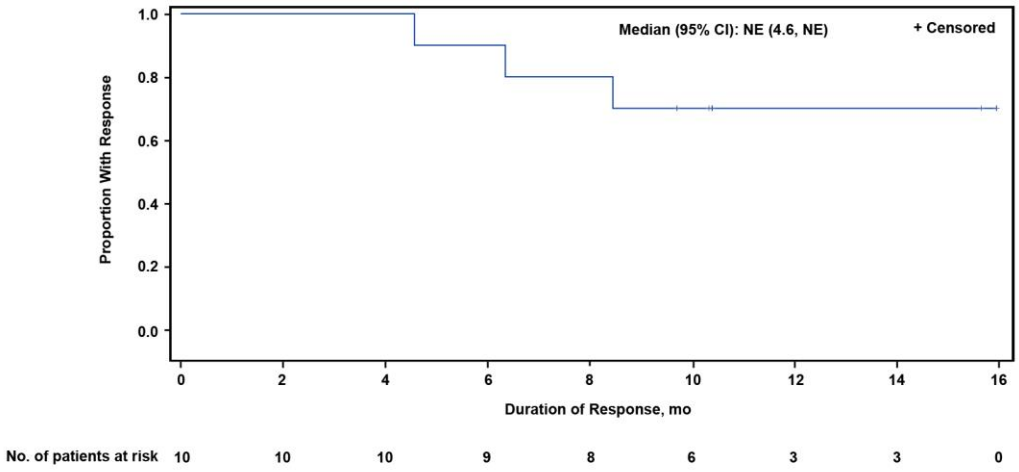
eTable 5. ORR Analysis by Biomarker Status and Prior Platinum Use

Biomarker Status	ORR[a] with Prior Platinum Use, n/N (% [90% CI])	ORR[a] Without Prior Platinum Use, n/N (% [90% CI])
t*BRCA*mut	0/5 (0% [0–45])	7/10 (70% [39–91])
t*BRCA*wt	3/19 (16% [4–36])	0/8 (0% [0–31])
t*BRCA* unknown	0/2 (0% [0–78])	0/3 (0% [0–63])
HRRmut	1/7 (14% [1–52])	7/13 (54% [29–78])
HRRwt	2/16 (13% [2–34])	0/6 (0% [0–39])
HRR unknown	0/3 (0% [0–63])	0/2 (0% [0–78])
PD-L1 positive	2/16 (13% [2–34])	7/12 (58% [32–82])
PD-L1 negative	1/8 (13% [1–47])	0/5 (0% [0–45])
PD-L1 unknown	0/2 (0% [0–78])	0/4 (0% [0–53])

[a] ORR includes only confirmed responses using RECIST v1.1

Abbreviations: CI, confidence interval; ORR, objective response rate; PD-L1, programmed death-ligand 1; mut, mutation; t, tumor; wt, wild type.

eFigure. Duration of Response for All Patients Who Achieved Confirmed CR or PR



eReferences

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