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African American Women Who Receive Primary Anthracycline- and Taxane-Based Chemotherapy for Triple-Negative Breast Cancer Suffer Worse Outcomes Compared With White Women

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To the Editor

We read with great interest the manuscript by Dawood et al¹ from the M. D. Anderson Cancer Center (MDACC; Houston, TX) entitled, “Triple Receptor–Negative Breast Cancer: The Effect of Race on Response to Primary Systemic Treatment and Survival Outcomes.” We have also recently evaluated a data set of women with triple receptor–negative breast cancer who received primary systemic therapy (PST) at our institution and report our observations below.

Breast cancer is a heterogeneous disease composed of a number of recognized biologic and pathologic subtypes. The so called “triple receptor–negative breast cancer,” used to describe all tumors that are estrogen receptor–, progesterone receptor–, and human epidermal growth factor receptor 2–negative, may include basal-like and non–basal-like tumors.

Chemotherapy is the only systemic treatment available for women with primary triple receptor–negative breast cancer to improve long-term outcomes. Triple receptor–negative breast cancer is more prevalent among premenopausal African American women and is associated with a shorter disease-free interval and overall survival than white women.^{2,3} This disparity has been often attributed to lack of access to healthcare, poor follow-up, low socioeconomic status, body mass index, and possibly lower doses of adjuvant therapy. Dawood et al⁴ have previously reported that African American women with metastatic breast cancer are at greater risk of death compared with white women.

African American women with triple receptor–negative breast cancer often present with a stage II or III breast cancer and may be recommended PST. Although PST does not improve

disease-free survival or overall survival, it may enhance breast conservation and provide prognostic information to individual women.⁵ Women with poor response to PST and a large residual disease are more likely to suffer a recurrence and die of their disease compared with women with a pathological complete response (pCR).

Based on available evidence and anecdotal observations, we hypothesized that African American women with triple receptor–negative breast cancers have worse outcomes in part because of resistance to standard chemotherapy. To test our hypothesis, we compared pCR rate, recurrence-free and overall survival, in African American versus white and other women with triple receptor–negative breast cancer who received preoperative anthracycline- and/or taxane-based therapy.

In 2002, members of the multidisciplinary breast cancer program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University Hospital (Baltimore, MD) developed an algorithm for PST management used by the clinicians from all specialties, which led to uniform identification, staging, and treatment criteria. Briefly, women with a clinical stage II or III breast cancer appropriate for PST based on International Consensus Recommendations^{5,6} had nodal evaluation by a fine-needle aspiration⁷ or sentinel node mapping before initiating chemotherapy. The breast cancer program screens and collects demographics and key medical characteristics on all new patients to the medical oncology clinic. All patients with a clinical stage II or III breast cancer at the time of initial consultation who received PST are included in the database. Approximately 2 to 4 weeks following PST, women undergo breast-conserving surgery or a mastectomy at the Johns Hopkins at the discretion of the treating surgeon and patient preference. Women with a positive axillary lymph node before chemotherapy undergo axillary lymph node dissection at time of definitive surgery.

We reviewed the breast cancer PST database from May 2002 to December 2007. Eligible subjects for the investigation included women with histologically confirmed, estrogen receptor–, progesterone receptor–, and human epidermal growth factor receptor 2–negative, clinical stage II or III, invasive breast cancer who received chemotherapy with doxorubicin and cyclophosphamide, with or without a taxane before or after the doxorubicin and cyclophosphamide combination. The Johns Hopkins Medicine institutional review board provided an exemption for this retrospective review.

We studied patient and tumor characteristics including age, race, family history, menopausal status, initial clinical stage, initial clinical tumor size and nodal status. Study end points included pCR (no residual invasive cancer in the breast and lymph nodes), recurrence-free survival, and overall survival in African American versus white/other women. Differences in patient and tumor characteristics across race were compared with Fisher's exact test, exact χ^2 test, or Wilcoxon rank sum test, where appropriate. Survival outcomes including recurrence-free survival and overall survival were analyzed using the Kaplan-Meier method and compared between race groups by the log-rank test.

We identified 38 women that met the predefined criteria; 15 were African American, 23 were white or other race (Table 1). Consistent with the literature, African American women

were more likely to be younger than 50 years of age and be pre- or perimenopausal at the time of initial diagnosis. There was no statistically significant difference between initial clinical stage and type of chemotherapy administered to the groups. Following therapy, 13% of the African American women had a pCR compared with 52% in white/other women ($P = .034$). Fewer white/other women had a stage III residual pathological stage compared with African American women (12% and 53%, respectively).

With a median follow-up of 2.1 years (range, 0.6 to 6.5 years), Kaplan-Meier curves indicate a trend for shorter recurrence-free survival ($P = .045$) and overall survival ($P = .028$) for African American women compared with white/other women (Fig 1). The trends remained similar after controlling for patient and tumor characteristics.

We compared outcomes of African American versus white women with stage II or III breast cancer who have received PST. In our cohort, African Americans were less likely to achieve a pCR and more likely to suffer a recurrence and death compared with white/other women. Our results are different than the data reported by MDACC investigators. In the MDACC report, African American women had a similar age range, menopausal status, histology, and other tumor characteristics at baseline compared with white women, but were slightly more likely to have a clinical stage III disease. In our data set, African Americans were more likely to be younger and premenopausal. Following therapy, the African American women were more likely to have large residual disease, defined as pathological stage II or III.

While our study was conducted retrospectively, patients were seen and treated in one institution following carefully crafted prospective algorithms. Our data set is smaller than that described by Dawood et al,¹ but the African American population in our cohort may be more likely to represent a group of women with basal-like tumors.² Our results, coupled with the MDACC report, suggest that additional studies are required to assess the outcomes of African American women who received optimal systemic therapy in the adjuvant or neoadjuvant setting. Moreover, identification of biomarkers that may separate triple receptor–negative breast cancers that are sensitive to standard therapy from those that are resistant and associated with poor outcomes is essential.

In summary, our results support a poor outcome for young African American women with triple receptor–negative breast cancer despite the use of standard modern chemotherapy. Clinical trials investigating the role of other chemotherapy regimens or novel agents in young African American women with triple receptor–negative breast cancer should be considered. A change in therapy should be considered as soon as a suboptimal response is recognized. Furthermore, studies incorporating novel agents in women with large residual disease following PST are required.

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Fig 1.

(A) Recurrence-free survival by race. (B) Overall survival by race. AA, African American; CA, white.

Table 1
 Characteristics of Patients With Triple Receptor–Negative Breast Cancer by Race (N = 38)*

Characteristic	Race						P†
	Total (N = 38)		African American (n = 15)		White/Other (n = 23)		
	No.	%	No.	%	No.	%	
Age, years							
50	23	61	14	93	9	39	.002
> 50	15	39	1	7	14	61	
Median	48		43		52		
Range	33–67		34–62		33–67		.014
Menopausal status							
Pre/perimenopausal	23	61	12	80	11	48	.036
Postmenopausal	14	37	2	13	12	52	
Unknown	1	3	1	7	0	0	
No. of first-degree relative affected							
I	8	21	3	20	5	22	> .999
None	30	79	12	80	18	78	
Clinical stage at baseline*							
I	1	2	0	0	1	4	
II	22	55	8	53	14	56	0.684
III	17	43	7	47	10	40	
Clinical tumor size at baseline*							
T1 or T2	21	53	7	47	14	56	0.745
T3 or T4	19	48	8	53	11	44	
Nodal status at baseline*							
Node negative	10	25	2	13	8	32	
Node positive	28	70	12	80	16	64	.269

Characteristic	Race							
	Total (N = 38)		African American (n = 15)		White/Other (n = 23)		P [†]	
	No.	%	No.	%	No.	%		
Unknown	2	5	1	7	1	4		
PST regimen								
ACT/ACP	33	86	13	87	20	87		
AC	4	11	1	7	3	13	> .999	
P alone	1	3	1	7	0	0		
pCR [*]								
Yes	15	38	2	13	13	52		
No	24	60	12	80	12	48	.034	
Other [‡]	1	2	1	7	0	0		
Pathological stage following PST [*]								
0	15	38	2	13	13	52		
I	4	10	0	0	4	16		
II	9	22	4	27	5	20	.001	
III	11	28	8	53	3	12		
Other [‡]	1	3	1	7	0	0		

NOTE. Comparisons were made excluding unknowns. Percentages may not add up to 100 due to rounding.

Abbreviations: PST, primary systemic therapy; A, doxorubicin; C, cyclophosphamide; T, docetaxel; P, paclitaxel; pCR, pathological complete response.

^{*}Total number of tumors = 40. Two women had synchronous tumors (one white woman with a stage I and II tumors, and one other woman with stage II and III tumors).

[†]P values were obtained using Fisher's exact test, exact χ^2 test, or Wilcoxon rank sum test, as appropriate.

[‡]One woman had progressive disease and metastases while on primary systemic therapy.