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Black Race and Distant Recurrence after Neoadjuvant or Adjuvant Chemotherapy in Breast Cancer

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Abstract

Background: Black race compared to white race is associated with more advanced stage and biologically aggressive breast cancer. Consequently, black patients are more frequently treated with neoadjuvant chemotherapy (NAC) than white patients. However, it is unclear how distant recurrence-free survival (DRFS) of black patients treated with NAC, compares to DRFS of black patients treated with adjuvant chemotherapy (AC). We evaluated the association between race, distant recurrence, and type of chemotherapy (AC or NAC) in localized or locally advanced breast cancer.

Patients and Methods: We evaluated DRFS in 807 patients, including 473 black, 252 white, 56 Hispanic, and 26 women of other or mixed race. The association between AC or NAC and DRFS

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was examined using multivariate Cox proportional hazard models that included race, age, stage, estrogen receptor (ER) and triple negative (TN) status.

Results: When the black and white subjects were pooled for the analysis the features associated with worse DRFS included stage III disease and age<50 years, but not ER-negative disease, TN disease, the use of NAC, or black race. However, in the analysis stratified by race NAC was associated with worse DRFS compared to AC in black (HR=2.70; 95% CI=1.73–4.22; p<0.0001), but not in white women (HR=1.29, 95% CI=0.56–2.95; p=0.36).

Conclusion: Black patients treated with NAC had worse DRFS than black patients treated with AC, or white patients treated with either NAC or AC. These findings need to be validated in a large-scale observational study and the effect of NAC on the breast cancer microenvironment in black women needs to be further evaluated.

Keywords

breast cancer; distant recurrence; black patients; neoadjuvant chemotherapy; adjuvant chemotherapy

Introduction

Black women with operable breast cancer have higher recurrence and mortality rates than white women [1]. This has been attributed to more advanced stage at diagnosis [2], higher rates of ER-negative (ER-) and/or triple-negative (TN) disease [3–5], lower socioeconomic status [6], more comorbidities [7], and higher rates of toxicity due to therapy [8]. However, black women have lower overall survival and cancer-specific survival compared to white women when treated with systemic and local therapy, even after controlling for demographic and prognostic tumor variables [9]. Some reports have also indicated that black women treated with neoadjuvant chemotherapy (NAC) have higher recurrence rates and breast cancer mortality than white women treated with NAC [10], while others did not find a difference [11].

Since black women typically present with more advanced stage and more aggressive ER-disease than white women [10], they are treated with NAC more frequently than white women [12] because NAC decreases tumor burden and improves surgical outcome [13]. Large prospective randomized studies of distant recurrence free survival (DRFS) and overall survival (OS) in predominantly white patients with localized breast cancer have not shown differences between those treated with NAC compared to those treated with adjuvant chemotherapy (AC) [14,15]. However, data comparing DRFS in black women treated with AC versus black women treated with NAC are currently not available. Since breast cancer behaves more aggressively in blacks than in whites, and blacks are more commonly treated with NAC, it is important to investigate how DRFS in black patients treated with NAC compares to DRFS of black patients treated with AC and patients of other racial background treated with and AC or NAC. To address this question we performed a retrospective study to evaluate the association between DRFS and type of chemotherapy (AC versus NAC) in a multiracial cohort treated at an academic medical center in which patients received multidisciplinary care.

Methods

Data collection

The research protocol was approved by the Einstein/Montefiore institutional review board. Patient data were obtained from Clinical Looking Glass (CLG, http://exploreclg.montefiore.org/), an interactive software application developed at Montefiore Medical Center that integrates demographic, clinical, and administrative data sets, and which additionally allows for data extraction in a programmable format for statistical assessment [16].

We manually evaluated charts from all 214 patients treated with NAC to obtain clinical stage. Use of clinical stage, as opposed to pathological stage, was essential for multivariate analysis to avoid chemotherapy-induced down-staging that might have occurred in NAC treated patients if pathological stage was used.

Patient selection

The study was conducted in a cohort of 807 women (473 black, 252 white, 56 Hispanic and 26 others) with a first diagnosis of invasive breast cancer made between 2000 and 2016 at Montefiore Medical Center in the Bronx, NY who received either NAC or AC for non-metastatic breast cancer. The cohort only included patients with stage IIA to IIIC at presentation.

The exclusion criteria included: bilateral breast cancer, unclear record of the chemotherapy schedule in relationship to surgery, and insufficient data regarding their initial breast cancer diagnosis and treatment, and multiple cancers (Figure 1). The patients were grouped in 2 cohorts: 1) Black and white cohort (N=725), consisting of only black and white patients treated with either NAC or AC, and 2) Neoadjuvant cohort (N=214), consisting of only patients treated with NAC, as indicated in the consort diagram (Figure 1).

Statistical Analysis

Bivariate comparisons in age, stage, ER, PR, HER2, and TN status were made between NAC and AC groups within white and black patients separately using a chi-square test, except for the continuous age where a two-sampled t-test was used. Distant recurrence-free survival (defined as a metastasis at a distant organ) was the end-point measurement used in this analysis. Kaplan-Meier (KM) survival curves and log-rank tests were used to compare DRFS between NAC and AC combined, as well as separate, for black and white patients. A multivariate Cox model was used to examine the effect of NAC vs AC on DRFS separately for blacks and whites, while adjusting for patient age, stage of tumor, and hormonal receptor status (including ER, PR, HER2, and TN). PR and HER2 were later removed from the model because of non-statistical significance. A formal comparison of the effect of NAC vs AC between black and white was made by combining the whites and blacks together and examining the interaction between NAC and race.

We used a propensity score approach to further examine if our results were subject to bias due to potential confounding that led to imbalanced groups between the NAC and AC

groups. Specifically, separately for blacks and whites, a logistic regression model was used to model on the use of NAC versus AC treatment with patients' age and tumor characteristics including tumor size, lymph node status, stage, ER, PR, and Her2 status as variables in the model. Then an inverse probability weighting method (IPW) was used to incorporate the propensity score into the multivariate Cox models and the robust variance was used to account for the weighting [17,18]. We did not use propensity score matching here because of the limited sample size. The IPW method to adjust for propensity has been widely adopted to control for potential bias induced by self-selected exposure in observational studies.

All the p-values were reported as two-sided. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC 2014).

Results

Black and White Cohort

Demographic and tumor characteristics for the "Black and white" cohort (black, n=473; white, n=252) treated with either NAC or AC are shown in the Table 1. Compared to patients treated with AC, white patients treated with NAC were significantly more likely to have ER- (p=0.01), PR- (p<0.0001), and TN disease (p=0.02), whereas black patients treated with NAC were significantly more likely to be <50 years old (p=0.007) and have stage III disease (p<0.0001), as well as ER- (p=0.003), PR- (p=0.005), and TN disease (p=0.0002). Six out of 92 (6.2%) black and 3 out of 40 (7.5%) white patients treated with NAC in this cohort achieved pathologic complete response evidenced by absence of tumor cells in the breast and lymph nodes. Pooled data for the entire cohort are shown in the Table 2.

The Kaplan-Meier curve shows that in this cohort, composed of predominantly back patients (65% blacks, 35% whites), NAC-treated patients (70% blacks, 30% whites) have lower DRFS than AC-treated patients (64% blacks, 36% whites) (Figure 2A; p<0.001). When the stratification included not only treatment scheme (AC/NAC), but also race (Figure 2B), the Kaplan-Meier curve for DRFS showed that black patients receiving NAC have significantly lower DRFS rates compared to white patients receiving either AC or NAC, or black patients receiving AC (p<0.001 for all groups).

Multivariate analysis of DRFS adjusted for race, age, stage, tumor size, ER, and triplenegative status for black and white patients combined is shown in Table 3 (top panel). Factors associated with significantly worse DRFS included stage III disease (p<0.0001; HR=4.43, 95% CI=3.12–6.37) and age <50 years (p<0.001; HR=1.78, 95% CI=1.26–2.53), but not black race (p=0.76), the use of NAC (p=0.36), ER-negative disease (p=0.17), or TN disease (p=0.23). However, NAC was associated with worse DRFS in black (HR=2.54, 95% CI=1.64–3.93) but not white (HR=1.46, 95% CI=0.63–3.33) patients. We used the inverse probability weighting (IPW), as an additional statistical method to control for baseline imbalance [17,18] and confirmed that NAC was associated with worse DRFS in black (HR = 3.61, 95%CI = 1.59, 8.20, p = 0.002), but not in white (HR = 0.72, 95CI = 0.04, 13.5, p = 0.82) women with breast cancer (Supplementary Tables 1a and 1b). Although we identified a much larger treatment effect of NAC in blacks as compared to whites, we failed to detect a

significant interaction between race and treatment, mostly likely due to the limited sample size (p=0.24).

In a stratified analysis (Table 3; bottom panel), stage and age showed the same trends as in the combined analysis for white and black patients independently. However, NAC was an independent indicator of poor prognosis in blacks (p<0.0001; HR=2.7, 95% CI 1.73–4.22), but not in whites (p=0.36; HR=1.29, 95% CI=0.56–2.95).

Neoadjuvant cohort

We also evaluated the characteristics and DRFS in a multiracial and multiethnic cohort of 214 patients consisting of 132 patients treated with NAC described above (40 white, 92 black), and an additional 82 patients (56 Hispanics, and 26 races other than black or white; Table 4). In this cohort, black race was associated with significantly higher rates of ER- (p=0.008) and TN disease (p=0.003) for the four race categories, but no significant differences (p>0.05) were found in patient age, stage, PR, HER2, status at the time of diagnosis.

The Kaplan-Meier curve for DRFS stratified by race for patients treated with NAC is presented in Figure 2C. As shown, black patients have lower DRFS than Hispanic, white, and other races (p<0.05 for all groups).

Multivariate analysis of DRFS adjusted for race, age, stage, ER status, and TN status indicates that stage III disease is an independent indicator of worse DRFS in patients receiving NAC (Table 5. top panel; p<0.0001; HR=3.09, 95% CI=1.77–5.40). Also, black patients receiving NAC have worse DRFS rates when compared to white patients (p=0.08; HR=2.09, 95% CI=0.91–4.79), but no such difference is observed for Hispanics (p=0.33; HR=1.57, 95% CI=0.63–3.94) or patients grouped as other races (p=0.95; HR=0.99, CI=0.29–3.16).

All the aforementioned analyses were additionally performed after pooling all patients other than black into a single category, designated as “non-black” (Table 6). Black patients receiving NAC have lower DRFS than non-black patients, as shown through multivariate analysis (Table 5, bottom panel; p=0.05, HR=1.68, 95% CI=1.00–2.85) and the corresponding Kaplan-Meier curve (Figure 2D; p<0.01; median survival: black, 1820 days; non-black, 3748 days).

Treatment considerations

There was no difference between black and white subjects in regards to taxanecontaining versus non-taxane chemotherapy (p=0.4). However, chemotherapy was more often combined with endocrine therapy in white than in black patients (p<0.001) (Table 7).

Although patients receiving NAC were more often treated with taxane-containing chemotherapy compared to patient receiving AC (p=0.01), there was no difference in overall treatment combinations between the NAC and AC groups (p=0.7) (Table 8).

Discussion

Black race has been associated with higher recurrence rates and breast cancer mortality [10]. Previous randomized trials showed similar outcomes for patients with localized breast cancer treated with NAC or AC, however these studies included predominately white women [15,14]. The main objective of this retrospective study was to evaluate the association between black race and distant recurrence free survival (DRFS) in patients with stage II-III breast cancer receiving neoadjuvant chemotherapy (NAC) or adjuvant chemotherapy (AC). In the first part of the study we compared DRFS in a cohort of black and white women treated with AC and NAC, whereas in the second part we investigated the DRFS in multi-racial and multi-ethnic cohort treated with NAC. Using Cox proportional hazard models adjusted for age, stage, ER expression, and triple negative status, we found that blacks treated with NAC have significantly worse DRFS compared to blacks treated with AC, while whites treated with either NAC or AC have similar DRFS. Although the race-treatment interaction was not statistically significant, our findings suggest that despite receiving NAC black women have worse DRFS than white women receiving the same therapy. In addition to tumor characteristics, other potential confounders for which we could not control for may explain this difference in outcome following NAC in black patients. In particular, our database has limited information regarding other patient characteristics such as education, socioeconomic status, comorbidities and others which could have been potential cofounders.

Population-based studies indicate that black women are treated significantly more often with NAC compared to other racial groups [12], which is attributed to more advanced stage, and higher rates of ER- and TN disease [19], which is more common in blacks [20]. Large prospective clinical trials, performed predominantly in white patient populations, showed similar OS and DRFS in patients treated with either NAC or AC [15,14]. Our analysis, stratified according to treatment plan (AC, NAC) and race (black, white) is consistent with prior reports indicating that whites have similar DRFS when treated with either NAC or AC, but indicates a discordance in outcomes for black women receiving NAC compared to AC, an observation that requires further evaluation using larger scale observational study that can control for additional patient related potential confounders and ultimately in a randomized controlled trial. Although we identified much larger treatment effect of NAC in blacks as compared to whites, we failed to detect a significant interaction between race and treatment, mostly likely due to the limited sample size.

Some evidence indicates racial differences in the breast tumor microenvironment (TME) that could explain our findings [21,22]. Although it is known that NAC induces pro-metastatic changes in breast cancers, racial differences in these changes have not been thoroughly evaluated [23,24]. NAC promotes the assembly of structures called tumor microenvironment of metastasis (TMEM) that serve as doorways for intravasation of tumor cells [24,23,25,26] and it increases the proportion of the highly invasive $Mena^{INV\text{-}hi}$/$Mena11a^{lo}$ ($Mena^{Calc\text{-}Hi}$) tumor cells which utilize the TMEM sites for hematogenous dissemination [25]. Functional TMEM sites are composed of a proangiogenic Tie2 expressing macrophage in contact with an endothelial cell and Mena-expressing cancer cell [25,26]. Interestingly, it has been reported that the density of Tie2 expressing pro-angiogenic macrophages is higher in blacks than in whites [27], raising the possibility that worse DRFS post-NAC in blacks versus

whites reported here may be a consequence of higher TMEM activity in blacks compared to whites. Furthermore, Martin et al. reported increased macrophage and microvascular density in the breast TME of blacks compared to whites [21], again pointing to the function of TMEM as a possible cause for observed differences in DRFS between black and white patients.

Another possible explanation for the difference in response to NAC between black and white patients may be due to body-mass index (BMI), which we did not control for due to limited information regarding the BMI in our data set. It has been reported that blacks have significantly higher BMI than whites, which is associated with higher circulating levels of cytokines and proinvasive changes in cancer cells and TME [22].

Although we showed worse DRFS in blacks treated with NAC compared to blacks treated with AC using rigorous statistical methods, our study has limitations inherent to all retrospective studies such as lack of randomization and lack of reliable information regarding BMI, as well as lack of information regarding other parameters such as education, socioeconomic status, and comorbidities which could have been potential cofounders. Our cohort showed a lower rate of pathologic complete response (pCR) than reported in other studies, but this was present in both black and white patients, and therefore unlikely to affect the observed difference in DRFS. However, using this retrospective cohort we recapitulated the findings from large randomized prospective clinical trials which found equal DRFS in white patients treated with NAC and AC. Likewise, our results support the findings of Woodward et al. (12), whose report indicated a tendency for worse DRFS and statistically worse overall survival (OS) in blacks compared to whites treated with doxorubicin-based NAC [10].

In summary, although black breast cancer patients are frequently treated with NAC, this approach does not seem to result in better, or even equivalent, DRFS as compared to black patients treated with AC. Although this may be a result of confounders which our study could not control for, the biologic factors contributing to our findings warrant further evaluation. Likewise, prospective randomized trials need to be initiated to determine which treatment approach would result in the most improved long-term survival in black breast cancer patients who have biologically more aggressive disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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List of Abbreviations:

AC	adjuvant chemotherapy

BMI	body mass index
DRFS	distant recurrence-free survival
ER	estrogen receptor
IPW	inverse probability weighting
KM	Kaplan-Meier
NAC	neoadjuvant chemotherapy
OS	overall survival
pCR	pathologic complete response
PR	progesterone receptor
TME	tumor microenvironment
TMEM	tumor microenvironment of metastasis
TN	triple negative

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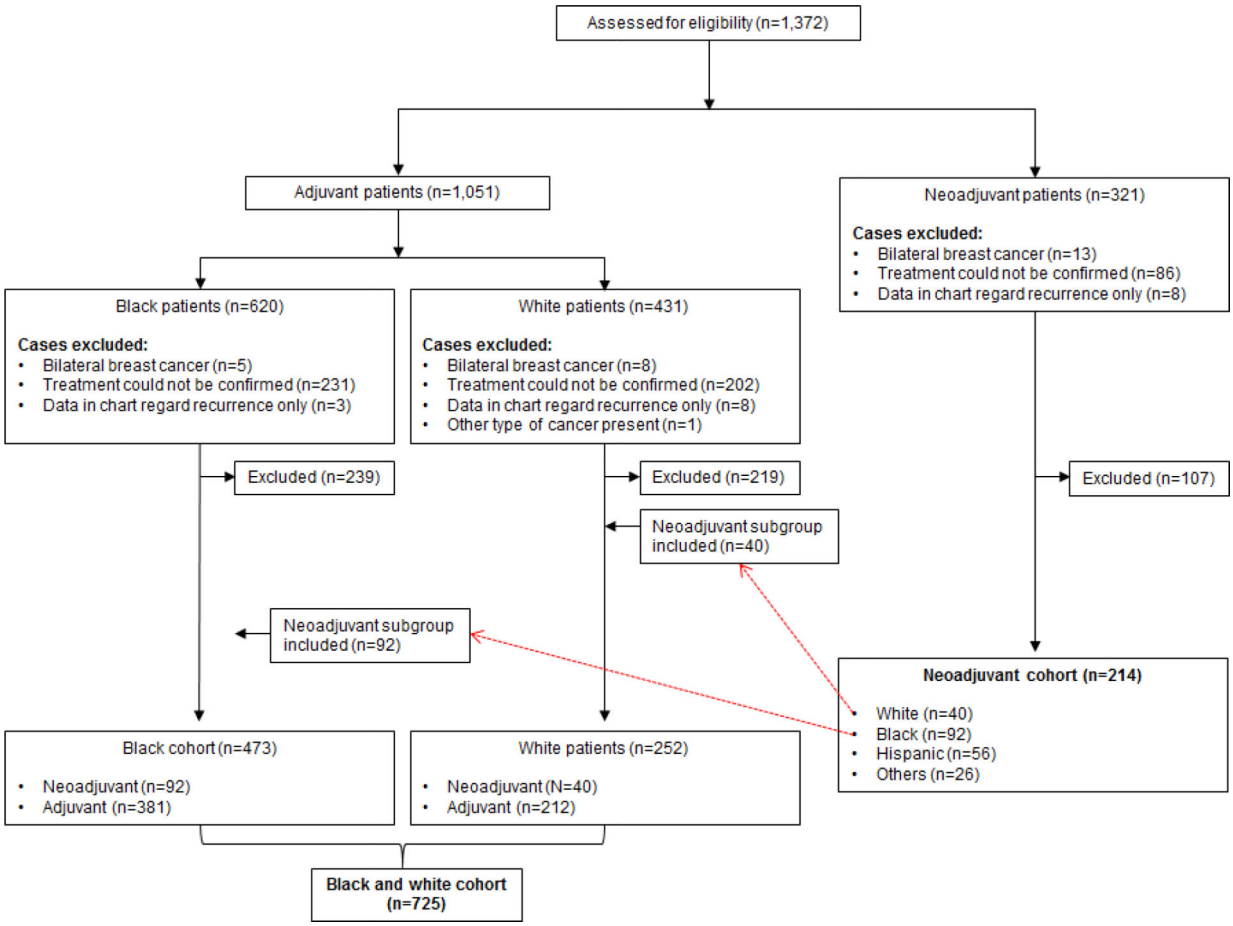

Figure 1.
Consort diagram.

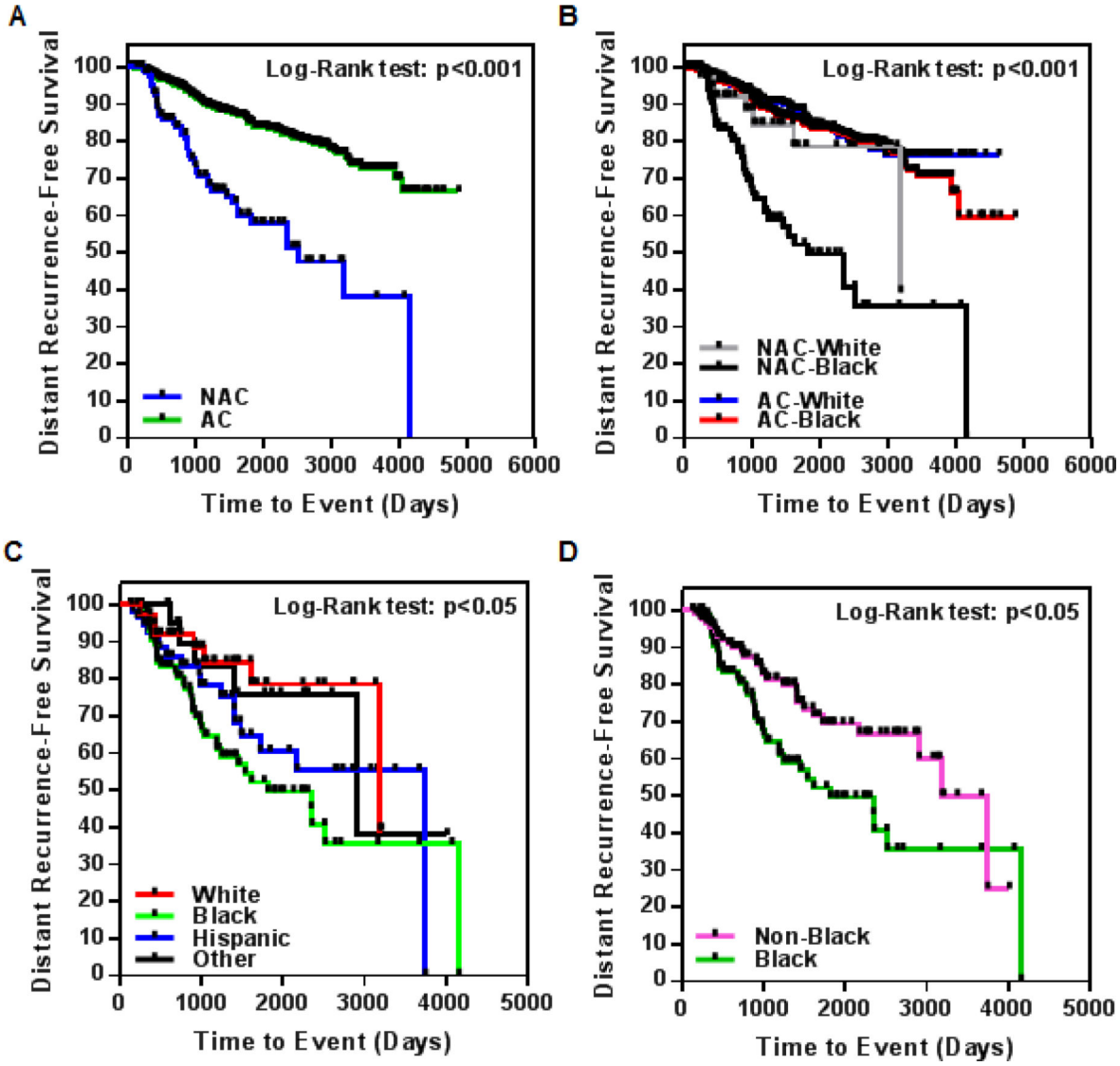

Figure 2.

(A-B) Kaplan-Meier curves demonstrating distant recurrence-free survival (DRFS) in black and white patients treated with either neoadjuvant (NAC) or adjuvant (AC) chemotherapy (A, non-stratified analysis; B, analysis stratified according to race and treatment). (C-D) KaplanMeier curves demonstrating DRFS in patients of various racial ethnicities, all treated with NAC. (C, race and ethnicity separated; D, DRFS for black vs. non-black races and ethnicities pooled).

Table 1.

Black and white patient cohort: patient and tumor characteristics

	White patients				Black patients			
Characteristic	**Neoadjuvant N (%)**	**Adjuvant N (%)**	**Total**	**Chi-Square (*p-value*)**	**Neoadjuvant N (%)**	**Adjuvant N (%)**	**Total**	**Chi-Square (*p-value*)**
All	40 (15.87%)	212 (84.13%)	252		92 (19.45%)	381 (80.55%)	473	
Age				0.92				0.007
<50	11 (27.50%)	60 (28.30%)	71		45 (48.91%)	129 (33.86%)	174	
>50	29 (72.50%)	152 (71.70%)	181		47 (51.09%)	252 (66.14%)	299	
Stage *				0.68				<0.0001
II	27 (67.50%)	150 (70.75%)	177		50 (54.35%)	287 (75.33%)	337	
III	13 (32.50%)	62 (29.25%)	75		42 (45.65%)	94 (24.67%)	136	
ER status				0.01				0.0003
Negative	15 (37.50%)	41 (19.34%)	56		53 (57.61%)	140 (36.75%)	193	
Positive	25 (62.50%)	171 (80.66%)	196		39 (42.39%)	241 (63.25%)	280	
PR status [1]				<0.0001				0.005
Negative	25 (62.50%)	68 (32.08%)	93		60 (66.67%)	190 (50.26%)	250	
Positive	15 (37.50%)	144 (67.92%)	159		30 (33.33%)	188 (49.74%)	218	
HER2 status [2]				<0.0001				0.09
Equivocal	4 (10.00%)	0 (0.00%)	4		1 (1.14%)	0 (0.00%)	1	
Negative	28 (70.00%)	170 (80.19%)	198		71 (80.86%)	281 (77.41%)	352	
Positive	8 (20.00%)	42 (19.81%)	50		16 (18.18%)	82 (22.59%)	98	
Triple-negative status [3]				0.02				0.0002
No	28 (70.00%)	181 (85.38%)	209		46 (57.27%)	262 (72.58%)	308	
Yes	12 (30.00%)	31 (14.62%)	43		42 (47.73%)	99 (27.42%)	141	

*Clinical stage was used for neoadjuvant and pathological stage for adjuvant cohort.

[1]PR status missing from 8 patients: Blacks/Neoadjuvant, N=90; Blacks/Adjuvant, N=378.

[2]HER2 status missing from 25 patients: Blacks/Neoadjuvant, N=88; Blacks/Adjuvant, N=363.

[3]Triple-negative status missing from 27 patients: Blacks/Neoadjuvant, N=88; Black/Adjuvant 361.

ER = estrogen receptor; PR = progesterone receptor; HER2 = Human Epidermal Growth Factor Receptor 2

Table 2.

Black and white patient cohort: patient and tumor characteristics

Black and white cohort pooled analysis				
Characteristic	**Neoadjuvant N (%)**	**Adjuvant N (%)**	**Total**	**Chi-Square (*p-value*)**
All	132 (18.21%)	593 (81.79%)	725	
Age				
<50	56 (42.42%)	189 (31.87%)	245	0.02
>50	76 (57.58%)	404 (68.13%)	480	
Stage*				
II	77 (58.33%)	437 (73.69%)	514	0.0004
III	55 (41.67%)	156 (26.31%)	211	
ER status				
Negative	68 (51.52%)	181 (30.52%)	249	<0.0001
Positive	64 (48.48%)	412 (69.48%)	476	
PR status[1]				
Negative	85 (65.38%)	258 (43.73%)	343	<0.0001
Positive	45 (34.62%)	332 (56.27%)	377	
HER2 status[2]				
Equivocal	5 (3.91%)	0 (0.00%)	5	<0.0001
Negative	99 (77.34%)	451 (78.43%)	550	
Positive	24 (18.75%)	124 (21.57%)	186	
Triple-negative status[3]				
No	74 (57.81%)	443 (77.31%)	517	<0.0001
Yes	54 (42.19%)	130 (22.69%)	184	

*Clinical stage was used for neoadjuvant and pathological stage for adjuvant cohort.

[1]PR status missing from 4 patients: Neoadjuvant, N=131; Adjuvant, N=590.

[2]HER2 status missing from 22 patients: Neoadjuvant, N=128; Adjuvant, N=575.

[3]Triple-negative status missing from 24 patients: Neoadjuvant, N=128; Adjuvant, N=573

ER = estrogen receptor; PR = progesterone receptor; HER2 = Human Epidermal Growth Factor Receptor 2

Table 3.

Multivariate analysis of DRFS in the Black and white patient cohort

Pooled (non-stratified) analysis (*n=725*, 100%)		
Characteristic	***p-value***	**Hazard ratio (95% CI)**
Black[1]	0.76	NAC:1.86 (0.82–4.22) AC: 1.07 (0.70–1.65)
Neoadjuvant	0.36	Black: 2.54 (1.64–3.93) White: 1.46 (0.64–3.33)
Race*Treatment interaction	0.24	-
Stage III*	<0.0001	4.46 (3.12–6.37)
Age <50	0.001	1.78 (1.26–2.53)
ER-	0.17	1.50 (0.84–2.69)
Triple-negative	0.23	1.44 (0.79–2.63)

Stratified-by-race analysis				
	White patients (*n=252*, 35%)		**Black patients (*n=473*, 65%)**	
Characteristic	***p-value***	**Hazard ratio**	***p-value***	**Hazard ratio**
Neoadjuvant	0.36	1.29 (0.56–2.95)	<0.0001	2.7 (1.73–4.22)
Stage III*	<0.0001	7.60(3.77–15.31)	<0.0001	3.66 (2.38–5.55)
Age <50	0.03	2.04 (1.10–3.92)	0.02	1.63 (1.08–2.47)
ER^-	0.05	2.95 (1.02–8.56)	0.70	1.14 (0.58–2.28)
Triple-negative	0.68	1.28 (0.40–4.11)	0.24	1.53 (0.76–3.09)

*Clinical stage was used for neoadjuvant and pathological stage for adjuvant cohort.

[1]The reference race is white.

AC = adjuvant chemotherapy; NAC = neoadjuvant chemotherapy; DRFS = distant recurrence-free survival; ER = estrogen receptor; CI = confidence interval

Table 4.

Neoadjuvant cohort: patient and tumor characteristics

Characteristic	Black N (%)	White N (%)	Hispanic N (%)	Other N (%)	Total	Chi-square (*p-value*)
All	92 (42.99%)	40(18.69%)	56 (26.17%)	26(12.15%)	214	
Age						
<50	45 (48.91%)	11 (27.50%)	25 (44.64%)	11 (42.31%)	92	0.15
>50	47(51.09%)	29 (72.50%)	31 (55.36%)	15(57.69%)	122	
Clinical stage						
I, II	50 (54.35%)	27 (67.50%)	28 (50.00%)	15(57.69%)	120	0.38
III	42 (45.65%)	13 (32.50%)	28 (50.00%)	11 (42.31%)	94	
ER status[1]						
Negative	53 (57.61%)	15 (37.50%)	16(30.19%)	10(40.00%)	94	0.008
Positive	39 (42.39%)	25 (62.50%)	37 (69.81%)	15(60.00%)	116	
PR status[2]						
Negative	60 (66.67%)	25 (62.50%)	24 (48.00%)	15(60.00%)	124	0.19
Positive	30 (33.33%)	15 (37.50%)	26 (52.00%)	10(40.00%)	81	
HER2 status[3]						
Equivocal	1 (1.14%)	4(10.00%)	2 (3.85%)	1 (4.00%)	8	0.20
Negative	71 (80.68%)	28 (70.00%)	37 (71.15%)	16(64.00%)	152	
Positive	16(18.18%)	8 (20.00%)	13(25.00%)	8 (32.00%)	45	
Triple-negative status[4]						0.003
No	46 (52.27%)	28 (70.00%)	40 (80.00%)	20 (80.00%)	134	
Yes	42 (47.73%)	12 (30.00%)	10(20.00%)	5 (20.00%)	69	

[1]ER status missing from 4 patients: Hispanics, N=53; Others, N=25.

[2]PR status missing from 9 patients: Blacks, N=90; Hispanics, N=50; Others, N=25.

[3]HER2 status missing from 9 patients: Blacks, N=88; Hispanics, N=52; Others, N=25.

[4]Triple-negative status missing from 11 patients: Blacks, N=88; Hispanics, N=50; Others, N=25

ER = estrogen receptor; PR = progesterone receptor; HER2 = Human Epidermal Growth Factor Recept

Table 5.

Multivariate analysis of DRFS in the Neoadjuvant cohort (non-black patients separated)

Characteristic	*p-value*	Hazard ratio
Black[1]	0.08	2.09 (0.91–4.79)
Hispanic	0.33	1.57 (0.63–3.94)
Other	0.95	0.99 (0.29–3.16)
Clinical stage III	<0.0001	3.09 (1.77–5.40)
Age <50	0.78	1.08 (0.65–1.79)
ER$^-$	0.32	1.51 (0.67–3.41)
Triple-negative	0.27	1.60 (0.70–3.68)

Multivariate analysis of DRFS in the Neoadjuvant cohort (non-black patients pooled together)

Characteristic	*p-value*	Hazard ratio
Black[2]	0.05	1.68 (1.00–2.85)
Clinical stage III	<0.0001	3.18 (1.83–5.54)
Age <50	0.68	1.11 (0.67–1.84)
ER$^-$	0.36	1.45 (0.65–2.23)
Triple-negative	0.23	1.65 (0.73–3.73)

[1]The reference race is white.

[2]The reference race is non-black.

DRFS = distant recurrence-free survival; ER = estrogen receptor

Table 6.

Neoadjuvant cohort: patient and tumor characteristics (all non-black patients pooled as one group)

Characteristic	Black N (%)	Non-Black N (%)	Total	Chi-square test (*p-value*)
All	92 (42.99%)	122 (57.01%)	214	
Age				0.13
<50	45 (48.91%)	47 (38.52%)	92	
>50	47 (51.09%)	75 (61.48%)	122	
Clinical stage				0.66
I,II	50 (54.35%)	70 (57.38%)	120	
III	42 (45.65%)	52 (42.62%)	94	
ER status				0.0009
Negative	53 (57.61%)	41 (34.75%)	94	
Positive	39 (42.39%)	77 (65.25%)	116	
PR status[1]				0.11
Negative	60 (66.67%)	64 (55.65%)	124	
Positive	30 (33.33%)	51 (44.35%)	81	
HER2 status[2]				0.09
Equivocal	1 (1.14%)	7 (5.98%)	8	
Negative	71 (80.68%)	81 (69.23%)	152	
Positive	16 (18.18%)	29 (24.79%)	45	
Triple-negative status[3]				0.003
No	46 (52.27%)	88 (76.52%)	134	
Yes	42 (47.73%)	27 (23.48%)	69	

[1] PR status missing from 9 patients: Blacks, N=90; Non-blacks, N=115.

[2] HER2 status missing from 9 patients: Blacks, N=88; Non-blacks, N=117.

[3] Triple-negative status missing from 11 patients: Blacks, N=88; Non-blacks, N=115.

ER = estrogen receptor; PR = progesterone receptor; HER2 = Human Epidermal Growth Factor Receptor 2

Table 7.

Chemotherapy regimen in black versus white patients.

Treatment	Black N (%)	White N (%)	Total	Chi-square (*p-value*)
All	473	252	725	
Chemotherapy[1]				0.40
Taxane-containing	227 (87.98%)	110 (90.91%)	337	
No taxane	31 (12.02%)	11 (9.09%)	42	
All Treatments				<0.01
Chemo	278 (58.77%)	107 (42.46%)	385	
Chemo + Endocrine	143 (30.23%)	118 (46.83%)	261	
Chemo + Trastuzumab	21 (4.44%)	8 (3.17%)	29	
Chemo + Endocrine + Trastuzumab	31 (6.55%)	19 (7.54%)	50	

[1]Detailed chemotherapy information missing from 428 patients: Black N=258; Adjuvant, N=121

Table 8.

Chemotherapy regimen in patients receiving neoadjuvant versus adjuvant chemotherapy. Treatment.

Treatment	Neoadjuvant N (%)	Adjuvant N (%)	Total	Chi-square (*p-value*)
All	214 (26.52%)	593 (73.48%)	807	
Chemotherapy[1]				0.01
Taxane-containing	136 (95.10%)	253 (87.24%)	389	
No taxane	7 (4.90%)	37 (12.76%)	44	
All Treatments				0.70
Chemo	113 (52.80%)	310 (52.28%)	423	
Chemo + Endocrine	73 (34.11%)	221 (37.27%)	294	
Chemo + Trastuzumab	10 (4.67%)	21 (3.54%)	31	
Chemo + Endocrine + Trastuzumab	18 (8.41%)	41 (6.91%)	59	

[1]Detailed chemotherapy information missing from 374 patients: Neoadjuvant N=143; Adjuvant, N=290.