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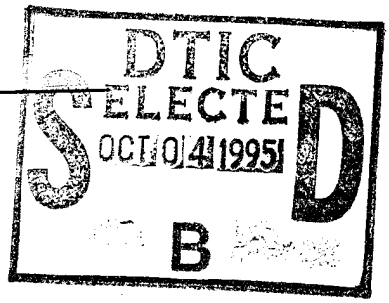

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African-American and caucasian women with newly diagnosed breast cancer were enrolled in the study. Upon enrollment, demographic data, tumor characteristics, and tumor staging data were obtained. Tumor samples were evaluated for estrogen and progesterone receptor levels, DNA ploidy, S-phase fraction, HER-2/neu expression, p53 protein accumulation, cathepsin D levels, and glutathione levels. Treatment choices, treatment received, relapse site and date, and date and cause of death were recorded in follow-up. To date, 90 women have been enrolled in the study (49 black and 41 white) and tumor samples have been analyzed in 70 women. While there have been differences between the black and white women noted in some of the above described parameters, none, as yet, reaches statistical significance.

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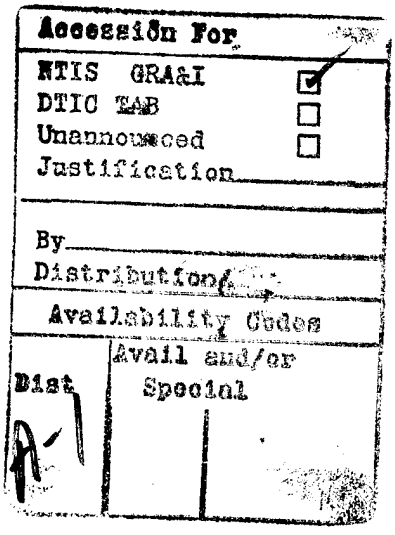

Introduction

Breast cancer is the most common invasive malignancy affecting American women, accounting for 28% of all tumors diagnosed in this group.[1] It is also a leading cause of cancer related death in the United States. Although the age-adjusted incidence of breast cancer in black women in the U.S. is less than that seen in white women, the mortality rates observed in blacks and whites are virtually identical.[2] This discrepancy is the result of a significantly lower five year survival rate for black women when compared to white women with breast cancer. The most recent results from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute have documented an 80% five year relative survival for white women diagnosed with breast cancer between 1983 and 1989; the corresponding rate for black women was only 64%.[3] While improvements in the detection and treatment of breast cancer over the last 30 years have led to an improved five year relative survival, there is no evidence that these advances have had an influence on the racial differences in survival.

In order to improve the survival of black women with breast cancer, an understanding of the factors which contribute to their poorer prognosis is necessary. It is known that black women generally have more advanced disease than white women at the time of initial presentation. A tendency toward larger primary tumors as well as a lower incidence of disease confined to the breast and a higher incidence of distant metastases at the time of diagnosis have been documented.[3-13] Environmental, behavioral, and biological factors have also been used to explain the higher incidence of advanced disease in black women with breast cancer. In particular, attention has focused on issues relating to access to medical care and preventive health services. The use of screening mammography has not been shown to be significantly different between healthy black and white women, although the only study of racial differences in breast cancer that has addressed this issue has noted a lower incidence of prior mammography in black women with breast cancer than in their white counterparts.[12,14] Black women with breast cancer have been found to more often rely on hospital-based or public clinics for their health care, and have been noted by some investigators to have a longer interval between symptom recognition and medical consultation.[7,15-17] The difference in median time to medical consultation between black and white women has generally been short, however, and has not adequately explained the significant difference in stage of disease at presentation.

There are also several biological differences in breast cancers of black and white women which may contribute to the differences in disease stage and survival seen in these populations. There is an increased incidence of medullary carcinoma among black women, accounting for 6-9% of all breast cancers, compared to white women, where this tumor histology is seen in 2-3% of women.[2,6,18] Black women have also been noted to have a higher incidence of poorly differentiated tumors of the breast, whether evaluated by architectural grade or nuclear grade, and in one large study higher grade tumors were significantly correlated with disease of more advanced stage.[5,12,19] A majority of studies which have compared hormone receptor levels in black and white women have documented a lower than expected incidence of estrogen receptor positive tumors in

black women with breast cancer.[5,6,12,14,19-23] One group of investigators has examined some of the more recently identified markers of breast tumor biology, including DNA ploidy, S-phase fraction, HER-2/*neu* protein levels and p53 protein accumulation. (52) White women had a significantly lower S-phase fraction than either the black or Hispanic populations.[24] This finding is not unexpected in light of the higher frequency of poorly differentiated tumors in African American women. The Black/White Cancer Survival Study, the most comprehensive study to date of racial survival differences in breast cancer found that tumor biologic characteristics (tumor grade and hormone receptor status) were second only to tumor stage in contributing to the observed survival difference.[25]

There are a limited number of studies which have evaluated the treatment of breast cancer in African American women. The Black/White Cancer Survival Study Group has reported that in women of equivalent stage, black women were just as likely to have surgical therapy as part of their primary treatment plan as white women. (73) They did find that black women were less likely to have breast conserving surgery and more likely to have a modified radical mastectomy.[26] The use of systemic adjuvant therapy, either chemotherapy or endocrine therapy has generally not been found to vary significantly according to race, although the data in this area is quite limited.[24,27-9] Even less information is available regarding the efficacy of systemic therapy in preventing relapse or improving survival in African American women with breast cancer. One study, presented only in abstract form, suggested that black women enrolled on Eastern Cooperative Oncology Group chemotherapy studies for breast cancer had a poorer survival than matched controls, although there is not enough information presented to adequately analyze the reported findings.[30]

Confounding all of this information is the issue of socioeconomic status and its close correlation with race. Observed differences in outcome, particularly if influenced by access to medical care, could certainly be a result of socioeconomics and not race. Attempts to control for socioeconomic factors (performed indirectly using census tract data) have not resulted in uniform agreement. Some studies have demonstrated a disappearance of racial differences in survival while others continue to show a significant impact of race upon survival with breast cancer.[7,11,31-4] Notably, the only prospective study which has collected socioeconomic data from individual patients demonstrated a continued effect of race on stage of disease at presentation.[12] In addition, the noted differences in tumor biology (histology, tumor grade, and hormone receptor status) are less easily explained solely by socioeconomic issues and thus raise the possibility of other factors significantly contributing to the observed survival difference.

We have initiated a prospective study evaluating the clinical, pathologic, and biologic characteristics of newly diagnosed breast cancers in a racially mixed, socioeconomically uniform cohort of patients seen at Truman Medical Center, the public hospital for Kansas City, Missouri. The objectives of the study are: 1) to determine if there are significant differences in breast cancer characteristics at presentation, prognostic factors, or treatment which could explain the survival differences noted between black and white women with the disease and 2) to determine if any documented differences are correlated with the survival of the women in the study.

Methods

Eligibility criteria. The study is being conducted at Truman Medical Center, the public hospital for Kansas City, Missouri. Women who meet the following eligibility requirements are being prospectively enrolled: 1) histologically confirmed invasive adenocarcinoma of the breast, 2) primary surgical therapy for the breast cancer performed at Truman Medical Center, 3) women of African-American or white ethnic background, 4) no prior exposure to radiation therapy or chemotherapy, and 5) written informed consent.

Demographic data. After study enrollment, demographic information is obtained, including age, race, menstrual history, estrogen exposure, family history of cancer, nutritional measurements, and weekly alcohol consumption.

Tumor analysis. Tumor tissue was obtained from either breast biopsy or mastectomy specimens, after gross examination by a pathologist, and tissue was placed in zinc-buffered formalin for routine histology, frozen for routine quantitative estrogen and progesterone receptor analysis, and sent fresh for drug metabolism parameters. Hematoxylin and eosin stained sections will be examined, and the tumors classified according to the criteria of the World Health Organization. Pathologic stages are defined according to the TNM classification.

DNA ploidy, cell cycle analysis, HER-2/*neu* protein content, p53 protein content, and cathepsin D levels were assessed by immunohistochemical analysis of paraffin embedded tissue. This analysis was performed by an outside reference laboratory with extensive experience in the area of cancer immunohistochemistry (Dianon Laboratories, Stratford, CT) using standard techniques.

HER-2/*neu* DNA amplification was determined by Southern blot analysis as described by Herold and Rothberg.[35] The pCER204 probe will be used for this purpose.[36]

Neovascularization in the tumor was evaluated in paraffin-embedded tissue primarily fixed in zinc-buffered formalin. Endothelial cells were stained using antisera against Factor VIII (Dako Polyclonal, Santa Barbara, CA) and the avidin-biotin peroxidase method. Representative areas of the tumor were selected, and microvessel density was assessed using MacMeasure morphometry software (Wayne Rasband, Research Services Branch, NIMH) and a microdigipad (GTCO, Bethesda, MD) with tracings of eighteen x400 photomicrographs of representative areas of each tumor.

Tumor drug metabolism parameters were assessed using fresh tissue. Fresh tumor specimens (at least 500 mg) were minced into small, 2-3 mm pieces and washed twice with cold isotonic saline.Glutathione (GSH) will be determined in tissue extracts by a specific, and sensitive fluorometric assay using o-phthaladehyde as the fluorescent agent.[37] GSH concentration will be expressed based on milligram protein and milligram DNA.

Patient follow-up. Breast cancer treatment recommendations and treatment received were recorded for each patient by review of the medical record. Patient outcome data including response to therapy, time to relapse, and survival were also obtained by review of the medical record.

Statistical analysis. Differences between blacks and whites in categorical breast cancer biologic characteristics will be analyzed by a chi-square test for independence. Continuous variables will be evaluated by the Student's t test and/or Mann-Whitney U test for ranked data. Relapse-free survival and overall survival will be estimated using life table analysis, with differences in survival between black and white patients assessed by a generalized Wilcoxon test.

Results

As of June 1, 1995, 90 women have been enrolled in the study, 49 black women and 41 white women. Tumor stage at the time of diagnosis is outlined in the table below. There were no significant differences in stage at presentation, although black women did appear to have a higher incidence of the smallest (T_1) primary tumors compared to the white women in this study. Lymph nodes were involved in an approximately equal number of women and the median number of positive nodes was 3 for both the black and white women. An equal number of black and white women had distant metastatic disease at the time of diagnosis.

Tumor Stage	**Black (49)**	**White (41)**
T stage	%	%
T_0	2.0	0
T_1	34.7	26.8
T_2	30.6	48.8
T_3	24.5	17.1
T_4	6.1	7.3
T_x	2.0	0
Axillary nodes		
(-)	44.9	41.5
(+)	42.9	48.7
Unknown	12.2	9.8
Metastases		
Yes	12.2	12.2

	Black	White
Overall AJCC Stage		
I	28.6	17.1
IIA	20.4	31.7
IIB	16.3	26.8
IIIA	14.3	7.3
IIIB	4.1	4.9
IV	12.2	12.2
Unknown	4.0	0

The predominant histologic type in both racial groups was ductal carcinoma, as expected, seen in 75% of black women and 90% of white women. Carcinoma-in-situ was noted in the tumor specimen in 55% of white women and 66% of black women.

Tumor biologic characteristics have been completely analyzed in approximately 70 women to date. The table below summarizes these results. The numbers in parentheses indicate the number of samples analyzed for the indicated marker. None of the differences noted between black and white women reach the level of statistical significance ($p = 0.05$) at this time.

Tumor Characteristic	Black	White
ER (+)[76]	52.0%	71.0%
PR (+)[76]	47.6%	64.7%
DNA index aneuploid[69]	57.2%	50.0%
S-phase fraction ≥ 8[51]	60.0%	50.0%
HER-2/*neu* expression ↑[70]	48.6%	31.5%
p53 expression ↑[70]	34.3%	48.6%
Cathepsin D expression ↑[70]	65.7%	74.3%
Mean microvessel density[46]	11.54	13.35
Glutathione levels (pmol/μprotein)[24]	9.71	11.89

Only preliminary data is currently available regarding treatment choices in the management of breast cancer in our patient population. Overall, 80% of the enrolled patients have had a modified radical mastectomy, 10% have had breast conserving surgery, and 10% have had only biopsy. Black women are slightly more likely to have breast conservation (15% vs. 5%), but this may be only a reflection of the higher incidence of T_1 tumors in black women. Twenty-eight percent of all women have

received breast radiotherapy after the primary surgery with no difference observed in black and white women. Chemotherapy was used in 47% of all women and hormonal therapy in 58%, with no racial differences noted. Overall therapy was judged to be adequate for disease stage in 75% of white women and 78% of black women. It is important to note that this information is incomplete, as many of the enrolled women are still receiving adjuvant therapy.

Conclusions

To date, patient accrual and sample processing has gone very smoothly. As a result, there is currently no need to modify the investigational approach. Patient enrollment goals are on schedule, and the planned accrual of 200 patients should be met in 1998. It is clear, however, that data collection will not be complete for approximately one year after the termination of accrual, as treatment assessment cannot be adequately made until the completion of adjuvant therapy.

The number of patients in the study is too small to make any conclusions about differences in breast cancer between black and white women. Several interesting trends can be noted, however. Black women have a higher incidence of T_1 tumors. Many of these small tumors were discovered on routine screening mammography and this disparity in the prevalence of the smallest cancers raises the question of a difference in mammographic screening practices between black and white women at our institution. We will be retrospectively reviewing this data on our enrolled patients, and have initiated a prospective study evaluating screening practices in the general medicine clinics. Tumor stage does not, at the present time, appear to be more advanced in black women in our patient population, with 12% of white and black women presenting with metastatic disease.

The expected difference in hormone receptor levels is being observed, but is not at a level to reach statistical significance at this time. While there are some racial differences noted in several of the studied prognostic factors, it is too early to tell if these trends will continue.

The most notable finding regarding therapy of breast cancer in our patient population is the low rate of breast conserving surgery. Reasons for this have not been explored at this time, but there are preliminary plans to investigate this issue in the future. Finally, the rate of therapy judged "inadequate" is quite high. This may be simply a result of analysis of treatment too early in the patient's course and further follow-up will correct this finding. Alternatively, it may be a real finding, in which case additional case analysis will be necessary. A major goal of this project over the second year of implementation will be to develop a system for analyzing therapy and the explanations for inadequate treatment.

REFERENCES

1. Silverberg E, and Lubera JA: Cancer statistics, 1989. CA--A Journal for Clinicians 39:3-20, 1989.
2. Cancer among blacks and other minorities: Statistical Profiles. National Cancer Institute, NIH Publication number 86-2785, March 1986.
3. Miller BA, Gloeckler Ries LA, Hankey BF, Kosary CL, Harras A, Devesa SS, et al.. SEER Cancer statistics review, 1973-1990. NIH Publication Number 93-2789; 1993.
4. Nemoto T, Vana J, Bedwani RN, Baker HW, McGregor FH, and Murphy GP: Management and survival of female breast cancer: Results of a national survey by the American College of Surgeons. Cancer 45:2917-2924, 1980.
5. Ownby HE, Frederick J, Russo J, Brooks SC, Swanson GM, Heppner GH, Brennan MJ, and the Breast Cancer Prognostic Study Associates: Racial differences in breast cancer patients. Journal of the National Cancer Institute 75:55-60, 1985.
6. Natarajan N, Nemoto T, Mettlin C, and Murphy GP: Race-related differences in breast cancer patients: Results of the 1982 national survey of breast cancer by the American College of Surgeons. Cancer 56:1704-1709, 1985.
7. Vernon SW, Tilley BC, Neale AV, and Steinfeldt L: Ethnicity, survival, and delay in seeking treatment for symptoms of breast cancer. Cancer 55:1563-1571, 1985.
8. Bain RP, Greenberg RS, and Whitaker JP: Racial differences in survival of women with breast cancer. Journal of Chronic Diseases 39:631-642, 1986.
9. Polednak AP: Breast cancer in black and white women in New York State: Case distribution and incidence rates by clinical stage at diagnosis. Cancer 58:807-815, 1986.
10. Satariano WA, Belle SH, and Swanson GM: The severity of breast cancer at diagnosis: A comparison of age and extent of disease in black and white women. American Journal of Public Health 76:779-782, 1986.
11. Wells BL, and Horm JW: Stage at diagnosis in breast cancer: Race and socioeconomic factors. American Journal of Public Health 82:1383-1385, 1992.
12. Hunter CP, Redmond CK, Chen VW, Austin DF, Greenberg RS, Correa P, Muss HB, Forman MR, Wesley MN, Blacklow RS, Kurman RJ, Dignam JJ, Edwards BK, Shapiro S and other members of the Black/White Cancer Survival Study Group: Breast cancer: Factors associated with stage at diagnosis in black and white women. Journal of the National Cancer Institute 83:1129-1137, 1993.
13. Mandelblatt J, Andrews H, Kerner J, Zauber A, and Burnett W: Determinants of late stage diagnosis of breast and cervical cancer: The impact of age, race, social class, and hospital type. American Journal of Public Health 81:646-649, 1991.
14. Ackermann SP, Brackbill RM, Bewerse BA, Sanderson LM: Cancer screening behaviors among U.S. women: Breast cancer, 1987-1989, and cervical cancer, 1988-1989. Morbidity and Mortality Weekly Reports 41(SS-2):17-34, 1992.
15. Dennis CR, Gardner B, and Lim B: Analysis of survival and recurrence vs. patient

and doctor delay in treatment of breast cancer. Cancer 35:714-720, 1975.

16. Mittra NK, Rush BF, and Verner E: A comparative study of breast cancer in the black and white populations of two inner-city hospitals. Journal of Surgical Oncology 15:11-17, 1980.
17. Coates RJ, Bransfield DD, Wesley M, Hankey B, Eley JW, Greenberg RS, Flanders D, Hunter CP, Edwards BK, Forman M, Chen VW, Reynolds P, Boyd P, Austin D, Muss H, Blacklow RS, and the Black/White Cancer Survival Study Group: Differences between black and white women with breast cancer in time from symptom recognition to medical consultation. Journal of the National Cancer Institute 84:938-950, 1992.
18. Freeman HP, and Wasfie TJ: Cancer of the breast in poor black women. Cancer 63:2562-2569, 1989.
19. Mohla S, Sampson CC, Khan T, Enterline JP, Leffall L, and White JE: Estrogen and progesterone receptors in breast cancer in black Americans: Correlation of receptor data with tumor differentiation. Cancer 50:552-559, 1982.
20. Lesser ML, Rosen PP, Senie RT, Duthie K, Menendez-Botet C, and Schwartz MK. Estrogen and progesterone receptors in breast carcinoma: Correlations with epidemiology and pathology. Cancer 48:299-309, 1981.
21. Pegoraro RJ, Karnan V, Nirmul D, and Joubert SM: Estrogen and progesterone receptors in breast cancer among women of different racial groups. Cancer Research 46:2117-2120, 1986.
22. Crowe JP, Gordon NH, Hubay CA, Pearson OH, Marshall JS, McGuire WL, and participating investigators: The interaction of estrogen receptor status and race in predicting prognosis for stage I breast cancer patients. Surgery 100:599-605, 1986.
23. Stanford JL, and Greenberg RS: Breast cancer incidence in young women by estrogen receptor status and race. American Journal of Public Health 79:71-73, 1989.
24. Elledge RM, Clark GM, Chamness GC, and Osborne CK: Tumor biologic factors and breast cancer prognosis among white, hispanic, and black women in the United States. J Natl Cancer Inst 86:705-12, 1994.
25. Eley JW, Hill HA, Chen VW, Austin DF, Wesley MN, Muss HB, Greenberg RS, et al.: Racial differences in survival from breast cancer: Results of the National Cancer Institute Black/White Cancer Survival Study. JAMA 272:947-54, 1994.
26. Pierce L, Fowble B, Solin LJ, Schultz DJ, Rosser C, and Goodman RL: Conservative surgery and radiation therapy in black women with early stage breast cancer: Patterns of failure and analysis of outcome. Cancer 69:2831-41, 1992.
27. Ownby HE, Frederick J, Russo J, Brooks SC, Swanson GM, Heppner GH, Brennan MJ, et al.: Racial differences in breast cancer patients. J Natl Cancer Inst 75:55-60, 1985.
28. Muss HB, Hunter CP, Wesley M, Correa P, Chen VW, Greenberg RS, Eley JW, et al.: Treatment plans for black and white women with stage II node-positive breast cancer. Cancer 70:2460-7, 1992.

29. Diehr P, Yergan J, Chu J, Feigl P, Glaefke G, Moe R, Bergner M, et al.: Treatment modality and quality differences for black and white breast-cancer patients treated in community hospitals. Med Care 27:942-58, 1989.
30. Zelen M, Betensky R, and Gelman R. Black vs. white survival in clinical trials: The ECOG experience. Proc Am Soc Clin Oncol 9:59, 1990.
31. Bassett MT, and Krieger N: Social class and black-white differences in breast cancer survival. American Journal of Public Health 76:1400-1403, 1986.
32. Dayal HH, Power RN, and Chiu C: Race and socio-economic status in survival from breast cancer. Journal of Chronic Diseases 35:675-683, 1982.
33. Farley TA, and Flannery JT: Late-stage diagnosis of breast cancer in women of lower socioeconomic status: Public health implications. American Journal of Public Health 79:1508-1512, 1989.
34. Gordon NG, Crowe JP, Brumberg DJ, and Berger NA: Socioeconomic factors and race in breast cancer recurrence and survival. American Journal of Epidemiology 135:609-618, 1992.
35. Herold KM, and Rothberg PG: Amplification and activation of the c-myc oncogene in adenocarcinoma of the large bowel. Familial Adenomatous Polyposis. p.361-369, 1990.
36. Ishii S, Imamota F, Yamanushi Y, Toyoshima K, and Yamamoto T: Characterization of the promoter region of the human c-*erbB-2* protooncogene. Proceedings of the National Academy of Sciences 84:4374-4378, 1987.
37. Hissin PJ, and Hilf R: A fluorometric method for determination of oxidized and reduced glutathione in tissues. Analytical Biochemistry 74:214-226, 1976.