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Princess Ekpo April 14, 2020

A Retrospective Review of Minority Enrollment and Clinical Outcomes in Breast Cancer Clinical Trials at Emory University

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Abstract

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Background: Black women are 40% more likely to die of breast cancer compared to White women. Inadequate representation of Blacks in clinical trials may contribute to health care inequity. Emory's Winship Cancer Institute (WCI) in Atlanta services a significant Black population and has a unique opportunity to engage these underrepresented patients in clinical trials. We aimed to assess clinical outcomes in Black versus White women with breast cancer enrolled on investigator-initiated clinical trials (IITs) at Emory.

Methods: Black and White women with breast cancer enrolled on IITs conducted at WCI between 1/2009 and 1/2019 were retrospectively evaluated. Descriptive statistics were generated for all patient characteristics. Univariate analyses and multiple logistic regression models were used to assess the effect of age and race on clinical response, length of time on trial, number of therapy lines prior to trial enrollment, and toxicity on trial. Overall survival patients with metastatic breast cancer (MBC) was assessed using Kaplan Meier analysis.

Results: One hundred and thirty-five women with breast cancer were included [White, n=92 (68.1%), and Black, n=43 (31.9%)]. There were 73 (54.1%) early-stage patients (stages I-III) and 62 patients with MBC. Mean BMI was higher for Black women in comparison to White women for both and early- and late-stage patients ($p<0.001$ and 0.044, respectively). Black women with MBC were enrolled on trial for less time than White women (5.62 months vs. 7.77 months, respectively, $p=0.22$) and more likely to have progressive disease (PD) on trial (45% in Blacks vs. 20% in Whites, $p=0.05$). There were no differences in toxicity rates and overall survival among patients enrolled on IITs based on race.

Conclusions: Black and White women with early-stage breast cancer have no significant difference in clinical outcomes. Black women with MBC who enrolled on IIT trials at Emory had worse treatment response and a trend towards poorer survival compared to White women. More research is needed to determine whether this is due to adverse biology. These results reinforce the need for exploration of biomarkers of response by race and ethnicity and improved representation of minorities in clinical trials to inform real-world efficacy.

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1. Background

Cancer is the second leading cause of death across the globe. In the United States, blacks have higher cancer-related mortality in comparison to whites for all cancer types, independent of sociodemographic factors and access to treatments.[1] For breast cancer, black women have a higher incidence of early-onset disease and a greater risk of mortality than any other race or ethnic group.[2] Triple-negative breast cancer (TNBC) is a subtype that exhibits aggressive metastasis, high risk of recurrence, and accounts for 10-30% of invasive breast cancers in the U.S.[3] The prevalence of TNBC and similar basal-like breast cancer subtypes is significantly higher in premenopausal black and Latino women.[4]

There have been tremendous advances over the last decade to investigate novel combinations of therapies, including targeted agents and immunotherapy, to improve the quality of life and prognosis of women with breast cancer.[5,6] Clinical trials evaluate the dose safety and efficacy of these newly designed therapies before their approvals by the U.S. Food Drug and Administration (FDA).[7] Based on the demographics of US cancer incidence, there is a disproportionate number of black patients enrolled in clinical trials leading to FDA approval of oncology drugs in comparison to white patients.[8] Black patients constituted only 4% of clinical trial participants in pivotal trials leading to FDA approval of oncologic therapies. Despite the policy prescriptions of the NIH Revitalization Act to promote clinical research equity regarding women and minorities, the underrepresentation of minorities in NCI-sponsored clinical trials has persisted 20 years later.[9]

There are known racial variations in tumor biology and response documented in the literature.[10–12] The differences in the drug metabolism across racial and ethnic groups also influence the differences in toxicity exhibited for these groups.[13] The generalizability of the efficacy and tolerability of cancer therapeutics in the overall cancer population has, therefore, been questioned given the poor representation of blacks and other minorities in the trials leading to their FDA approval.[14] The lack representative racial/ethnic participation in clinical research extends to the treatment of breast cancer and has the potential to further perpetuate existing cancer mortality disparities between minorities and whites.

In the Unites States, black women with breast cancer die at a significantly higher rate in comparison to white women with breast cancer. Among the most populous US cities, Atlanta had the largest increase in breast cancer mortality disparity between black women and white women from the year 2005 to 2014.[15] Several studies have identified potential reasons for the racial and ethnic disparities in cancer survival, including biological differences, socioeconomic factors and inadequate minority enrollment in drug testing.[16–19] There is currently limited knowledge of minority enrollment in breast cancer clinical trials in the Atlanta metropolitan area. This study evaluates minority enrollment in breast cancer clinical trials at Emory University, an Atlanta-

based institution, to determine the demographics of patients enrolled in breast cancer clinical trials and identify disparities in clinical outcomes between black and white women.

2. Methods

2.1 Patient Population

Patients with invasive breast cancer enrolled on investigator-initiated breast cancer clinical trials conducted at Winship Cancer Institute of Emory University between 2009 and 2019 were eligible. Trial-specific data was collected from the electronic clinical trial management system for selected studies while demographic data and breast cancer clinical outcomes were collected through the electronic medical record. We evaluated data from patients on eleven different investigator-initiated phase I clinical trials conducted at our center. The selected studies evaluated an investigational therapy in the neoadjuvant, adjuvant or metastatic setting. The Emory University Institutional Review Board approved this study.

2.2 Statistical Analyses

Descriptive statistics were generated for all patient characteristics. Frequency and percentage were reported for categorical variables, and mean, median, standard deviation, IQR, and range were reported for numeric variables. Differences between race was assessed using chi-sq. test for categorical variables and ANOVA for numeric variables and negative binomial regression for count data. Univariate (UVA) analysis based on chi-square for categorical and ANOVA for numeric variables was used to determine the effect of each clinicopathological variable on binary best response. Multiple logistic regression analyses (MVA) was performed adjusting for age and stage. For the secondary outcome, length of time on trial was square root transformed to meet the normality and heteroscedastic assumptions. univariate analysis based on ANOVA for categorical variables and a Pearson correlation test for numeric variables were conducted for determine the clinicopathological variables significantly associated with length of time on trial. Multiple linear regression analysis was performed adjusting for age and stage. A sensitivity analysis including Stage IV patients was also conducted. Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC), and statistical significance was assessed at the 0.05 level.

2.3 Clinical Outcomes

The primary endpoints reviewed in this study are: 1) best clinical response to therapeutic drug (stable disease, partial response or complete response versus progressive disease), 2) treatment discontinuation rate and reason for treatment discontinuation (adverse events, disease progression, patient withdrawal, or treatment completion), and 3) highest grade of hematologic

and non-hematologic toxicity according to NCI CTCAE v. 4.0 criteria. Overall survival was also assessed for stage IV patients.

3. Results

3.1 Entire study cohort

There were 135 patients included in the study cohort treated on investigator-initiated breast cancer therapeutic trials from 1/2009 to 1/2019. To allow for clinically relevant comparisons, we divided the cohort into early-stage and late-stage categories. There were 73 (54.1%) early-stage patients (stages I-III) and 62 late-stage (stage IV) patients. Table 1 displays the descriptive statistics of all included patients. The self-identified race was White for 92 (68.1%) patients and Black for 43 (31.9%) patients. Over 90% of the patients were enrolled on phase II trials most of whom received targeted (43%) or combined targeted therapy and chemotherapy (40.7%). All patients were female, and the mean age at trial consent was 53.70 (± 11.05) years. The mean BMI was 28.13 (± 7.25). The primary reason for treatment discontinuation was treatment completion (47%), followed by disease progression (35.1%), adverse events (9%), and patient withdrawal (9%).

3.2 Early-stage patients

Of the 73 early-stage patients included in this study, the self-identified race was White for 51 (69.9%) patients and Black for 22 (30.1%) patients. Table 1 shows the descriptive statistics for stage I-III patients. All patients were female, and the mean age at trial consent was 52.62 (± 11.38) years. The maximum number of lines prior to first clinical trial was 4. Fifty-four percent of the patients had a partial response to treatment. Patients were most likely to discontinue treatment after completing treatment per protocol criteria (79.2%). The highest grade for hematologic and non-hematologic toxicities was grade 1 for most early-stage patients (77.2% and 47.9%, respectively).

Based on the univariate analysis for race, the mean BMI for Black women (35.77) was higher than that of White women (26.71) (p-value <0.001) (Table 2). For early-stage patients, there were no significant differences in age and stage at time of trial, phase of trial, class of therapeutic drug and time on trial between Black and White women per univariate analyses (Table 2). There were also no differences displayed in the number of lines prior to first clinical trial, receptor status, adverse events, reason for treatment discontinuation, time on trial and best response between Black and White women (Table 2). There were no significant relationships identified between best response and any of the evaluated covariates (Table 3, 4A, 4B).

Based on multivariable analysis, women who were older at trial consent spent more time enrolled on trial after adjusting for race and BMI (p-value=0.031) (Table 6). There were no relationships exhibited between time enrolled on trial and race or BMI for early-stage patients (Table 5, 6, and 6B). There were also no relationships exhibited between reason for treatment discontinuation and race or BMI for early-stage patients (Table 7, 8, 8B).

3.3 Late-stage patients

Table 1 shows the descriptive statistics for the stage IV patients like those previously stated. Sixty-two women with MBC were included [White, n=41 (66%), and Black, n=21 (34%), p=0.55]. Over 90% of women were enrolled on phase II clinical trials and received targeted therapy. Mean age at clinical trial consent was 53.2 and 55.9 years in Black and White women, respectively (p=0.36). While most women had hormone-receptor positive disease, a higher percentage of Blacks had triple negative breast cancer (29% vs. 17% in Whites, p=0.39). Black women had fewer lines of systemic therapy prior to trial enrollment (2.86 vs. 4.24, respectively, p=0.021) and were enrolled on trial for less time than White women (5.62 months vs. 7.77 months, respectively, p=0.22). The mean BMI of Black women with MBC was significantly higher than that of White women (p=0.029). There were no significant differences in class of therapeutic drug and reason for treatment discontinuation between Black and White women. The odds of having progressive disease for Black women are 4.12 times higher than that of White women after adjusting for BMI and age (p-value=0.045) (Table 4B). There were no significant relationships identified between best response and age at trial consent or BMI (Tables 3, 4A, 4B). There are no relationships exhibited between time enrolled on trial and race, age at trial consent or BMI for late-stage patients (Tables 5, 6, and 6B).

There were no differences in toxicity rates among patients enrolled on IITs based on race. Black women were more likely to have progressive disease (PD) on trial (43% in Blacks vs. 22% in Whites, p=0.086). While there was no significant difference in overall survival (p=0.388), there was a trend towards shorter survival in Black women (38.12 months vs. 63.54 months, respectively). The difference in survival time between Black and White patients increased as patients stayed on the trial for longer (Figures 1 and 2).

Based on univariate cumulative logistic regression (Table 7), the odds of having adverse events (AEs) versus disease progression (DP)/ patient withdrawal/ treatment completion for the underweight BMI category are 2.76 times greater compared to obese. When controlling for race and age, the odds of having AEs vs DP/ patient withdrawal/ treatment completion for those who are of normal weight are 73% lower compared to obese and overweight patients are 87% lower compared to obese. The association of overweight compared to obese is significantly associated with reason for treatment discontinuation (p=0.014).

Based on multivariable cumulative logistic regression (Table 8B), the odds of having adverse events (AEs) vs disease progression (DP)/ patient withdrawal/ treatment completion for the underweight BMI category are 2.08 times greater compared to obese after holding race and age constant. For those who are of normal weight, the odds of having AEs vs DP/ patient withdrawal/ treatment completion are 76% lower compared to obese. For those who are overweight, the odds are 91% lower compared to obese controlling for race and age. The association of overweight compared to obese is significantly associated with reason for treatment discontinuation (p-value=0.09). There were no significant relationships exhibited between treatment discontinuation and race or age at trial consent for late-stage patients (Table 7, 8, 8B).

4. Discussion

This study evaluated minority enrollment and clinical outcomes in investigator-initiated trials (IITs) for breast cancer treatment over the past 10 years to identify any disparities at Winship Cancer Institute of Emory University, a National Cancer Institute (NCI)-designated comprehensive cancer center based in Atlanta. In recent years, breast cancer was identified as the leading cause of death among black women in Georgia and Atlanta was found to have the largest disparity in cancer mortality between Black and White females among the 50 largest cities in the United States.[15,20] The Glenn Family Breast Center at Winship Cancer Institute of Emory University and Grady Memorial Hospital offer a unique opportunity to increase clinical trial accrual in minority women given the high percentages of women of African or Hispanic ancestry in our catchment area. A current view of minority participation in IITs at Emory University was conducted to understand if disparities in minority enrollment and breast cancer clinical trials was also seen at our institution.

There were 31.9% black women and 68.1% white women enrolled on breast cancer IITs at Emory between 2009 and 2019. While minority representation in Emory's breast cancer IITs is higher than minority enrollment described in other cancer therapeutic trials, it is still less than what is expected based on the demographics of the general Atlanta population (Black 51.85% versus White 40.27%)[21] and the higher incidence of breast cancer among Black versus White women. The lack of patient-level demographics specific to breast cancer in Atlanta limits the ability to assess the true success of the Winship Cancer Institute in the recruitment of representative patient populations for clinical research. A recent study of 5 regionally diverse NCI-designated cancer centers displayed a lack of standardized declaration of their catchment areas and inconsistent tracking of race and socioeconomic status for therapeutic trials.[22]

Early-stage blacks were younger at trial consent in comparison to whites. This is likely due to fact that black women have the highest breast cancer incidence before age 40 in the United States.[20] Black women with metastatic breast cancer who enrolled on IITs at Emory University

had worse treatment response and a trend towards poorer survival compared to White women. One study evaluated racial disparities in cancer survival on cancer clinical trials for 19,457 patients of the Southwest Oncology Group. It revealed that Black women had significantly worse survival than White women for breast cancer (hazard ratio =1.49; p-value <0.001).[23] A more recent study of phase I clinical trials at Emory University that evaluated clinical outcomes found Black patients were younger and had significantly shorter survival in comparison to white women (7.4 vs. 11.4 months; p-value of 0.0227).[24] For all stages at diagnosis, breast cancer survival is lowest for Black women in the United States.[20] More research is needed to determine whether poorer survival in Black women is due to adverse biology. While most women had hormone-receptor positive disease, a higher percentage of Blacks had triple-negative breast cancer (TNBC). This is not surprising as the US incidence rates for TNBC are about two times higher in Black women in comparison to White women.[20] Several studies have shown the higher incidence of TNBC in women of African descent and how its aggressive nature is influenced by genetics and the environment.[25–27] This may be one of the factors contributing to poorer breast cancer survival in black women. These results reinforce the need for exploration of biomarkers of response by race and ethnicity and improved representation of minorities in clinical trials to inform real-world efficacy.

When looking at other factors including whether age and BMI at trial consent impacted breast cancer clinical outcomes for both early stage and late stage women, we found that a lower BMI was associated with increased adverse events when holding for age and race. In our study, Black women with breast cancer from all stages had significantly higher BMI than White women; however, we did not see an increase in adverse events in White women despite their lower BMIs. Recent studies suggest that lower BMI leads to worse clinical outcomes in patients with cancer [28], which again was not seen in our study. In fact, black women with stage IV disease were more likely to have progressive disease while on trial compared to white women and there were no differences in toxicity rates among patients enrolled on IITs based on race. This again suggests that there are differences in disease biology between black and white women that impact both adverse events, response to treatment and overall survival.

A review of 20 health research studies reported minimal differences in racial and ethnic minorities in willingness to participate in clinical trials in the United States.[29] Similarly, a National Cancer Institute/National Institute of Mental Health (NCI/NIMH)-funded study of 358 terminally ill cancer patients revealed that race/ethnicity was not associated with drug trial enrollment when socioeconomic status was held constant.[30] These studies suggest that low minority enrollment is not greatly due to a low willingness of minorities to participate in clinical trials. Though further research is warranted to truly explain the trends seen in representation of racial/ethnic minorities in clinical research, trust of care providers and effective communication may play larger roles in observed trends than willingness to participate.

This study served to characterize the representation of racial minorities and their clinical outcomes on IITs at Emory University. The next steps involve improving institutional clinical recruitment trial practices. Previous studies have identified several barriers to minority participation in clinical trials, including mistrust, language/transportation barriers, and decreased awareness about available trials.[31,32] Having minority study coordinators will not only help to diversify the healthcare workforce but also ensure that all patients appropriately being informed of clinical trial opportunities and standard of care. The most effective strategies at select US Cancer Centers for Excellence for increasing the inclusion of racial and ethnic minorities in cancer clinical trials included increased minority representation in research staff and engagement with providers and community leaders.[33] Patient-physician communication is oftentimes of poor quality between Black patients and non-Black physicians. A study at two NCI-designated comprehensive cancer centers using Partnering Around Cancer Clinical Trials (PACCT), a theoretical model, focused on improving the quality of patient-physician communication during discussions of new clinical trial information and patient understanding between racially incongruous pairs.[34] Publishing educational pamphlets, social media campaigns, and educational videos are among several strategies an institution can take to improve patient understanding. The use of digital technologies with careful consideration of underrepresented patient populations allows for broad recruitment for cancer clinical trials.[35]

This study did not assess how minority representation in IITs at Emory University changed over time. It would have been beneficial to know if there was an increase in this representation over time to see the true impact of current recruitment efforts. From 1990 to 2012, the enrollment disparity for Black patients was evaluated in 23,006 NCI lung cancer trial enrollees. This study showed that there were no significant improvements in representation over this period.[36] An evaluation of minority enrollment in 170 Gynecologic Oncology Group (GOG) studies revealed a 2.8-fold decrease in black enrollment between the years 1994-2002 and 2009-2013. This study found that enrollment of Black patients was significantly lower than that was expected based on age-adjusted cancer incidence.[37] Another limitation of our study was its relatively small sample size as we focused on only patients in IITs. Though minorities were still underrepresented, this systematic study showed that there is promise in improving the representation of racial minorities in the testing of new cancer therapeutics. The disparities in clinical outcomes between Black and White women with metastatic breast cancer indicate that there is still a need to modify clinical trial recruitment strategies to reach the goal of increasing diversity of trial enrollees. Racial minorities continue to suffer a disproportional cancer burden. Thus, efforts to increase their representation in the testing of new oncologic interventions are important to ensure the generalizability of clinical research.

Tables

Figure Legends

Figure 1: Kaplan-Meier curves by race on study survival time (os_surtime) showing similar survival in Black and White women in terms of median OS (18 vs. 17.1 months; p=0.2926). There is a trend exhibiting lower long-term survival in Black women compared to White women with the disparity in survival being most pronounced after 36 months.

Figure 2: A. Quantile survival analysis plots by race for patients with metastatic breast cancer, and B. Forest plot for survival time difference between Black and White women with metastatic breast cancer

References

1. Aizer AA, Wilhite TJ, Chen M-H, et al. Lack of reduction in racial disparities in cancer-specific mortality over a 20-year period. *Cancer*. 2014;120(10):1532-1539. doi:10.1002/cncr.28617

2. Ries L, Harkins D, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2003. *Public Health Fac Publ*. January 2006. https://scholarworks.gsu.edu/iph_facpub/132.

3. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry. *Cancer*. 2007;109(9):1721-1728. doi:10.1002/cncr.22618

4. Dent R, Trudea M, Pritchard K, et al. Triple-negative Breast Cancer: Clinical Features and Patterns of Recurrence. Clinical cancer research : an official journal of the American Association for Cancer Research. doi:10.1158/1078-0432.CCR-06-3045

5. Lee YT, Tan YJ, Oon CE. Molecular Targeted Therapy: Treating Cancer With Specificity. European journal of pharmacology. doi:10.1016/j.ejphar.2018.07.034

6. Granier C, Karaki S, Roussel H, et al. [Cancer immunotherapy: Rational and recent breakthroughs]. *Rev Med Interne*. 2016;37(10):694-700. doi:10.1016/j.revmed.2016.05.023

7. Ramamoorthy A, Knepper TC, Merenda C, et al. Demographic Composition of Select Oncologic New Molecular Entities Approved by the FDA Between 2008 and 2017. *Clin Pharmacol Ther*. 2018;104(5):940-948. doi:10.1002/cpt.1180

8. Loree J, Anand S, Dasari A, et al. Disparity of Race Reporting and Representation in Clinical Trials Leading to Cancer Drug Approvals From 2008 to 2018. JAMA oncology. doi:10.1001/jamaoncol.2019.1870

9. Chen MS, Lara PN, Dang JHT, Paterniti DA, Kelly K. Twenty years post-NIH Revitalization Act: enhancing minority participation in clinical trials (EMPaCT): laying the groundwork for improving minority clinical trial accrual: renewing the case for enhancing minority participation in cancer clinical trials. *Cancer*. 2014;120 Suppl 7:1091-1096. doi:10.1002/cncr.28575

10. Martin DN, Boersma BJ, Yi M, et al. Differences in the tumor microenvironment between African-American and European-American breast cancer patients. *PloS One*. 2009;4(2):e4531. doi:10.1371/journal.pone.0004531

11. Kinseth MA, Jia Z, Rahmatpanah F, et al. Expression differences between African American and Caucasian prostate cancer tissue reveals that stroma is the site of aggressive changes. *Int J Cancer*. 2014;134(1):81-91. doi:10.1002/ijc.28326

12. Mitchell KA, Zingone A, Toulabi L, Boeckelman J, Ryan BM. Comparative Transcriptome Profiling Reveals Coding and Noncoding RNA Differences in NSCLC from African Americans and European Americans. *Clin Cancer Res Off J Am Assoc Cancer Res*. 2017;23(23):7412-7425. doi:10.1158/1078-0432.CCR-17-0527

13. Yasuda S, Zhang L, Huang S-M. The Role of Ethnicity in Variability in Response to Drugs: Focus on Clinical Pharmacology Studies. Clinical pharmacology and therapeutics. doi:10.1038/clpt.2008.141

14. Bickell N, Wang J, Oluwole S, et al. Missed Opportunities: Racial Disparities in Adjuvant Breast Cancer Treatment. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. doi:10.1200/JCO.2005.04.5799

15. Hunt BR, Hurlbert MS. Black:white disparities in breast cancer mortality in the 50 largest cities in the United States, 2005-2014. *Cancer Epidemiol*. 2016;45:169-173. doi:10.1016/j.canep.2016.07.018

16. Tariq K, Latif N, Zaiden R, Jasani N, Rana F. Breast Cancer and Racial Disparity Between Caucasian and African American Women, Part 1 (BRCA-1). Clinical advances in hematology & oncology : H&O. https://pubmed.ncbi.nlm.nih.gov/24518421/. Published August 2013. Accessed April 10, 2020.

17. Yedjou CG, Sims JN, Miele L, et al. Health and Racial Disparity in Breast Cancer. *Adv Exp Med Biol*. 2019;1152:31-49. doi:10.1007/978-3-030-20301-6_3

18. Nazha B, Mishra M, Pentz R, Owonikoko TK. Enrollment of Racial Minorities in Clinical Trials: Old Problem Assumes New Urgency in the Age of Immunotherapy. *Am Soc Clin Oncol Educ Book*. 2019;(39):3-10. doi:10.1200/EDBK_100021

19. Foy KC, Fisher JL, Lustberg MB, Gray DM, DeGraffinreid CR, Paskett ED. Disparities in breast cancer tumor characteristics, treatment, time to treatment, and survival probability among African American and white women. *NPJ Breast Cancer*. 2018;4:7. doi:10.1038/s41523-018-0059-5

20. DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(6):438-451. doi:10.3322/caac.21583

21. United States Census Bureau, American FactFinder. 2010 Census.

22. Hawk E, Habermann E, Ford J, et al. Five National Cancer Institute-designated Cancer Centers' Data Collection on Racial/Ethnic Minority Participation in Therapeutic Trials: A Current View and Opportunities for Improvement. Cancer. doi:10.1002/cncr.28571

23. Albain KS, Unger JM, Crowley JJ, Coltman CA, Hershman DL. Racial Disparities in Cancer Survival Among Randomized Clinical Trials Patients of the Southwest Oncology Group. *JNCI J Natl Cancer Inst*. 2009;101(14):984-992. doi:10.1093/jnci/djp175

24. Owonikoko TK, Busari AK, Kim S, et al. Race, age and gender-based characteristics and toxicities of targeted therapies on phase I trials. *Oncology*. 2018;95(3):138. doi:10.1159/000488763

25. Brewster A, Chavez-MacGregor M, Brown P. Epidemiology, Biology, and Treatment of Triple-Negative Breast Cancer in Women of African Ancestry. The Lancet. Oncology. doi:10.1016/S1470-2045(14)70364-X

26. Jiagge E, Jibril AS, Chitale D, et al. Comparative Analysis of Breast Cancer Phenotypes in African American, White American, and West Versus East African patients: Correlation Between African Ancestry and Triple-Negative Breast Cancer. *Ann Surg Oncol*. 2016;23(12):3843-3849. doi:10.1245/s10434-016-5420-z

27. Kohler B, Sherman R, Howlader N, et al. Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State. Journal of the National Cancer Institute. doi:10.1093/jnci/djv048

28. Shachar SS, Williams GR. The obesity paradox in cancer – moving beyond BMI. *Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol*. 2017;26(1):13-16. doi:10.1158/1055-9965.EPI-16-0439

29. Wendler D, Kington R, Madans J, et al. Are racial and ethnic minorities less willing to participate in health research? *PLoS Med*. 2006;3(2):e19. doi:10.1371/journal.pmed.0030019

30. Jimenez R, Zhang B, Joffe S, et al. Clinical Trial Participation among Ethnic/Racial Minority and Majority Patients with Advanced Cancer: What Factors Most Influence Enrollment? *J Palliat Med*. 2013;16(3):256-262. doi:10.1089/jpm.2012.0413

31. Salman A, Nguyen C, Lee Y, Cooksey-James T. A Review of Barriers to Minorities' Participation in Cancer Clinical Trials: Implications for Future Cancer Research. Journal of immigrant and minority health. doi:10.1007/s10903-015-0198-9

32. Schmotzer GL. Barriers and facilitators to participation of minorities in clinical trials. *Ethn Dis*. 2012;22(2):226-230.

33. Regnante JM, Richie NA, Fashoyin-Aje L, et al. US Cancer Centers of Excellence Strategies for Increased Inclusion of Racial and Ethnic Minorities in Clinical Trials. *J Oncol Pract*. March 2019. doi:10.1200/JOP.18.00638

34. Eggly S, Hamel L, Heath E, et al. Partnering Around Cancer Clinical Trials (PACCT): Study Protocol for a Randomized Trial of a Patient and Physician Communication Intervention to Increase Minority Accrual to Prostate Cancer Clinical Trials. BMC cancer. doi:10.1186/s12885-017-3804-5

35. Borno HT, Bakke BM, Kaplan C, et al. A step towards equitable clinical trial recruitment: a protocol for the development and preliminary testing of an online prostate cancer health

information and clinical trial matching tool. *Pilot Feasibility Stud*. 2019;5. doi:10.1186/s40814-019-0516-4

36. Pang HH, Wang X, Stinchcombe TE, et al. Enrollment Trends and Disparity Among Patients With Lung Cancer in National Clinical Trials, 1990 to 2012. *J Clin Oncol Off J Am Soc Clin Oncol*. 2016;34(33):3992-3999. doi:10.1200/JCO.2016.67.7088

37. Scalici J, Finan M, Black J, et al. Minority Participation in Gynecologic Oncology Group (GOG) Studies. Gynecologic oncology. doi:10.1016/j.ygyno.2015.05.014

Entire patient cohort:

Table 1: Descriptive Statistics of Patient Characteristics and Clinical Outcomes

Variable	Level	N (%) = 135
Race	White	92 (68.1)
	Black or African American	43 (31.9)
Gender	F	135 (100.0)
Stage at Time of Trial	Stage I-III	73 (54.1)
	Stage IV	62 (45.9)
Phase of Trial	Phase I	5 (3.7)
	Phase II	130 (96.3)
Class of Therapeutic Drug	Targeted therapy	58 (43.0)
	Chemotherapy	22 (16.3)
	Combined	55 (40.7)
Reason for Treatment Discontinuation	AE/SE/Complications/ Other	12 (9.0)
	DP, relapse during active treatment	47 (35.1)
	Patient withdrawal	12 (9.0)
	Treatment completed per protocol criteria	63 (47.0)
	Missing	1

Variable	Level	N (%) = 135
Highest Grade of Hematologic Toxicity	Grade 1	84 (79.2)
	Grade 2	7 (6.6)
	Grade 3	12 (11.3)
	Grade 4	3 (2.8)
	Missing	29
Highest Grade of Non-Hematologic Toxicity	Grade 1	61 (45.9)
	Grade 2	39 (29.3)
	Grade 3	28 (21.1)
	Grade 4	5 (3.8)
	Missing	2
Best Response	Complete Response	10 (7.5)
	Partial Response	47 (35.1)
	Progressive Disease	32 (23.9)
	Stable Disease	45 (33.6)
	Missing	1
Best response	Partial Response or Complete/Stable Disease	102 (76.1)
	Progressive Disease	32 (23.9)
	Missing	1

Variable	Level	N (%) = 135
Receptor Status	HR Positive	88 (65.7)
	Triple Positive	6 (4.5)
	Triple Negative	36 (26.9)
	HR Negative Her2+	4 (3.0)
	Missing	1
Age at trial consent (quartile)	>=31, <=45	34 (25.2)
	>45, <=54	37 (27.4)
	>54, <=62	31 (23.0)
	>62, <=79	33 (24.4)
BMI category	Under Weight	6 (4.4)
	Normal Weight	46 (34.1)
	Overweight	40 (29.6)
	Obese	43 (31.9)
Age at trial consent	Mean	53.70
	Median	54.00
	Minimum	31.00
	Maximum	79.00
	Std Dev	11.05
	Missing	0.00

Variable	Level	N (%) = 135
Height (m)	Mean	1.64
	Median	1.63
	Minimum	1.51
	Maximum	1.83
	Std Dev	0.07
	Missing	0.00
Weight (kg)	Mean	75.18
	Median	71.70
	Minimum	43.30
	Maximum	134.70
	Std Dev	19.26
	Missing	0.00
BMI	Mean	28.13
	Median	27.59
	Minimum	16.50
	Maximum	54.30
	Std Dev	7.25
	Missing	0.00
Number of Prior Lines Prior to First Clinical Trial	Mean	1.76
	Median	0.00
	Minimum	0.00
	Maximum	11.00
	Std Dev	2.50
	Missing	0.00

Variable	Level	N (%) = 135
Time on Trial (months)	Mean	6.08
	Median	4.86
	Minimum	0.00
	Maximum	28.40
	Std Dev	4.96
	Missing	0.00
Time to death (months)	Mean	20.31
	Median	14.25
	Minimum	1.98
	Maximum	63.54
	Std Dev	15.75
	Missing	92.00
Overall Survival Time (months)	Mean	10.37
	Median	5.82
	Minimum	0.00
	Maximum	63.54
	Std Dev	11.53
	Missing	0.00

Early-stage patients:

Table 1: Descriptive Statistics of Patient Characteristics and Clinical Outcomes for Early-Stage Patients

Variable	Level	N (%) = 73
Race	White	51 (69.9)
	Black or African American	22 (30.1)
Gender	F	73 (100.0)
Stage at Time of Trial	Stage I-III	73 (100.0)
Phase of Trial	Phase II	73 (100.0)
Class of Therapeutic Drug	Targeted therapy	1 (1.4)
	Chemotherapy	18 (24.7)
	Combined	54 (74.0)
Reason for Treatment Discontinuation	AE/SE/Complications/ Other	3 (4.2)
	DP, relapse during active treatment	5 (6.9)
	Patient withdrawal	7 (9.7)
	Treatment completed per protocol criteria	57 (79.2)
	Missing	1

Variable	Level	N (%) = 73
Highest Grade of Hematologic Toxicity	Grade 1	44 (77.2)
	Grade 2	4 (7.0)
	Grade 3	7 (12.3)
	Grade 4	2 (3.5)
	Missing	16
Highest Grade of Non-Hematologic Toxicity	Grade 1	34 (47.9)
	Grade 2	20 (28.2)
	Grade 3	15 (21.1)
	Grade 4	2 (2.8)
	Missing	2
Best Response	Complete Response	10 (13.9)
	Partial Response	39 (54.2)
	Progressive Disease	14 (19.4)
	Stable Disease	9 (12.5)
	Missing	1
Best response	Partial Response or Complete/Stable Disease	58 (80.6)
	Progressive Disease	14 (19.4)
	Missing	1
Receptor Status	HR Positive	42 (57.5)
	Triple Positive	4 (5.5)
	Triple Negative	23 (31.5)
	HR Negative Her2+	4 (5.5)

Variable	Level	N (%) = 73
Age at trial consent (quartile)	>=31, <=45	25 (34.2)
	>45, <=54	13 (17.8)
	>54, <=62	18 (24.7)
	>62, <=79	17 (23.3)
BMI category	Under Weight	2 (2.7)
	Normal Weight	22 (30.1)
	Overweight	20 (27.4)
	Obese	29 (39.7)
Age at trial consent	Mean	52.62
	Median	54.00
	Minimum	34.00
	Maximum	76.00
	Std Dev	11.38
	Missing	0.00
Height (m)	Mean	1.64
	Median	1.63
	Minimum	1.51
	Maximum	1.76
	Std Dev	0.06
	Missing	0.00

Variable	Level	N (%) = 73
Weight (kg)	Mean	78.66
	Median	79.30
	Minimum	46.90
	Maximum	134.70
	Std Dev	19.68
	Missing	0.00
BMI	Mean	29.44
	Median	29.02
	Minimum	17.89
	Maximum	54.30
	Std Dev	7.54
	Missing	0.00
Number of Prior Lines Prior to First Clinical Trial	Mean	0.05
	Median	0.00
	Minimum	0.00
	Maximum	4.00
	Std Dev	0.47
	Missing	0.00
Time on Trial (months)	Mean	5.42
	Median	5.09
	Minimum	0.03
	Maximum	14.05
	Std Dev	2.78
	Missing	2.00

Variable	Level	N (%) = 73
Time to death (months)	Mean	9.85
	Median	9.85
	Minimum	9.85
	Maximum	9.85
	Std Dev	
	Missing	72.00
Overall Survival Time (months)	Mean	5.43
	Median	5.09
	Minimum	0.03
	Maximum	14.05
	Std Dev	2.81
	Missing	2.00

Table 2: Univariate Association for Patient Characteristics and Clinical Outcomes with Race for Early-Stage Patients

Covariate	Statistics	Level	Race: White N=51	Race: Black or African American N=22	Parametric P-value*	Non-Parametric P-value**
Class of Therapeutic Drug	N (Col %)	Targeted therapy	1 (1.96)	0 (0)	0.541	0.574
	N (Col %)	Chemotherapy	11 (21.57)	7 (31.82)		
	N (Col %)	Combined	39 (76.47)	15 (68.18)		
Reason for Treatment Discontinuation	N (Col %)	AE/SE/Complications/ Other	3 (6)	0 (0)	0.563	0.644
	N (Col %)	DP, relapse during active treatment	3 (6)	2 (9.09)		
	N (Col %)	Patient withdrawal	4 (8)	3 (13.64)		
	N (Col %)	Treatment completed per protocol criteria	40 (80)	17 (77.27)		
Highest Grade of Hematologic Toxicity	N (Col %)	Grade 1	32 (80)	12 (70.59)	0.155	0.137
	N (Col %)	Grade 2	1 (2.5)	3 (17.65)		
	N (Col %)	Grade 3	6 (15)	1 (5.88)		
	N (Col %)	Grade 4	1 (2.5)	1 (5.88)		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=51	Black or African American N=22		
Highest Grade of Non-Hematologic Toxicity	N (Col %)	Grade 1	24 (47.06)	10 (50)	0.474	0.521
	N (Col %)	Grade 2	16 (31.37)	4 (20)		
	N (Col %)	Grade 3	9 (17.65)	6 (30)		
	N (Col %)	Grade 4	2 (3.92)	0 (0)		
Best Response	N (Col %)	Complete Response	8 (15.69)	2 (9.52)	0.912	0.956
	N (Col %)	Partial Response	27 (52.94)	12 (57.14)		
	N (Col %)	Progressive Disease	10 (19.61)	4 (19.05)		
	N (Col %)	Stable Disease	6 (11.76)	3 (14.29)		
Best response	N (Col %)	Partial Response or Complete/Stable Disease	41 (80.39)	17 (80.95)	0.956	1.000
	N (Col %)	Progressive Disease	10 (19.61)	4 (19.05)		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=51	Black or African American N=22		
Receptor Status	N (Col %)	HR Positive	31 (60.78)	11 (50)	0.258	0.273
	N (Col %)	Triple Positive	4 (7.84)	0 (0)		
	N (Col %)	Triple Negative	13 (25.49)	10 (45.45)		
	N (Col %)	HR Negative Her2+	3 (5.88)	1 (4.55)		
Age at trial consent (quartile)	N (Col %)	>=31, <=45	15 (29.41)	10 (45.45)	0.422	0.440
	N (Col %)	>45, <=54	10 (19.61)	3 (13.64)		
	N (Col %)	>54, <=62	12 (23.53)	6 (27.27)		
	N (Col %)	>62, <=79	14 (27.45)	3 (13.64)		
BMI category	N (Col %)	Under Weight	2 (3.92)	0 (0)	**<.001**	**<.001**
	N (Col %)	Normal Weight	21 (41.18)	1 (4.55)		
	N (Col %)	Overweight	15 (29.41)	5 (22.73)		
	N (Col %)	Obese	13 (25.49)	16 (72.73)		

Covariate	Statistics	Level	Race: White N=51	Race: Black or African American N=22	Parametric P-value*	Non-Parametric P-value**
Age at trial consent	N		51	22	0.176	0.170
	Mean		53.8	49.86		
	Median		55	49.5		
	Min		34	36		
	Max		76	65		
	Std Dev		11.68	10.39		
Height (m)	N		51	22	0.745	0.857
	Mean		1.64	1.63		
	Median		1.64	1.63		
	Min		1.51	1.54		
	Max		1.76	1.73		
	Std Dev		0.07	0.06		
Weight (kg)	N		51	22	**<.001**	**<.001**
	Mean		71.73	94.71		
	Median		69.9	93.1		
	Min		46.9	56.5		
	Max		117.5	134.7		
	Std Dev		16.01	18.19		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=51	Black or African American N=22		
BMI	N		51	22	**<.001**	**<.001**
	Mean		26.71	35.77		
	Median		25.97	36.27		
	Min		17.89	20.26		
	Max		47.37	54.3		
	Std Dev		5.61	7.74		
Number of Prior Lines Prior to First Clinical Trial	N		51	22	1.000***	
	Mean		0.08	0		
	Median		0	0		
	Min		0	0		
	Max		4	0		
	Std Dev		0.56	0		
Time on Trial (months)	N		50	21	0.237	0.579
	Mean		5.67	4.81		
	Median		5.11	4.63		
	Min		0.03	0.73		
	Max		14.05	9.02		
	Std Dev		3.09	1.81		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=51	Black or African American N=22		
Overall Survival Time (months)	N		50	21	0.228	0.571
	Mean		5.7	4.81		
	Median		5.11	4.63		
	Min		0.03	0.73		
	Max		14.05	9.02		
	Std Dev		3.12	1.81		

* The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.

** The non-parametric p-value is calculated by the Kruskal-Wallis test for numerical covariates and Fisher's exact test for categorical covariates.

Table 3: Univariate Association with Best Treatment Response for Early-Stage Patients

Covariate	Statistics	Level	Best response – Partial Response or Complete/Stable Disease N=58	Best response – Progressive Disease N=14	Parametric P-value*	Non-Parametric P-value**
Race	N (Col %)	White	41 (70.69)	10 (71.43)	0.956	1.000
	N (Col %)	Black or African American	17 (29.31)	4 (28.57)		
Age at trial consent (quartile)	N (Col %)	>=31, <=45	21 (36.21)	3 (21.43)	0.372	0.422
	N (Col %)	>45, <=54	11 (18.97)	2 (14.29)		
	N (Col %)	>54, <=62	12 (20.69)	6 (42.86)		
	N (Col %)	>62, <=79	14 (24.14)	3 (21.43)		
BMI category	N (Col %)	Under Weight	1 (1.72)	1 (7.14)	0.505	0.436
	N (Col %)	Normal Weight	17 (29.31)	5 (35.71)		
	N (Col %)	Overweight	17 (29.31)	2 (14.29)		
	N (Col %)	Obese	23 (39.66)	6 (42.86)		

Covariate	Statistics	Level	Best response – Partial Response or Complete/Stable Disease N=58	Best response – Progressive Disease N=14	Parametric P-value*	Non-Parametric P-value**
Age at trial consent	N		58	14	0.216	0.305
	Mean		52.03	56.21		
	Median		52	58.5		
	Min		34	39		
	Max		75	76		
	Std Dev		11.46	10.24		
Height (m)	N		58	14	0.744	0.633
	Mean		1.64	1.63		
	Median		1.65	1.62		
	Min		1.51	1.52		
	Max		1.76	1.76		
	Std Dev		0.06	0.08		
Weight (kg)	N		58	14	0.808	0.892
	Mean		78.97	77.53		
	Median		79.65	80.6		
	Min		49.3	46.9		
	Max		134.7	105.7		
	Std Dev		19.9	20.16		

Covariate	Statistics	Level	Best response – Partial Response or Complete/Stable Disease N=58	Best response – Progressive Disease N=14	Parametric P-value*	Non-Parametric P-value**
BMI	N		58	14	0.862	0.949
	Mean		29.53	29.14		
	Median		29.09	27.61		
	Min		17.89	18.3		
	Max		54.3	42.88		
	Std Dev		7.67	7.53		

* The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.
** The non-parametric p-value is calculated by the Kruskal-Wallis test for numerical covariates and Fisher's exact test for categorical covariates.

Table 4: Multivariable Variable Analysis Logistic Regression of Best Treatment Response for Early-stage Patients

			Best response=Progressive Disease		

Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	21	1.08 (0.21-5.69)	0.924	0.924
	White	51	-	-	
BMI category	Normal Weight	22	0.55 (0.02-12.68)	0.706	0.481
	Obese	29	0.33 (0.01-7.78)	0.488	
	Overweight	19	0.14 (0.01-3.69)	0.240	
	Under Weight	2	-	-	
Age at trial consent	>45, <=54	13	1.25 (0.17-8.96)	0.824	0.328
	>54, <=62	18	4.34 (0.81-23.37)	0.087	
	>62, <=79	17	1.56 (0.25-9.78)	0.634	
	>=31, <=45	24	-	-	

* Number of observations in the original data set = 73. Number of observations used = 72.

Table 5: Univariate Association with Time on Trial for Early-stage Patients

			s_Time_Enrolled			
Variable	**Level**	**N**	**Mean**	**Median**	**ANOVA P-value**	**Kruskal-Wallis P-value**
Race	White	50	2.29	2.26	0.380	0.579
	Black or Af. Am.	21	2.15	2.15		
Age at trial consent (quartile)	>=31, <=45	25	2.01	2.26	0.061	0.491
	>45, <=54	13	2.33	2.17		
	>54, <=62	17	2.51	2.29		
	>62, <=79	16	2.27	2.16		
BMI category	Under Weight	2	2.21	2.21	0.999	0.997
	Normal Weight	22	2.26	2.28		
	Overweight	19	2.25	2.26		
	Obese	28	2.24	2.13		

		s_Time_Enrolled			
Variable	**N**	**Pearson CC**	**Pearson P-value**	**Spearman CC**	**Spearman P-value**
Age at trial consent	71	0.275	**0.020**	0.138	0.250
BMI	71	0.009	0.940	-0.007	0.955
Height (m)	71	0.016	0.897	0.002	0.988
Weight (kg)	71	0.011	0.928	-0.007	0.956

Table 6: Multivariable Variable Analysis Regression Model Time on Trial for Early-stage Patients

		s_Time_Enrolled				
Covariate	**Level**	**B**	**95%CI Low**	**95%CI Up**	**B P-value**	**Type3 P-value**
Race	Black or African American	-0.09	-0.45	0.28	0.634	0.634
	White	-	-	-	-	
Age at trial consent	>45, <=54	0.04	-0.42	0.50	0.853	0.079
	>54, <=62	0.25	-0.18	0.68	0.243	
	>=31, <=45	-0.26	-0.66	0.14	0.191	
	>62, <=79	-	-	-	-	
BMI category	Normal Weight	0.04	-0.36	0.44	0.853	0.951
	Overweight	-0.02	-0.40	0.35	0.897	
	Under Weight	-0.22	-1.13	0.70	0.635	
	Obese	-	-	-	-	

* Number of observations in the original data set = 73.
Number of observations used = 71.

Table 7: Univariate Association with Reason for Treatment Discontinuation for Early-stage Patients

			Reason for Treatment Discontinuation		

Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	22	1.08 (0.32-3.63)	0.906	0.906
	White	50	-	-	
Age at trial consent (quartile)	>=31, <=45	25	0.53 (0.14-1.95)	0.342	0.107
	>45, <=54	12	0.15 (0.02-1.38)	0.094	
	>54, <=62	18	0.09 (0.01-0.86)	**0.037**	
	>62, <=79	17	-	-	
BMI category	Under Weight	2	3.99 (0.21-76.26)	0.358	0.506
	Normal Weight	21	1.57 (0.35-7.05)	0.555	
	Overweight	20	2.74 (0.67-11.30)	0.162	
	Obese	29	-	-	
Age at trial consent		72	1.02 (0.97-1.07)	0.472	0.472
Weight (kg)		72	0.98 (0.95-1.01)	0.149	0.149
BMI		72	0.95 (0.87-1.03)	0.236	0.236

Covariate	Level	N	Reason for Treatment Discontinuation		
			Odds Ratio (95% CI)	OR P-value	Type3 P-value

The probability of having lower values of the outcome is being modeled.

Table 8: Multivariable Variable Analysis Logistic Regression with Reason for Treatment Discontinuation for Early-stage Patients

			Reason for Treatment Discontinuation		
Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	22	1.31 (0.30-5.74)	0.721	0.721
	White	50	-	-	
Age at trial consent	>45, <=54	12	0.16 (0.02-1.56)	0.114	0.120
	>54, <=62	18	0.09 (0.01-0.88)	0.039	
	>=31, <=45	25	0.59 (0.15-2.34)	0.449	
	>62, <=79	17	-	-	
BMI category	Normal Weight	21	1.45 (0.27-7.95)	0.667	0.528
	Overweight	20	2.90 (0.64-13.13)	0.167	
	Under Weight	2	3.69 (0.12-117.43)	0.460	
	Obese	29	-	-	

* Number of observations in the original data set = 73. Number of observations used = 72.

Late stage patients:

Table 1: Descriptive Statistics of Patient Characteristics and Clinical Outcomes for Late-stage Patients

Variable	Level	N (%) = 62
Race	White	41 (66.1)
	Black or African American	21 (33.9)
Gender	F	62 (100.0)
Stage at Time of Trial	Stage IV	62 (100.0)
Phase of Trial	Phase I	5 (8.1)
	Phase II	57 (91.9)
Class of Therapeutic Drug	Targeted therapy	57 (91.9)
	Chemotherapy	4 (6.5)
	Combined	1 (1.6)
Reason for Treatment Discontinuation	AE/SE/Complications/ Other	9 (14.5)
	DP, relapse during active treatment	42 (67.7)
	Patient withdrawal	5 (8.1)
	Treatment completed per protocol criteria	6 (9.7)

Variable	Level	N (%) = 62
Highest Grade of Hematologic Toxicity	Grade 1	40 (81.6)
	Grade 2	3 (6.1)
	Grade 3	5 (10.2)
	Grade 4	1 (2.0)
	Missing	13
Highest Grade of Non-Hematologic Toxicity	Grade 1	27 (43.5)
	Grade 2	19 (30.6)
	Grade 3	13 (21.0)
	Grade 4	3 (4.8)
Best Response	Partial Response	8 (12.9)
	Progressive Disease	18 (29.0)
	Stable Disease	36 (58.1)
Best response	Partial Response or Complete/Stable Disease	44 (71.0)
	Progressive Disease	18 (29.0)
Receptor Status	HR Positive	46 (75.4)
	Triple Positive	2 (3.3)
	Triple Negative	13 (21.3)
	Missing	1

Variable	Level	N (%) = 62
Age at trial consent (quartile)	>=31, <=45	9 (14.5)
	>45, <=54	24 (38.7)
	>54, <=62	13 (21.0)
	>62, <=79	16 (25.8)
BMI category	Under Weight	4 (6.5)
	Normal Weight	24 (38.7)
	Overweight	20 (32.3)
	Obese	14 (22.6)
Age at trial consent	Mean	54.98
	Median	53.00
	Minimum	31.00
	Maximum	79.00
	Std Dev	10.59
	Missing	0.00
Height (m)	Mean	1.64
	Median	1.63
	Minimum	1.51
	Maximum	1.83
	Std Dev	0.07
	Missing	0.00

Variable	Level	N (%) = 62
Weight (kg)	Mean	71.09
	Median	66.50
	Minimum	43.30
	Maximum	125.00
	Std Dev	18.07
	Missing	0.00
BMI	Mean	26.59
	Median	25.63
	Minimum	16.50
	Maximum	48.83
	Std Dev	6.62
	Missing	0.00
Number of Prior Lines Prior to First Clinical Trial	Mean	3.77
	Median	3.00
	Minimum	0.00
	Maximum	11.00
	Std Dev	2.41
	Missing	0.00
Time on Trial (months)	Mean	7.04
	Median	4.89
	Minimum	0.33
	Maximum	28.40
	Std Dev	6.51
	Missing	0.00

Variable	Level	N (%) = 62
Time to death (months)	Mean	20.55
	Median	14.68
	Minimum	1.98
	Maximum	63.54
	Std Dev	15.85
	Missing	20.00
Overall Survival Time (months)	Mean	16.36
	Median	13.32
	Minimum	0.33
	Maximum	63.54
	Std Dev	14.65
	Missing	0.00

Table 2: Univariate Association for Patient Characteristics and Clinical Outcomes with Race for Late-stage Patients

			Race			
Covariate	**Statistics**	**Level**	**White N=41**	**Black or African American N=21**	**Parametric P-value***	**Non-Parametric P-value****
Phase of Trial	N (Col %)	Phase I	4 (9.76)	1 (4.76)	0.494	0.654
	N (Col %)	Phase II	37 (90.24)	20 (95.24)		
Class of Therapeutic Drug	N (Col %)	Targeted therapy	38 (92.68)	19 (90.48)	0.350	0.530
	N (Col %)	Chemotherapy	3 (7.32)	1 (4.76)		
	N (Col %)	Combined	0 (0)	1 (4.76)		
Reason for Treatment Discontinuation	N (Col %)	AE/SE/Complications/Other	6 (14.63)	3 (14.29)	0.815	0.874
	N (Col %)	DP, relapse during active treatment	27 (65.85)	15 (71.43)		
	N (Col %)	Patient withdrawal	3 (7.32)	2 (9.52)		
	N (Col %)	Treatment completed per protocol criteria	5 (12.2)	1 (4.76)		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=41	Black or African American N=21		
Highest Grade of Hematologic Toxicity	N (Col %)	Grade 1	26 (81.25)	14 (82.35)	0.316	0.416
	N (Col %)	Grade 2	3 (9.38)	0 (0)		
	N (Col %)	Grade 3	2 (6.25)	3 (17.65)		
	N (Col %)	Grade 4	1 (3.13)	0 (0)		
Highest Grade of Non-Hematologic Toxicity	N (Col %)	Grade 1	17 (41.46)	10 (47.62)	0.406	0.500
	N (Col %)	Grade 2	11 (26.83)	8 (38.1)		
	N (Col %)	Grade 3	10 (24.39)	3 (14.29)		
	N (Col %)	Grade 4	3 (7.32)	0 (0)		
Best Response	N (Col %)	Partial Response	4 (9.76)	4 (19.05)	0.074	0.072
	N (Col %)	Progressive Disease	9 (21.95)	9 (42.86)		
	N (Col %)	Stable Disease	28 (68.29)	8 (38.1)		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=41	Black or African American N=21		
Best response	N (Col %)	Partial Response or Complete/Stable Disease	32 (78.05)	12 (57.14)	0.086	0.138
	N (Col %)	Progressive Disease	9 (21.95)	9 (42.86)		
Receptor Status	N (Col %)	HR Positive	31 (77.5)	15 (71.43)	0.385	0.486
	N (Col %)	Triple Positive	2 (5)	0 (0)		
	N (Col %)	Triple Negative	7 (17.5)	6 (28.57)		
Age at trial consent (quartile)	N (Col %)	>=31, <=45	6 (14.63)	3 (14.29)	0.736	0.753
	N (Col %)	>45, <=54	14 (34.15)	10 (47.62)		
	N (Col %)	>54, <=62	9 (21.95)	4 (19.05)		
	N (Col %)	>62, <=79	12 (29.27)	4 (19.05)		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=41	Black or African American N=21		
BMI category	N (Col %)	Under Weight	2 (4.88)	2 (9.52)	**0.044**	**0.029**
	N (Col %)	Normal Weight	21 (51.22)	3 (14.29)		
	N (Col %)	Overweight	11 (26.83)	9 (42.86)		
	N (Col %)	Obese	7 (17.07)	7 (33.33)		
Age at trial consent	N		41	21	0.357	0.231
	Mean		55.88	53.24		
	Median		55	51		
	Min		34	31		
	Max		74	79		
	Std Dev		10.63	10.54		
Height (m)	N		41	21	0.147	0.190
	Mean		1.64	1.62		
	Median		1.64	1.62		
	Min		1.51	1.55		
	Max		1.83	1.71		
	Std Dev		0.08	0.05		

Covariate	Statistics	Level	Race: White N=41	Race: Black or African American N=21	Parametric P-value*	Non-Parametric P-value**
Weight (kg)	N		41	21	0.505	0.220
	Mean		69.98	73.25		
	Median		63.1	73.2		
	Min		43.3	49.3		
	Max		125	119.9		
	Std Dev		19.24	15.73		
BMI	N		41	21	0.215	**0.044**
	Mean		25.84	28.05		
	Median		24.6	28.52		
	Min		16.5	17.58		
	Max		48.83	45.13		
	Std Dev		6.91	5.9		
Number of Prior Lines Prior to First Clinical Trial	N		41	21	**0.021*****	
	Mean		4.24	2.86		
	Median		3	3		
	Min		1	0		
	Max		11	5		
	Std Dev		2.68	1.42		

Covariate	Statistics	Level	Race: White N=41	Race: Black or African American N=21	Parametric P-value*	Non-Parametric P-value**
Time on Trial (months)	N		41	21	0.223	0.326
	Mean		7.77	5.62		
	Median		6.15	3.47		
	Min		0.33	0.5		
	Max		28.4	19.21		
	Std Dev		7.05	5.17		
Time to death (months)	N		25	17	0.522	0.888
	Mean		21.87	18.62		
	Median		13.82	15.7		
	Min		4	1.98		
	Max		63.54	37.62		
	Std Dev		18.56	10.97		
Overall Survival Time (months)	N		41	21	0.972	0.388
	Mean		16.41	16.26		
	Median		11.8	15.11		
	Min		0.33	1.98		
	Max		63.54	37.62		
	Std Dev		16.24	11.27		

Covariate	Statistics	Level	Race		Parametric P-value*	Non-Parametric P-value**
			White N=41	Black or African American N=21		

* The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.

** The non-parametric p-value is calculated by the Kruskal-Wallis test for numerical covariates and Fisher's exact test for categorical covariates.

*** p-value calculated using negative binomial model

Table 3: Univariate Association with Best Treatment Response for Late-Stage Patients

Covariate	Statistics	Level	Best response: Partial Response or Complete/Stable Disease N=44	Best response: Progressive Disease N=18	Parametric P-value*	Non-Parametric P-value**
Race	N (Col %)	White	32 (72.73)	9 (50)	0.086	0.138
	N (Col %)	Black or African American	12 (27.27)	9 (50)		
Age at trial consent (quartile)	N (Col %)	>=31, <=45	6 (13.64)	3 (16.67)	0.612	0.638
	N (Col %)	>45, <=54	17 (38.64)	7 (38.89)		
	N (Col %)	>54, <=62	11 (25)	2 (11.11)		
	N (Col %)	>62, <=79	10 (22.73)	6 (33.33)		
BMI category	N (Col %)	Under Weight	3 (6.82)	1 (5.56)	0.719	0.768
	N (Col %)	Normal Weight	16 (36.36)	8 (44.44)		
	N (Col %)	Overweight	16 (36.36)	4 (22.22)		
	N (Col %)	Obese	9 (20.45)	5 (27.78)		
Age at trial consent	N		44	18	0.890	0.871
	Mean		54.86	55.28		
	Median		53.5	53		
	Min		31	34		
	Max		74	79		
	Std Dev		10.22	11.77		

Covariate	Statistics	Level	Best response: Partial Response or Complete/Stable Disease N=44	Best response: Progressive Disease N=18	Parametric P-value*	Non-Parametric P-value**
Height (m)	N		44	18	0.890	0.846
	Mean		1.63	1.64		
	Median		1.63	1.64		
	Min		1.53	1.51		
	Max		1.83	1.8		
	Std Dev		0.07	0.08		
Weight (kg)	N		44	18	0.239	0.461
	Mean		69.35	75.34		
	Median		65.65	68.85		
	Min		43.3	49.3		
	Max		120.2	125		
	Std Dev		16.18	21.96		
BMI	N		44	18	0.241	0.495
	Mean		25.95	28.14		
	Median		25.63	25.78		
	Min		16.5	18.11		
	Max		47.25	48.83		
	Std Dev		5.83	8.23		

Covariate	Statistics	Level	Best response: Partial Response or Complete/Stable Disease N=44	Best response: Progressive Disease N=18	Parametric P-value*	Non-Parametric P-value**

* The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.
** The non-parametric p-value is calculated by the Kruskal-Wallis test for numerical covariates and Fisher's exact test for categorical covariates.

Table 4: Multivariable Variable Analysis Logistic Regression of Best Treatment Response for Late-stage Patients

			Best response=1		
Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	21	4.12 (1.03-16.49)	0.045	**0.045**
	White	41	-	-	
BMI category	Normal Weight	24	2.48 (0.17-35.75)	0.506	0.542
	Obese	14	2.11 (0.13-33.33)	0.597	
	Overweight	20	0.79 (0.06-11.22)	0.862	
	Under Weight	4	-	-	
Age at trial consent	>45, <=54	24	0.58 (0.10-3.43)	0.545	0.639
	>54, <=62	13	0.40 (0.05-3.35)	0.397	
	>62, <=79	16	1.23 (0.21-7.33)	0.821	
	>=31, <=45	9	-	-	

* Number of observations in the original data set = 62. Number of observations used = 62.

Table 5: Univariate Association with Time on Trial for Patients with Metastatic Breast Cancer

			s_Time_Enrolled			
Variable	**Level**	**N**	**Mean**	**Median**	**ANOVA P-value**	**Kruskal-Wallis P-value**
Race	White	41	2.50	2.48	0.278	0.326
	Black or Af. Am.	21	2.16	1.86		
Age at trial consent (quartile)	>=31, <=45	9	2.43	2.03	0.494	0.502
	>45, <=54	24	2.40	2.21		
	>54, <=62	13	1.99	2.03		
	>62, <=79	16	2.66	2.94		
BMI category	Under Weight	4	2.43	2.35	0.925	0.856
	Normal Weight	24	2.46	2.26		
	Overweight	20	2.43	2.47		
	Obese	14	2.19	2.03		

		s_Time_Enrolled			
Variable	**N**	**Pearson CC**	**Pearson P-value**	**Spearman CC**	**Spearman P-value**
Age at trial consent	62	0.079	0.541	0.100	0.440
BMI	62	-0.107	0.409	-0.114	0.379
Height (m)	62	0.088	0.494	0.108	0.405
Weight (kg)	62	-0.074	0.568	-0.073	0.574

Table 6: Multivariable Variable Analysis Regression Model Time on Trial for Late-stage Patients

		s_Time_Enrolled				
Covariate	**Level**	**B**	**95%CI Low**	**95%CI Up**	**B P-value**	**Type3 P-value**
Race	Black or African American	-0.40	-1.10	0.30	0.260	0.260
	White	-	-	-	-	
Age at trial consent	>45, <=54	-0.17	-0.98	0.65	0.684	0.469
	>54, <=62	-0.72	-1.66	0.22	0.130	
	>=31, <=45	-0.22	-1.23	0.79	0.664	
	>62, <=79	-	-	-	-	
BMI category	Normal Weight	-0.01	-0.90	0.88	0.988	0.892
	Overweight	0.26	-0.61	1.14	0.549	
	Under Weight	0.23	-1.16	1.62	0.742	
	Obese	-	-	-	-	

* Number of observations in the original data set = 62.
Number of observations used = 62.

Table 7: Univariate Association with Reason for Treatment Discontinuation

			Reason for Treatment Discontinuation		
Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	21	1.24 (0.41-3.75)	0.702	0.702
	White	41	-	-	
Age at trial consent (quartile)	>=31, <=45	9	1.83 (0.33-10.23)	0.493	0.867
	>45, <=54	24	0.93 (0.25-3.50)	0.914	
	>54, <=62	13	1.21 (0.26-5.65)	0.809	
	>62, <=79	16	-	-	
BMI category	Under Weight	4	2.76 (0.29-25.84)	0.375	**0.029**
	Normal Weight	24	0.27 (0.06-1.24)	0.092	
	Overweight	20	0.13 (0.03-0.67)	**0.014**	
	Obese	14	-	-	
Age at trial consent		62	1.00 (0.95-1.05)	0.958	0.958
Weight (kg)		62	1.01 (0.98-1.04)	0.590	0.590
BMI		62	1.01 (0.94-1.10)	0.763	0.763

Covariate	Level	N	Reason for Treatment Discontinuation		
			Odds Ratio (95% CI)	OR P-value	Type3 P-value

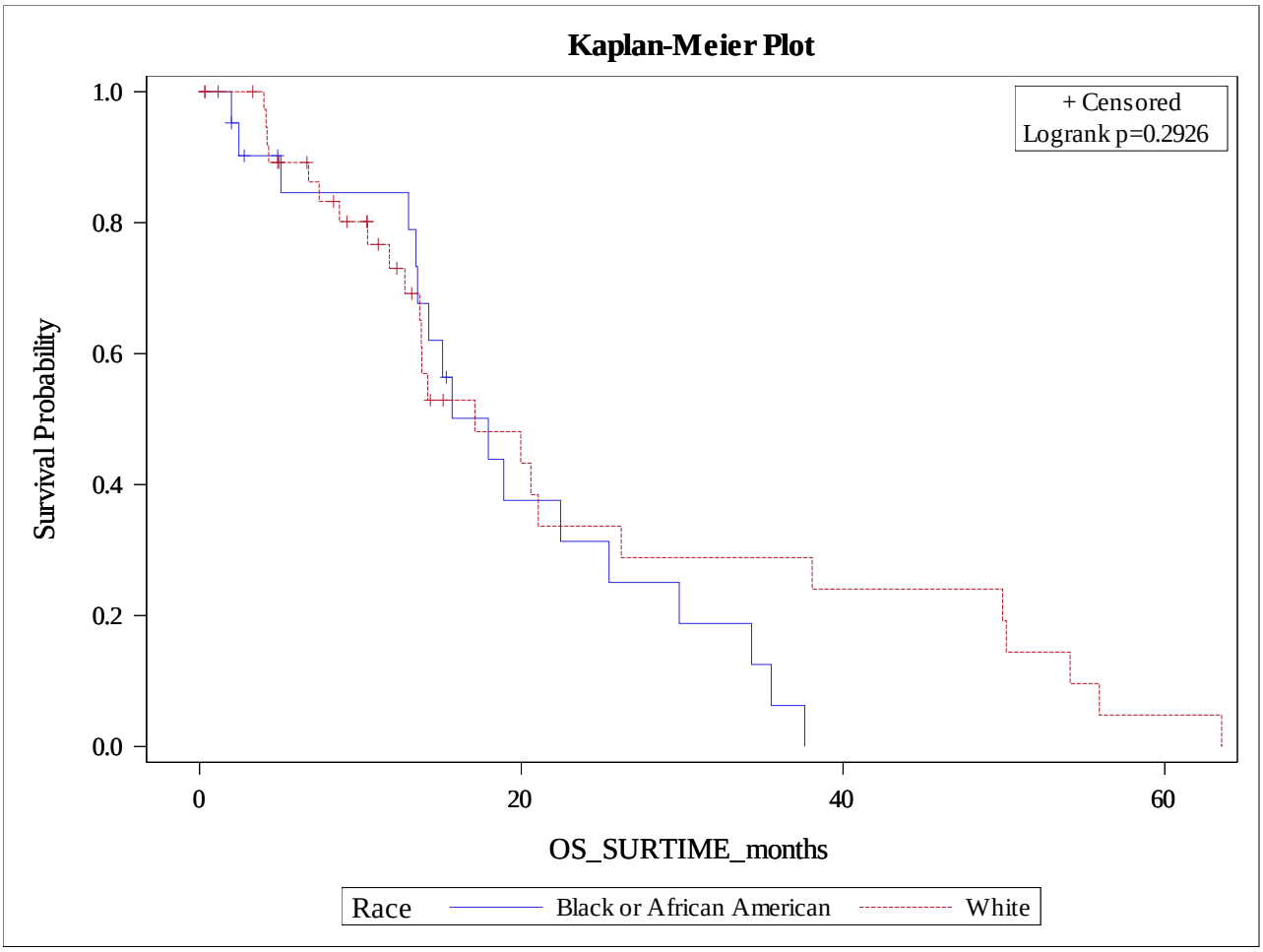
The probability of having lower values of the outcome is being modeled.

Table 8: Multivariable Variable Analysis Logistic Regression with Reason for Treatment Discontinuation

			Reason for Treatment Discontinuation		
Covariate	**Level**	**N**	**Odds Ratio (95% CI)**	**OR P-value**	**Type3 P-value**
Race	Black or African American	21	1.19 (0.35-4.00)	0.781	0.781
	White	41	-	-	
Age at trial consent	>45, <=54	24	0.55 (0.13-2.29)	0.412	0.568
	>54, <=62	13	1.19 (0.23-6.09)	0.833	
	>=31, <=45	9	1.68 (0.28-10.18)	0.575	
	>62, <=79	16	-	-	
BMI category	Normal Weight	24	0.24 (0.05-1.26)	0.093	**0.019**
	Overweight	20	0.09 (0.02-0.53)	0.007	
	Under Weight	4	2.08 (0.20-21.29)	0.536	
	Obese	14	-	-	

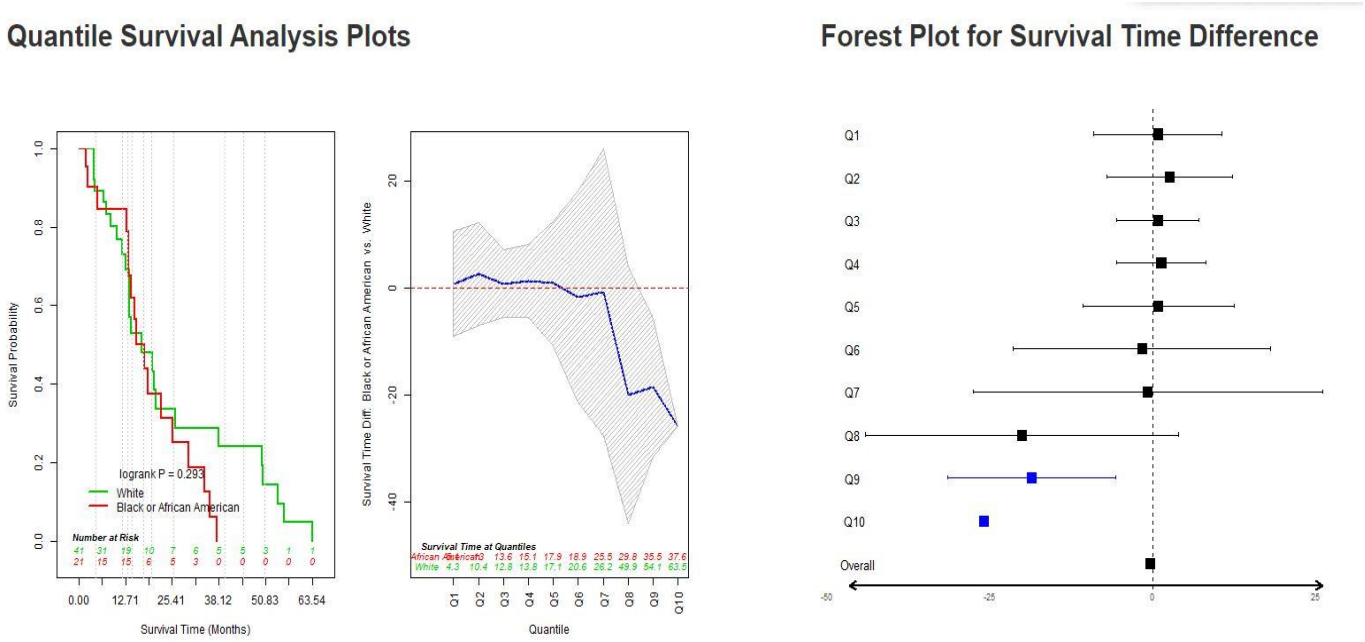
* Number of observations in the original data set = 62. Number of observations used = 62.

Figure 1:



Race	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	36 Mo Survival	60 Mo Survival
Black or African American	21	17 (81%)	4 (19%)	18 (13.5, 25.5)	84.6% (59.3%, 94.8%)	6.3% (0.4%, 24.7%)	0.0% (NA, NA)
White	41	25 (61%)	16 (39%)	17.1 (12.8, 26.2)	73.0% (54.2%, 85.1%)	28.9% (12.4%, 47.7%)	4.8% (0.3%, 19.8%)

Figure 2:


Quantile Survival Analysis Plots
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
logrank P = 0.293
White
Black or African American
Number at Risk
41 31 19 10 7 6 5 5 3 1 1
21 15 15 6 5 3 0 0 0 0 0
0.00 12.71 25.41 38.12 50.83 63.54
Survival Time (Months)
Survival Time Diff: Black or African American vs. White
20
0
-20
-40
Survival Time at Quantiles
White 4.3 10.4 12.8 13.8 17.1 20.6 26.2 49.9 54.1 63.5
Q1 Q2 Q3 Q4 Q5 Q6 Q7 Q8 Q9 Q10
Quantile
Forest Plot for Survival Time Difference
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
Overall
-50
-25
0
25