San Antonio Breast Cancer Symposium®
December 9-12, 2025

Investigating Genomic and Treatment Heterogeneity in ER-/HER2+ and Triple Negative Breast Cancers

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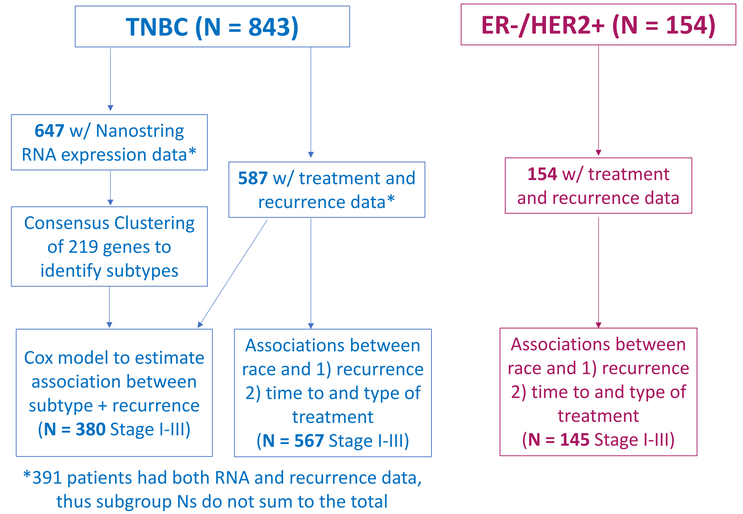
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Background

- Black women experience higher risk of breast cancer (BC) recurrence than non-Black women. Contributors include:
  - Higher incidence of proliferative IHC subtypes such as triple negative [TNBC] and ER-/HER2+ BC
  - Disparities in healthcare access and treatment among Black vs non-Black women
- Biologic heterogeneity exists within ER- clinical breast cancer subtypes
  - 6 TNBC molecular subtypes: Basal-like 1/2 (BL1/2), Luminal/Androgen Receptor (LAR), Immunomodulatory (IMM), Mesenchymal and Mesenchymal Stem Cell-like
- Among ER-s, we aimed to:
  - **1)** Understand biologic heterogeneity and treatment patterns by race
  - **2)** Evaluate the impact of biologic heterogeneity and treatment on outcomes

Methods

*All analyses use the Carolina Breast Cancer Study (CBCS), Phases I-III

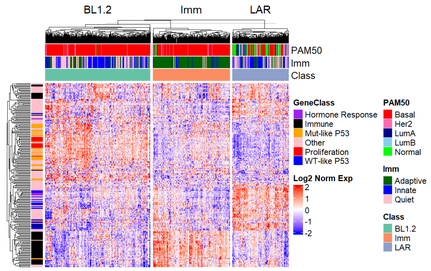


*391 patients had both RNA and recurrence data, thus subgroup Ns do not sum to the total

Results

Figure 1. Biologic heterogeneity in TNBC reflects proliferation and immune infiltration. A) We identified three molecular subtypes of TNBC mirroring previous classifications: "Immunogenic" with high Adaptive expression, "Luminal/Androgen Receptor (LAR)" with higher ESR1 expression, and "Basal-like 1/2" with high proliferation. **B)** Black and younger participants had significantly fewer LAR and Immunogenic tumors (vs. BL1/2).

A. Three TNBC Subtypes Identified in CBCS



B. TNBC Subtypes Associate with Demographic and Molecular Features

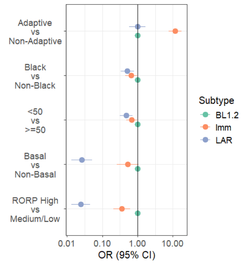
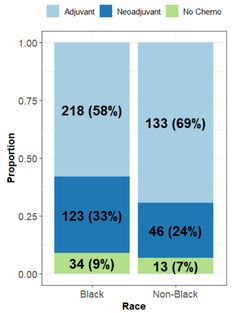


Figure 2. Differences in treatment patterns and timing by race among TNBCs. A) Black TNBC participants were more likely than non-Black participants to receive neoadjuvant chemotherapy (vs. adjuvant; RFD = 10%, 95% CI = 2%, 18%). There was no difference in the prevalence of receiving no chemotherapy by race. **B)** Among those receiving either adjuvant or neoadjuvant chemotherapy, Black women had longer times between diagnosis and first treatment (Difference in median time to treatment of 6 days for both groups).

A. Chemotherapy Sequence by Race



B. Time to Treatment by Race and Chemo Sequence

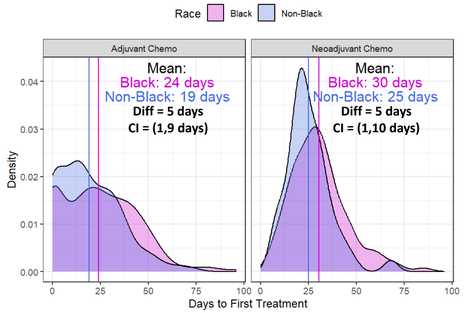
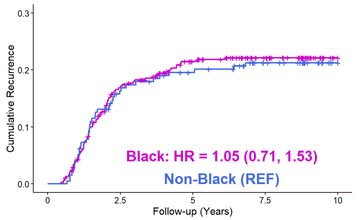


Figure 3. Associations between race and recurrence among TNBCs. A) Among TNBCs, risk of recurrence was similar among Black vs Non-Black women. **B)** BL1/2 and LAR subtypes have the highest recurrence risk.

A. Race and Recurrence Among TNBCs.



B. Molecular Subtype and Recurrence Among TNBCs.

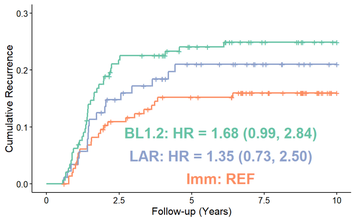
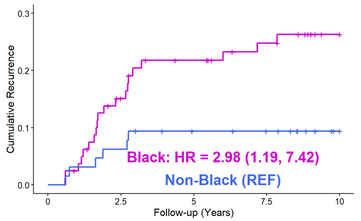


Figure 4. Associations between race and recurrence among ER-/HER2+s. A) Among ER-/HER2+s, Black women had higher risk of recurrence than non-Black women. **B) P**revalence of trastuzumab receipt was similar by race. Black women had nonsignificantly longer time to receipt.

A. Race and Recurrence Among ER-/HER2+s.



B. Race and Treatment Among ER-/HER2+s.

	Trastuzumab Treated	Mean (SD) Days to Trastuzumab
Black	76 (94%)	78 (57)
Non-Black [REF]	59 (92%)	72 (70)
Effect Estimate	OR = 1.29 (0.34, 4.83)	Diff = 6 days (-16, 28)

Conclusions

- Results support previous TNBC classification schema even with smaller RNA panels. Black patients are more likely to have proliferative Basal-like 1/2 subtypes than non-Black patients
- We observed no differences in recurrence by race among TNBC. Black women showed differences in TNBC subtype prevalence and temporal order of surgery vs. chemotherapy, as well as ~1 week longer times to first treatment.
- Black ER-/HER2+ patients experienced higher rates of recurrence. We did not observe differences in trastuzumab receipt by race.
- Results highlight persistent disparities in outcomes among ER-/HER2+ disease and underscore the centrality of immunogenicity as a prognostic feature in TNBC.

Acknowledgements: This research was supported by a grant from UNC Lineberger Comprehensive Cancer Center, which is funded by the University Cancer Research Fund of North Carolina, the Susan G Komen Foundation (OGUNC1202, OG22873776, SAC210102, TREND21686258), National Cancer Institute (R01CA253450), the National Cancer Institute Specialized Program of Research Excellence (SPORE) in Breast Cancer (NIH/NCI P50-CA058223), the Breast Cancer Research Foundation (HEI-23-003), and the US Department of Defense (HT94252310235). The authors would like to acknowledge the University of North Carolina BioSpecimen Processing Facility for sample processing, storage, and sample disbursements (http://bsp.web.unc.edu/) and the Breast Cancer Research Foundation HEI-23-003. We are grateful to CBCS participants and study staff. This presentation is the intellectual property of the author/presenter. Contact them at sarahvan@email.unc.edu for permission to reprint and/or distribute.