Identification of racial disparities across MammaPrint® and BluePrint® subtypes in HR+HER2- breast cancer

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Background

- Black women in the United States diagnosed with breast cancer have a 30% higher mortality rate than White women, even after adjusting for socioeconomic factors.[1]
- Racial disparities in outcomes are observed even among patients receiving comparable systemic treatments, suggesting, in part, a biological basis for racial survival disparities observed in patients diagnosed with hormone receptor positive (HR+) breast cancer.[2]
- Higher incidences of genomically high risk tumors have been observed in Black participants in studies utilizing MammaPrint risk of distant recurrence and BluePrint molecular subtyping.[3,4]
- In this study, we utilized MammaPrint and BluePrint to examine whether tumor genomic differences contribute to racial survival disparities among women with HR+, human epidermal growth factor receptor 2-negative (HER2-) early-stage breast cancer.

Methods

- This study included 1,018 participants with HR+HER2- early breast cancer with 3-year follow-up data. A reference cohort of 509 black females was used to propensity score match 509 White patients enrolled in FLEX by age and menopausal status.
- MammaPrint and BluePrint Genomic Test Results:

MammaPrint	Low Risk 1.000 to 0.000	High 1 Risk 0.000 to -0.569	High 2 Risk -0.570 to -1.000
BluePrint	Luminal A-Type	Luminal B-Type	Basal-Type

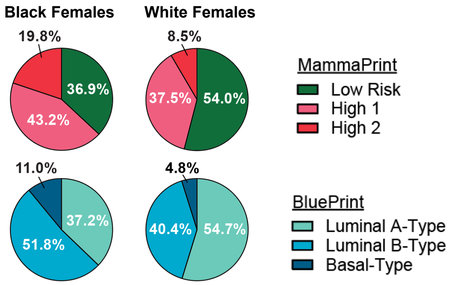
- Recurrence-free survival (RFS) was compared between race and molecular subtype using Kaplan-Meier estimates and log-rank tests.
- A Cox proportional hazards model was used to analyze the association of MammaPrint, BluePrint, race, and clinicopathologic features with RFS.

Table 1. Clinical Characteristics

	Black (N=509)	White (N=509)	All (N=1018)	P-value
Age (Years)				
Mean (SD)	54 (± 13)	54 (± 13)	54 (± 13)	0.983
Menopausal Status				
Post-	250 (51.9%)	251 (52.1%)	501 (52.0%)	1
Pre-/Peri-	232 (48.1%)	231 (47.9%)	463 (48.0%)	
Tumor Stage				
T1	203 (56.7%)	202 (63.9%)	405 (60.1%)	0.645
T2	124 (34.6%)	94 (29.7%)	218 (32.3%)	
T3	24 (6.7%)	17 (5.4%)	41 (6.1%)	
T4	7 (2.0%)	3 (0.9%)	10 (1.5%)	
Lymph Node Status				
LN-	241 (70.1%)	240 (82.5%)	481 (75.7%)	0.002
LN+	103 (29.9%)	51 (17.5%)	154 (24.3%)	
Grade				
G1	113 (23.5%)	143 (30.0%)	256 (26.8%)	<0.001
G2	225 (46.8%)	259 (54.4%)	484 (50.6%)	
G3	143 (29.7%)	74 (15.5%)	217 (22.7%)	
ER Staining				
>10%	469 (95.9%)	492 (97.8%)	961 (96.9%)	0.257
1-10%	20 (4.1%)	11 (2.2%)	31 (3.1%)	

Data presented N (%) unless indicated otherwise; Unknown values excluded; N, sample size; SD, standard deviation: ER, estrogen receptor

Figure 1. MammaPrint and BluePrint distribution by race in participants with HR+HER2- tumors



All participants were included in MammaPrint comparisons. Participants with unknown BluePrint results were excluded from BluePrint comparisons (N=492 and N=475 for Black and White participants, respectively)

Figure 2A. 3-year RFS by Race

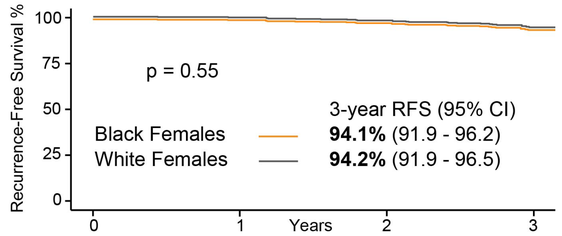


Figure 2B. 3-year RFS by MammaPrint

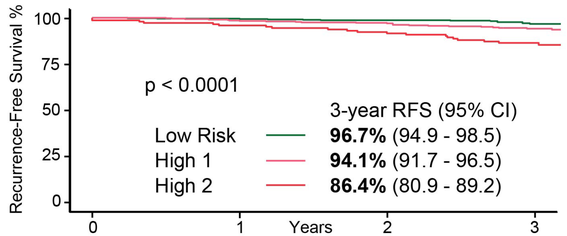
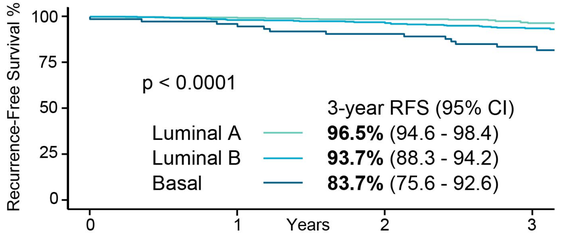


Figure 2C. 3-year RFS by BluePrint



RFS, recurrence-free survival; CI, confidence interval

Table 2. Multivariate Cox proportional hazards model

Variable	HR (multivariate)	Variable	HR (multivariate)
MP/BP Group		**Tumor Stage**	
Low Risk/Luminal A	-	T1	-
High Risk/Luminal B	3.50 (1.26-9.76, p=0.017)	T2	1.37 (0.65-2.90, p=0.412)
High Risk/Basal	5.84 (1.59-21.37, p=0.008)	T3	2.78 (1.08-7.13, p=0.033)
Menopausal Status		**Lymph Node Status**	
Pre-/Peri-	-	LN-	-
Post-	2.45 (1.23-4.88, p=0.011)	LN+	2.94 (1.50-5.79, p=0.002)
Race		**Grade**	
White	-	G1	-
Black	1.14 (0.54-2.41, p=0.731)	G2	1.20 (0.38-3.79, p=0.754)
		G3	1.60 (0.47-5.50, p=0.453)

Data presented as HR (95% CI, p-value). T4 not included due to small sample size N=10. HR, hazard ratio; MP, MammaPrint; BP, BluePrint

Results

- Black participants were significantly more likely to have nodal involvement, higher grade (**Table 1**), and were more likely to be treated with chemotherapy, compared to White participants (73.6% vs. 47.1%, respectively; p<0.001)
- Genomically High Risk tumors were more common among Black compared to White females (**Figure 1**):
  - High 2: p<0.001; Luminal B-Type: p=0.002; Basal-Type: p<0.001
- No significant difference in 3-yr RFS was observed for Black females, compared to White females (p=0.55; **Figure 2A**)
- 3-year RFS by MammaPrint and BluePrint (**Figures 2B-C**):
  - Low Risk: 96.7%, High 1: 94.1%, High 2: 86.4%; p<0.0001
  - Luminal A-Type: 96.5%; Luminal B-Type: 93.7%; Basal-Type: 83.7%; p<0.0001
- In the multivariate model, High Risk Luminal B- and Basal-Type tumors had significantly worse 3-year outcomes compared to Luminal A-Type tumors. Post-menopausal status, T3 tumor size, and lymph node involvement were also associated with 3-year outcomes (**Table 2**)
- Race and tumor grade were not significantly associated with 3-year outcomes when adjusted for other covariates (**Table 2**)

Conclusions

- MammaPrint and BluePrint classification identified higher incidence of High 2, Luminal B, and Basal molecular subtypes among Black females, compared to White, with HR+HER2- early breast cancer.
- Notably, 3-yr RFS was driven by MammaPrint + BluePrint, independent of race, after adjusting for other covariates.
- These data highlight the importance of tumor genomic testing to inform treatment decisions as we strive to reduce racial survival disparities among Black females with breast cancer.

References: 1. Carey LA et al., JAMA 2006; 2. Giaquinto AN et al., CA Cancer J Clin 2022; 3. Patel R et al., ASCO 2024; 4. Hoskins K et al., ASCO 2021