# MammaPrint® and BluePrint® identify racial disparities among women with HR+HER2- early-stage breast cancer

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## BACKGROUND

- Black women are 41% more likely to die from breast cancer compared to White women yet remain underrepresented in clinical trials and population studies.[1]
- TailorX and RxPonder have raised questions about the prognostic accuracy of the genomic test used in these trials, which was shown to underestimate risk in Black women.[2-3]
- The 70-gene MammaPrint® (MP) risk of distant recurrence signature was shown in the MINDACT trial to identify patients with clinically high risk, but genomically Low Risk tumors who have excellent outcomes without chemotherapy.[4-5]
- The 80-gene BluePrint® (BP) molecular subtyping signature categorizes tumors as Luminal-, HER2-, or Basal-Type.
- MP and BP are prognostic of therapeutic response and long-term outcomes.[4-6]

## OBJECTIVES

To identify genomic differences contributing to survival disparities, MP and BP distribution and outcomes based on MP and BP classification were evaluated in Black and White women with HR+HER2- breast cancer.

## METHODS

- **Patients**: This study included 568 Black women enrolled in BEST from 2005-2015 (n = 139; R01-CA204819) and the ongoing FLEX study (n = 429; NCT03053193). White women enrolled in FLEX (n = 568) were matched to Black patients controlling for age, tumor size, and nodal status. All patients had stage I-III, HR+HER2- breast cancer.
- **MammaPrint and BluePrint testing**:

| Test | MammaPrint | BluePrint |
|---|---|---|
| Risk and Subtype Characterization | Low Risk | Luminal A-Type |
| | High Risk | Luminal B-Type |
| | | HER2-Type |
| | | Basal-Type |

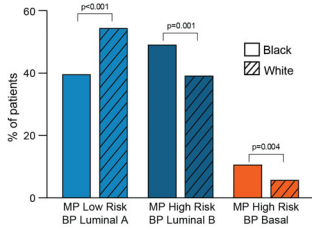
- **Endpoints and Statistical Analysis**:
  - Primary endpoint: 3- and 10-year Recurrence-Free Survival (RFS)
  - Secondary endpoint: 10-year Overall Survival (OS).
  - Differences in RFS and OS was evaluated by Kaplan-Meier analyses and log-rank test.
  - Median follow up was 3.0 years for FLEX patients (n = 500) and 10.1 years for patients in BEST (n = 135).

**Table 1. Clinical characteristics**

| n (%) | Black n = 568 | White n = 568 | Total n = 1136 |
|---|---|---|---|
| **Menopausal status** | | | |
| Pre/peri- | 229 (41.9) | 180 (34.1) | 409 (38.1) |
| Post- | 317 (58.1) | 348 (65.9) | 665 (61.9) |
| **Histological grade** | | | |
| Low, G1 | 133 (24.4) | 147 (26.8) | 280 (25.6) |
| Intermediate, G2 | 253 (46.4) | 313 (57.0) | 566 (51.7) |
| High, G3 | 159 (29.2) | 89 (16.2) | 248 (22.7) |
| **Tumor size** | | | |
| T1 | 282 (57.7) | 293 (59.1) | 575 (58.4) |
| T2 | 168 (34.4) | 173 (34.9) | 341 (34.6) |
| T3-T4 | 39 (7.9) | 30 (6.0) | 69 (7.0) |
| **Lymph node status** | | | |
| LN- | 342 (72.5) | 342 (72.5) | 684 (72.5) |
| LN+ | 130 (27.5) | 130 (27.5) | 260 (27.5) |

*unknown not shown

**Figure 1. MP and BP subtype**




*5 patients with BP HER2-type not shown

**Figure 2. 3-year RFS classified by MP and BP in White (A) and Black patients (B)**

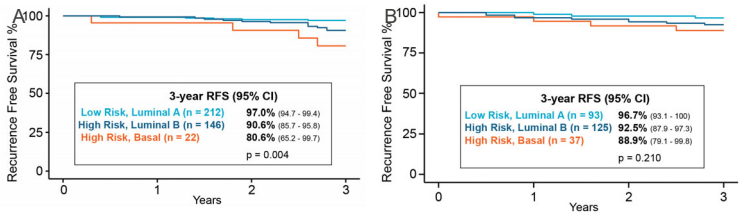
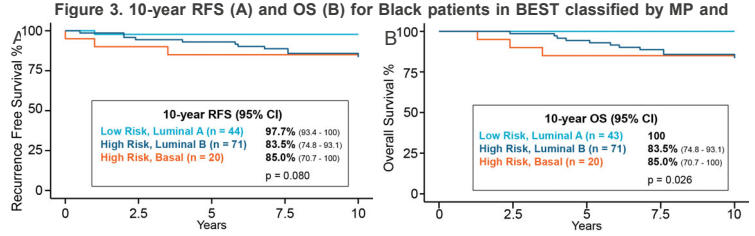



**Figure 3. 10-year RFS (A) and OS (B) for Black patients in BEST classified by MP and**




## RESULTS

- Black patients had significantly more aggressive MP High Risk tumors, including Luminal B- (48.9%) and Basal-Type tumors (10.7%) compared to White patients (39.3% and 6.0%, respectively; p=0.001 and p = 0.004, respectively; Figure 1).
- 3-year RFS was 93.6% (95% CI 90.7 – 96.7) for Black patients and 93.6% (95% CI 91.1 – 96.3) for White patients.
- Within each race, 3-year RFS differed when stratified by MP and BP, with Basal-Type tumors exhibiting the worst outcome (Figure 2A-B).
- 10-year RFS and OS rates for Black women were 88.4% (95% CI 82.9 – 94.2) and 89.0% (95% CI 83.7 – 94.7), respectively.
- When stratified by MP and BP, Black patients with Low Risk, Luminal A tumors had excellent 10-year RFS (97.7%) and OS (100%) compared to patients with High Risk, Luminal B or Basal-Type tumors. Patients with Basal-Type tumors had earlier events compared with Luminal tumors (Figure 3).

## CONCLUSIONS

- MP and BP more precisely stratified tumors resulting in distinct 3- and 10-year outcomes, independent of race, beyond clinical subtype alone.
- We identified racial differences in the distribution of MP and BP subtypes, but within each subtype, survival outcomes at 3 years were comparable between Black and White patients.
- Black patients with Low Risk, Luminal A-Type tumors had excellent 10-year survival outcomes, similar to outcomes observed in MINDACT, where the patient cohort was predominantly white, suggesting equivalent outcomes among diverse patients when classified by MP and BP, in contrast to other genomic tests. Patients with Low Risk tumors, independent of race, may be candidates to avoid overtreatment.[4-5]
- HR+, BP Basal-Type tumors occur more frequently in Black patients and exhibit worse outcomes compared to Luminal tumors. These patients may be undertreated if not recognized by genomic testing. More aggressive treatment can improve outcomes, as demonstrated by improved OS in HR+, Basal-Type tumors that achieved pathologic Complete Response.[7]
- These data highlight the importance of genomic testing to help optimize treatment and reduce outcome disparities in Black women.

## REFERENCES

1. Giaquinto AN, et al. CA Cancer J Clin, 2022. 2. Albain et al. J Natl Cancer Inst 2021. 3. Abdou et al. Cancer Res 2023. 4. Cardoso et al. New Engl J Med 2016. 5. Piccart et al. Lancet Oncol 2021. 6. Whitworth et al. Ann Surg Oncol, 2022. 7. Whitworth et al. JCO Precis Oncol 2022.