Real-World Evidence of MammaPrint® and BluePrint® Utility for Informing Axillary Surgery Decisions in the Neoadjuvant Setting

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Introduction

- Decisions regarding the extent of axillary surgery in HR+HER2- early-stage breast cancer (EBC) are primarily based on clinical factors, including age, T-stage, and N-stage
- The ACOSOG Z0011[1] trial found sentinel lymph node dissection (SLND) noninferior to axillary lymph node dissection (ALND) for T1-2 and 1-2 LN+ for 10-year Overall Survival, however, the role of genomics for axillary surgery decision-making remains unclear
- The NBRST[2,3] and I-SPY2[4] trials have shown that the risk of distant recurrence and molecular subtyping signatures, MammaPrint and BluePrint, can predict distinct pathological Complete Response (pCR) rates to neoadjuvant chemotherapy (NCT) in EBC
- To identify the role of genomic profiling in axillary decision making in FLEX, we evaluated the association of MammaPrint and BluePrint with the likelihood of achieving pCR (ypT0/isN0) and avoiding ALND in patients with HR+HER2- EBC

Methods

Study Cohort

- Patients with HR+HER2- tumors treated with NCT with available surgical treatment information enrolled in the ongoing prospective, observational FLEX Trial (NCT03053193), were included in this study (N = 603)

MammaPrint and BluePrint Genomic Testing Results:

MammaPrint	Low Risk 1.000 to 0.000	High 1 Risk (H1)* 0.000 to -0.569	High 2 Risk (H2) -0.570 to -1.000	
BluePrint	Luminal A	Luminal B	Luminal B	Basal

*MammaPrint High risk subtypes also included BluePrint Basal (H1: n = 8) and HER2 (H2: n = 2) subtypes, which were excluded from the analysis

Statistics

- Differences in clinical characteristics, pCR rates, and type of nodal dissection were assessed by Chi-Squared or Fisher's exact tests
- Multivariate logistic regression assessed the associations of MammaPrint/BluePrint with pCR likelihood and ALND, adjusting for clinical factors
- P-values less than 0.05 were considered significant

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Table 1. Clinical Characteristics

Characteristic	Low (n=60)	High 1 (n=333)	High 2 (n=210)	Overall (n=603)	P-value
Age					
<50	26 (44.1%)	119 (35.8%)	85 (40.7%)	230 (38.3%)	0.54
>=50	33 (55.9%)	213 (64.2%)	124 (59.3%)	370 (61.7%)	
Menopausal Status					
Pre-/Peri-	26 (45.6%)	120 (38.8%)	72 (36.7%)	218 (38.8%)	0.675
Post-	31 (54.4%)	189 (61.2%)	124 (63.3%)	344 (61.2%)	
Race/Ethnicity					
White	44 (78.6%)	240 (76.9%)	142 (74.0%)	426 (76.1%)	
Black	8 (14.3%)	44 (14.1%)	32 (16.7%)	84 (15.0%)	0.998
Latin American	3 (5.4%)	18 (5.8%)	12 (6.3%)	33 (5.9%)	
AAPI	0 (0%)	7 (2.2%)	5 (2.6%)	12 (2.1%)	
Other	1 (1.8%)	3 (0.9%)	1 (0.5%)	5 (0.9%)	
Tumor Stage					
T1	3 (7.1%)	62 (23.4%)	38 (23.2%)	103 (21.9%)	
T2	18 (42.9%)	137 (51.7%)	100 (61.0%)	255 (54.1%)	0.0025
T3	17 (40.5%)	51 (19.2%)	15 (9.1%)	83 (17.6%)	
T4	4 (9.5%)	15 (5.7%)	11 (6.7%)	30 (6.4%)	
Clinical Nodal Status					
LN-	14 (33.3%)	95 (37.4%)	77 (48.7%)	186 (41.0%)	0.314
LN+	28 (66.6%)	159 (62.6%)	81 (51.2%)	268 (59.0%)	
Grade					
G1	6 (10.9%)	28 (9.2%)	1 (0.5%)	35 (6.3%)	<0.001
G2	47 (85.5%)	176 (57.5%)	41 (20.7%)	264 (47.2%)	
G3	2 (3.6%)	102 (33.3%)	156 (78.8%)	260 (46.5%)	
ER %					
Low (<10%)	0 (0%)	3 (0.9%)	44 (23.4%)	47 (8.2%)	<0.001
Medium (10-50%)	0 (0%)	11 (3.4%)	42 (22.3%)	53 (9.2%)	
High (>50%)	60 (100%)	313 (95.7%)	102 (54.3%)	475 (82.6%)	
Surgery Type					
Breast conserving	17 (30.4%)	132 (40.5%)	100 (48.1%)	249 (42.2%)	0.095
Mastectomy	39 (69.6%)	194 (59.5%)	108 (51.9%)	341 (57.8%)	
CT Regimen					
TC	10 (16.7%)	74 (22.3%)	23 (11.0%)	107 (17.8%)	
AC-T	37 (61.7%)	216 (65.1%)	125 (59.5%)	378 (62.8%)	<0.001
Capecitabine	1 (1.7%)	7 (2.1%)	19 (9.0%)	27 (4.5%)	
Platinum-Containing	1 (1.7%)	5 (1.5%)	23 (11.0%)	29 (4.8%)	
Other	11 (18.3%)	30 (9.0%)	20 (9.5%)	61 (10.1%)	
BluePrint					
Luminal A	58 (100.0%)	0 (0%)	0 (0%)	58 (10.4%)	
Luminal B	0 (0%)	317 (96.4%)	91 (44.5%)	408 (68.5%)	<0.001
Basal	0 (0%)	8 (3.6%)	112 (54.5%)	120 (20.7%)	
HER2	0 (0%)	0 (0%)	2 (1.0%)	2 (0.4%)	

Data presented as n (%); Not all patients received BluePrint testing; Unknown values excluded; n, sample size; AAPI, Asian American and Pacific Islander; AIAN, American Indian or Alaska Native; ER, estrogen receptor; TC, taxanes; AC-T, anthracyclines and taxanes

Figure 1. Pathological Complete Response (pCR) to NCT by (A) MammaPrint or (B) BluePrint

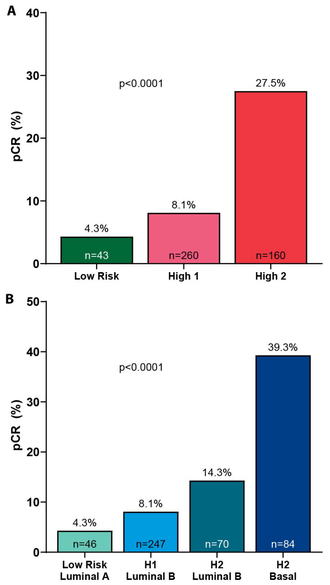

Table 2. Multivariate logistic regression analysis for association of clinical and MammaPrint/BluePrint with pCR

Characteristic	Odds Ratio	95% CI	P-value
MP and BP			
H1/Luminal B	1		
H2/Luminal B	1.71	0.58-4.77	0.314
H2/Basal	5.18	2.06-13.82	**0.001**
Menopausal Status			
Post-	1		
Pre-/Peri-	0.87	0.41-1.81	0.717
Tumor Stage			
T1/T2	1		
T3/T4	0.61	0.19-1.58	0.344
Lymph Node Status			
LN-	1		
LN+	0.69	0.34-1.42	0.314
Tumor Grade			
Non-G3	1		
G3	1.16	0.46-2.86	0.754

Data presented as Odds Ratio (95% CI, p-value).

Figure 2. Distribution of axillary surgery type after NCT by (A) MammaPrint or (B) BluePrint

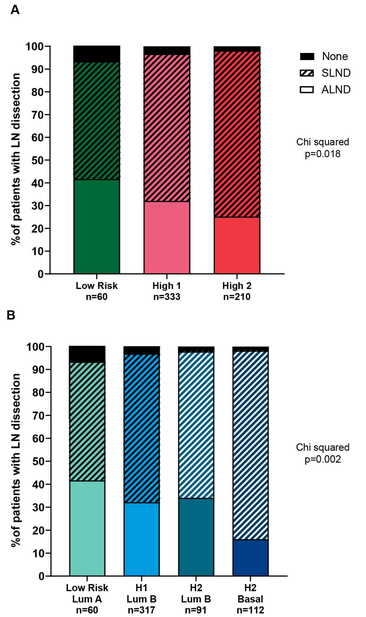

Table 3. Multivariate logistic regression analysis for association of clinical and MammaPrint/BluePrint with receiving ALND

Characteristic	Odds Ratio	95% CI	P-value
MP and BP			
Low Risk/Luminal A	1		
H1/Luminal B	0.69	0.32-1.51	0.35
H2/Luminal B	0.68	0.26-1.81	0.442
H2/Basal	0.31	0.10-0.89	**0.031**
Menopausal Status			
Post-	1		
Pre-/Peri-	1.03	0.65-1.64	0.899
Tumor Stage			
T1/T2	1		
T3/T4	1.37	0.80-2.35	0.25
Lymph Node Status			
LN-	1		
LN+	3.45	2.11-5.78	**<0.001**
Tumor Grade			
Non-G3	1		
G3	1.08	0.63-1.86	0.781

Data presented as Odds Ratio (95% CI, p-value).

Results

- Most patients were postmenopausal (61%), had T2+ tumors (78%), had nodal involvement (59%), and were treated with anthracyclines (63%) . Most H2 tumors (77%) had ER% staining ≥10% and were more likely to be Grade 3 (79%; p<0.001), compared to H1 and Low-Risk tumors (**Table 1**)
- Patients with H2 tumors were significantly more likely to achieve a pCR (27.5%) compared to Low-Risk (4.3%) or H1-Risk (8.1%; p<0.001). Addition of BluePrint showed patients with H2/Basal-Type tumors had the highest pCR (39.3%; p<0.0001) (**Figure 1**)
- Multivariate analysis revealed that patients with H2 (OR=3.16, 95% CI 1.43-7.28, p=0.005; data not shown) or H2/Basal-Type tumors were significantly more likely to achieve pCR (OR=5.18, p=0.001) when accounting for menopausal status, T-stage, nodal status, and grade (**Table 2**)
- H2 was significantly more likely to avoid ALND (74.8%) compared to patients with Low-Risk (58.3%) and H1 tumors (67.9%; p=0.018). BluePrint revealed patients with H2/Basal-Type had the highest rates of undergoing SLND (**Figure 2**)
- Multivariate analysis showed that patients with H2/Basal-Type tumors had a significantly lower Odds Ratio of undergoing ALND (OR=0.31; p=0.031), while LN+ at presentation was strongly associated with undergoing ALND (OR=3.45, p<0.001) (**Table 3**)

Conclusions

- MammaPrint and BluePrint not only predict response to NCT in HR+HER2- EBC but also correlate with axillary surgery outcomes. Patients with H2 or Basal-Type tumors were significantly more likely to achieve pCR and more likely to avoid ALND
- I-SPY2[4] showed that patients with MammaPrint H2 tumors achieve even greater pCR rates with emerging treatments such as immunotherapy, which is currently under evaluation in the Phase-III SWOG S2206 (NCT06058377) trial
- These results suggest that MammaPrint/BluePrint can inform neoadjuvant planning and highlight the importance of using MammaPrint/BluePrint on core needle biopsies in patients with HR+HER2- EBC to help enable downstaging and less invasive axillary surgery

References: 1. Giuliano et al., JAMA. 2017.; **2.** Whitworth et al., Ann Surg Oncol. 2022.**; 3.** Beitsch et al., ASCO. 2023.; **4.** Pusztai et al., Cancer Cell. 2021.