The impact of the 80-gene signature on pCR and chemotherapy treatment decisions in early-stage breast cancer: A FLEX analysis

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Introduction

- Hormone receptor-positive (HR+), HER2-negative early-stage breast cancer (EBC) displays notable heterogeneity and diverse responses to neoadjuvant chemotherapy (NCT)
- Genomic profiling has demonstrated utility in guiding pre-operative treatment decisions by predicting the probability of achieving a pathological complete response (pCR) and chemosensitivity[1]
- Breast cancer subtyping based solely on receptor status by IHC may not fully capture tumor biology or sufficiently guide personalized treatment decisions[1,2]
- The BluePrint® 80-gene signature provides insight into the intrinsic subtypes of EBC, identifying patients that have tumors that may be more likely to benefit from more aggressive treatments
- This study evaluated pCR rates to NCT by BluePrint molecular subtypes in MammaPrint® High Risk tumors and the role of BluePrint in guiding adjuvant chemotherapy (CT) treatment decisions from patients enrolled in FLEX- a prospective, longitudinal, observational real world data study

Methods

Study Cohort

- Patients included in this analysis were enrolled in the FLEX trial (NCT03053193), received MammaPrint and BluePrint, and had HR+HER2- EBC
- The analysis included patients eligible for CT with MammaPrint High Risk tumors, which were grouped into patients who received:
  1. NCT and had available pCR data (N=401)
  2. Adjuvant CT with treatment recommendation data based on BluePrint results (N=868)
- MammaPrint High Risk of recurrence results were further characterized by BluePrint molecular subtyping signature as Luminal B or Basal[1,2]

Statistics

- Differences in clinical characteristics, pCR rates, and treatment differences were evaluated by Chi-Squared test or Fisher's exact tests
- P-values of less than 0.05 were considered significant

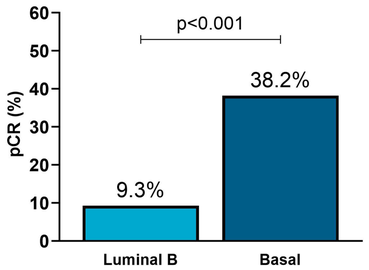
Results

Table 1. Clinical Characteristics of FLEX patients with HR+HER2- disease treated with NCT and available pCR data

	Luminal B (N=312)	Basal (N=89)	Overall (N=401)	P-value
Age (Years)				
Mean (SD)	54 (± 12)	54 (± 13)	54 (± 12)	0.971
Menopausal Status				
Post-	182 (61.9%)	54 (65.1%)	236 (62.6%)	0.877
Pre-/Peri-	112 (38.1%)	29 (34.9%)	141 (37.4%)	
Race				
White	223 (75.9%)	61 (76.3%)	284 (75.9%)	0.806
Black	43 (14.6%)	15 (18.8%)	58 (15.5%)	
Latin American	19 (6.5%)	1 (1.3%)	20 (5.3%)	
AAPI	6 (2.0%)	3 (3.8%)	9 (2.4%)	
AIAN	1 (0.3%)	0 (0%)	1 (0.3%)	
Mixed	2 (0.7%)	0 (0%)	2 (0.5%)	
Tumor Stage				
T1	55 (22.3%)	21 (29.6%)	76 (23.9%)	0.887
T2	137 (55.5%)	39 (54.9%)	176 (55.3%)	
T3	39 (15.8%)	8 (11.3%)	47 (14.8%)	
T4	16 (6.5%)	3 (4.2%)	19 (6.0%)	
Lymph Node Status				
LN-	82 (33.9%)	43 (65.2%)	125 (40.6%)	<0.001
LN+	160 (66.1%)	23 (34.8%)	183 (59.4%)	
Grade				
G1	19 (6.5%)	0 (0%)	19 (5.1%)	<0.001
G2	147 (50.5%)	7 (8.3%)	154 (41.1%)	
G3	125 (43.0%)	77 (91.7%)	202 (53.9%)	

Data presented as n (%); Unknown values excluded; N, sample size; AAPI, Asian American and Pacific Islander; AIAN, American Indian or Alaska Native

Figure 1. pCR data Luminal B vs Basal tumors



NCT-treated cohort with pCR data (N=401)

- BluePrint classified 78% of tumors as Luminal B and 22% as Basal **(Table 1)**
  - LN+ was more common in Luminal B (66.1%) vs Basal tumors (34.8%; p<0.001)
  - More Basal tumors were grade 3 (91.7%) compared to Luminal B (43.0%; p<0.001)
- Patients with Basal tumors were significantly more likely to achieve a pCR (38.2%) vs Luminal B (9.3%; p<0.001) **(Figure 2)**

CT treatment Recommendation Cohort (N=868)

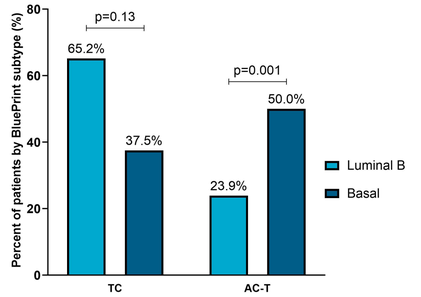
- 93% of the patients had tumors classified as BluePrint Luminal B and 7% as Basal **(Table 2)**
  - Among Basal, 88.1% were LN-, 41.5% were ER >50%, and 81.7% were grade 3, compared to 79.6% (p = 0.283), 97.2% (p<0.001) and 18.8% (p < 0.001) for Luminal B, respectively
  - Only 13.2% of Basal tumors had an ER expression of <10%
  - 98.4% of patients with Basal tumors received CT vs. 76.9% of Luminal B (p=0.19)
  - Basal-type patients are more likely to receive neoadjuvant therapy (27.4% vs. 11.9%; p=0.006)
- CT recommendations showed that patients with Basal tumors were twice as likely to receive AC-T (50.0% vs. 23.9%; p=0.001) and less likely to receive TC (37.5% vs. 65.2%; p=0.13) **(Figure 2)**
- The Basal subtype was more frequently treated with CT (98.4%) and neoadjuvant therapy (27.4%) compared to Luminal B (77%, p<0.001; 11.9%, p=0.006, respectively) and with a more aggressive CT regimen than docetaxel/cyclophosphamide (Basal: 50.0%, Luminal B: 25.7%; p<0.001)
- When restricted to Grade 3 tumors, Basal-type tumors were more often treated with AC-T (39.6% vs. 21.2%; p=0.02) compared to Luminal B (data not shown)
  - Similarly, among tumors with ER staining >50%, Basal were more likely to receive AC-T (40.9% vs. 16.7%; p=0.04) compared to Luminal B

Table 2. Clinical Characteristics of FLEX patients with HR+HER2- disease in the treatment recommendation cohort

	Luminal B (N=806)	Basal (N=62)	Overall (N=868)	P-value
Age (Years)				
Mean (SD)	61 (± 11)	57 (± 12)	61 (± 11)	0.078
Race				
White	624 (82.4%)	38 (65.5%)	662 (81.2%)	0.114
Black	81 (10.7%)	15 (25.9%)	96 (11.8%)	
Latin American	34 (4.5%)	3 (5.2%)	37 (4.5%)	
AAPI	16 (2.1%)	2 (3.4%)	18 (2.2%)	
AIAN	2 (0.3%)	0 (0%)	2 (0.2%)	
Menopausal Status				
Post-	615 (81.3%)	45 (80.4%)	660 (81.3%)	0.973
Pre-/Peri-	141 (18.7%)	11 (19.6%)	152 (18.7%)	
Tumor Stage				
T1	464 (64.8%)	30 (49.2%)	494 (63.6%)	0.211
T2	232 (32.4%)	28 (45.9%)	260 (33.5%)	
T3	17 (2.4%)	2 (3.3%)	19 (2.4%)	
T4	3 (0.4%)	1 (1.6%)	4 (0.5%)	
Lymph Node Status				
LN-	546 (79.6%)	52 (88.1%)	598 (80.3%)	0.283
LN+	140 (20.4%)	7 (11.9%)	147 (19.7%)	
Grade				
G1	148 (19.0%)	0 (0%)	148 (17.7%)	<0.001
G2	484 (62.2%)	11 (18.3%)	495 (59.1%)	
G3	146 (18.8%)	49 (81.7%)	195 (23.3%)	
ER Staining (%)				
Low (<10%)	4 (0.5%)	7 (13.2%)	11 (1.3%)	<0.001
Medium (10-50%)	18 (2.3%)	24 (45.3%)	42 (5.0%)	
High (>50%)	768 (97.2%)	22 (41.5%)	790 (93.7%)	
Treatment Type				
Neoadjuvant therapy	96 (11.9%)	17 (27.4%)	113 (13.0%)	0.0055
Adjuvant therapy	710 (88.1%)	45 (72.6%)	755 (87.0%)	
Systemic Treatment				
ET only	184 (22.8%)	1 (1.6%)	185 (21.4%)	<0.001
ET+CT	612 (75.9%)	56 (90.3%)	668 (77.2%)	
ET,CT + TT	9 (1.1%)	5 (8.1%)	11 (1.3%)	
Chemotherapy				
TC	366 (65.2%)	18 (36.0%)	384 (62.8%)	<0.001
AC-T	134 (23.9%)	24 (48.0%)	158 (25.9%)	
Platinum containing	10 (1.8%)	1 (2.0%)	11 (1.8%)	
Other	51 (9.1%)	7 (14.0%)	58 (9.5%)	

Data presented as n (%); Unknown values excluded; N, sample size; AAPI, Asian American and Pacific Islander; AIAN, American Indian or Alaska Native; ER, estrogen receptor; ET, endocrine therapy; CT, chemotherapy; TT, targeted therapy; TC, taxane; AC-T, anthracyclines with taxane

Figure 2. Choice of treatment according to BluePrint results



Conclusions

- Distinct pCR rates among breast cancer molecular subtypes underscore the utility of BluePrint in guiding treatment decisions
- Patients with Basal tumors were significantly more likely to achieve a pCR (38.2%) vs Luminal B (9.3%; p<0.001)
- Despite all patients with MammaPrint High Risk, HR+ HER2- tumors qualifying for CT, patients with HR+HER2- Basal tumors were significantly more likely to receive:
  - Neoadjuvant therapy
  - Chemotherapy
  - AC-T instead of TC
- These findings suggest that physicians used BluePrint results to guide treatment decisions

References: 1. Whitworth et al., Ann Surg Oncol. 2022; **2.** Groenendijk FH, et al. NPJ Breast Cancer. 2019;5:15. | Adam Brufsky is a paid consultant and receives research funding from Agendia | This study was funded by Agendia |