Pathologic Complete Response (pCR) Rates According to MammaPrint and BluePrint Results are Consistent Among Pre- and Post-Menopausal Patients

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Background

Increased use of multi-gene expression profiling has enabled refinement of early-stage breast cancer management. Clinical trials have demonstrated that risk of recurrence testing identifies breast cancer patients who derive benefit from adjuvant chemotherapy and those who can avoid it without affecting long-term clinical outcomes[1]. Recent sub-analyses of pre-menopausal patients suggest a significant clinical benefit to adjuvant chemotherapy in this patient group[2,3]; however, it has yet to be demonstrated whether this is due to a direct cytotoxic effect or secondary ovarian suppression. Here, we report the first age-based analysis of the 70-gene (MammaPrint, MP) and 80-gene (BluePrint, BP) assays in the pre-operative setting.

Methods

The prospective NBRST trial[4] (NCT0147910) evaluated the utility of MP and BP in the pre-operative treatment setting. From 2011 to 2014, the study enrolled 1069 patients from 67 institutions and included women with invasive breast cancer of any pathology-defined subtype, regardless of hormone or HER2 receptor status. Complete clinical data were available for 1025 patients. Patients received neoadjuvant chemotherapy (NAC; n=954) or neoadjuvant endocrine therapy (NET; n=67) according to NCCN guideline recommendations. Pathological complete response (pCR), is defined as the absence of invasive carcinoma in both the breast and axilla at microscopic examination of resection specimen. Differences in clinical characteristics and molecular subtype were assessed by Chi-Squared or Fisher's exact test. Comparison of response rates was performed using two-proportion *z*-test.

Results

Table 1. Clinical characteristics of patients aged ≤ 50 or > 50

Characteristics	≤ 50 years old (n=434)	> 50 years old (n=591)	p-Value
Menopausal status[a]			
Pre-	378 (88.7%)	51 (8.7%)	<0.001
Post-	48 (11.3%)	536 (91.3%)	
T stage			
T1	66 (15.2%)	82 (13.9%)	0.45
T2	237 (54.6%)	337 (57.0%)	
T3	105 (24.2%)	124 (21.0%)	
T4	22 (5.1%)	43 (7.3%)	
TX	4 (0.9%)	5 (0.8%)	
N stage			
N0	147 (33.9%)	262 (44.3%)	<0.001
N1	219 (50.5%)	259 (43.8%)	
N2	39 (9.0%)	25 (4.2%)	
N3	11 (2.5%)	11 (1.9%)	
NX	18 (4.1%)	34 (5.8%)	
Grade			
G1	22 (5.1%)	48 (8.1%)	0.03
G2	136 (31.3%)	216 (36.6%)	
G3	263 (60.6%)	307 (51.9%)	
GX	13 (3.0%)	20 (3.4%)	
IHC/FISH Classification[b]			
HR+HER2-	198 (45.7%)	296 (50.1%)	0.32
HER2+	125 (28.9%)	165 (27.9%)	
TN	110 (25.4%)	130 (22.0%)	
MammaPrint Risk			
Low Risk	59 (13.6%)	104 (17.6%)	0.10
High Risk	375 (86.4%)	487 (82.4%)	
BluePrint Classification			
Luminal A-type	58 (13.4%)	102 (17.3%)	0.03
Luminal B-type	130 (30.0%)	208 (35.2%)	
HER2-type	80 (18.4%)	88 (14.9%)	
Basal-type	166 (38.2%)	193 (32.7%)	

[a] 12 unknown excluded; [b] 1 unknown excluded

Approximately 88% of patients aged ≤ 50 were pre-menopausal and 91% of patients aged > 50 were post-menopausal (**Table 1**). T stage and distribution of IHC/FISH subtypes and MammaPrint risk were similar between patients ≤ 50 years old and patients > 50 years old. Younger patients were significantly more likely to have lymph node positive breast cancer, grade 3 tumors, and BluePrint HER2-type and Basal-type tumors (**Table 1**).

Figure 1: pCR by MammaPrint Risk

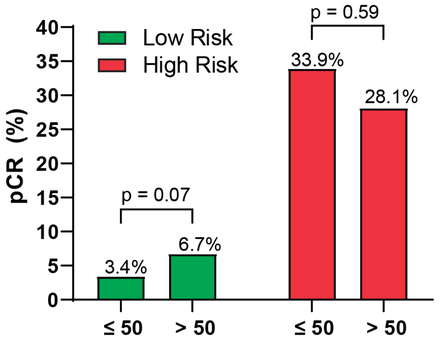
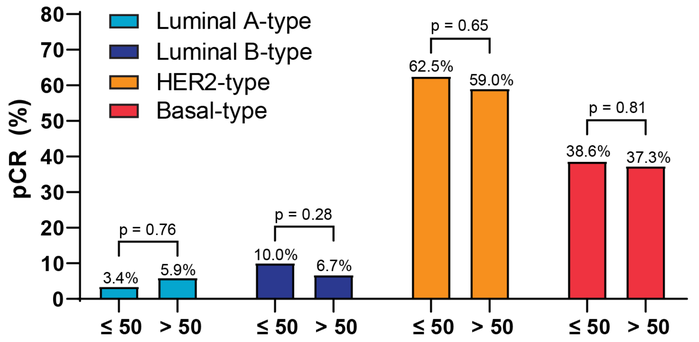


Figure 2: pCR by BluePrint subtype



MammaPrint High Risk tumors were associated with an increased likelihood of pCR compared to Low Risk tumors, which exhibited a low pCR rate (**Figure 1**). Among both Low Risk and High Risk groups, there was no significant difference in the pCR rate in patients aged ≤ 50 compared to patients aged > 50. pCR rates were highest in BluePrint HER2-type and Basal-type tumors and lowest in Luminal A-type and Luminal B-type tumors (**Figure 2**). Among the four molecular subtypes, there was no significant difference in the pCR rate based on an age 50 cutoff.

Conclusion

As expected, pCR rates were lowest in MammaPrint Low Risk, BluePrint Luminal A-type tumors and highest in High Risk, HER2-type and Basal-type tumors. These data demonstrate comparable chemosensitivity between tumors from patients aged ≤ 50 and patients aged > 50. These data suggest that there is no intrinsic difference in chemosensitivity in breast cancers due to age, and that age-related differences observed in treatment benefit in other studies are more likely due to host factors such as menopausal status. Overall, MammaPrint and BluePrint accurately predicted pCR in patients of all subtypes, regardless of age, supporting their use to better tailor pre-operative treatment and timing for surgery.

References

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