Genomic profiling of breast cancer in African-American women

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Introduction

Molecular profiling of breast cancer (BC) defined intrinsic subtypes with distinct gene expression and clinical outcome. In the United States, BC is less frequent in African-American females (AAF); however mortality is higher, particularly among younger women. Disparities in health care, and a higher proportion of unfavorable subtypes of breast cancer in AAF may account for this difference in outcome. Specifically, triple-negative breast cancer seems to be more frequent in AAF than on non-African American, particularly in younger women . Immunohistochemistry (IHC) markers have been used as a surrogate to identify intrinsic subtypes, but molecular profiling may provide more insight into the heterogeneity and biology of breast cancer.

The 70-gene signature (MammaPrint, Agendia Inc) classifies patients according to high or low risk of relapse and predicts for response to neoadjuvant chemotherapy. BluePrint (Agendia Inc), defines three molecular subtypes. The combination of MammaPrint High or Low Risk with BluePrint allows for further risk stratification and is correlated with the intrinsic subtypes Luminal A, Luminal B, HER2 and Basal-type.

Methods

Tumor gene expression in AAF presenting with early stage or locally advanced BC was performed using the Symphony platform on fresh and paraffin-embedded tissue (Agendia Inc), a microarray-based method which classifies tumors according to prognosis (MammaPrint, MP), molecular subtype (BluePrint, BP) and estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (HER2) mRNA levels (TargetPrint, TP). Genomic information was correlated with clinical and pathologic characteristics and Oncotype® DX recurrence score (RS) when available. We analyzed 100 patients with evaluable MP results. Patients' characteristics were summarized by frequencies and percentages. Statistical comparisons between the low and high risk groups were conducted using Fisher's exact test.

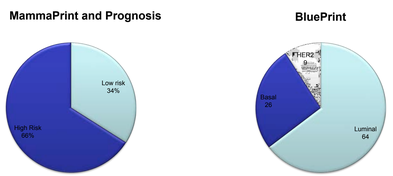
Results

We are presenting the results on 100 patients, with a median age of 60 (range 22-98)

Patient Characteristics

	Low Risk	High Risk	Total	p
	n (%)	n (%)		
All patients	34 (34)	66 (66)	100	
Age				0.02
Age ≤40	0 (0)	9 (100)	9	
Age >40	34 (37)	57(63)	91	
Stage				0.06
I	20(48)	22(52)	42	
II	10 (24)	32 (76)	42	
III	4 (25)	12 (75)	16	
Grade				
1	9(90)	1(10)	10	<0.0001
2	22(50)	22(50)	44	
3	3(6)	43(94)	46	
IHC ER expression (%)				<0.0001
0	0 (0)	26 (100)	26	
1-9	0 (0)	6 (100)	6	
≥ 10	34 (50)	34 (50)	68	
HER2 (IHC/FISH)				0.016
Positive	1 (7)	14(93)	15	
Negative	33 (39)	52(61)	85	

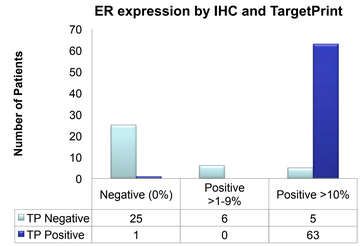
MammaPrint and Molecular Subtype

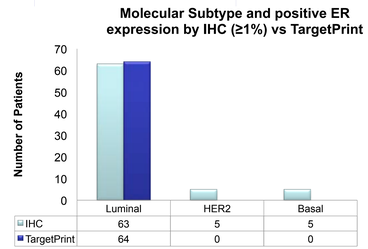


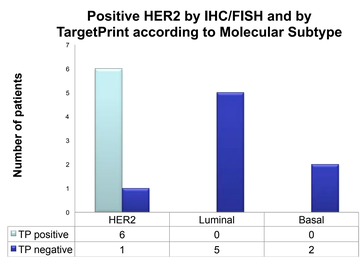
IHC/FISH and MammaPrint/Molecular Subtype

IHC/FISH	Luminal/ Low Risk	Luminal/ High Risk	HER2	Basal	Total
HR+/HER2-	33	25	0	5	63
HER2+	1	4	7	2	14
Triple Negative	0	1	2	19	22
Total	34	30	9	26	99

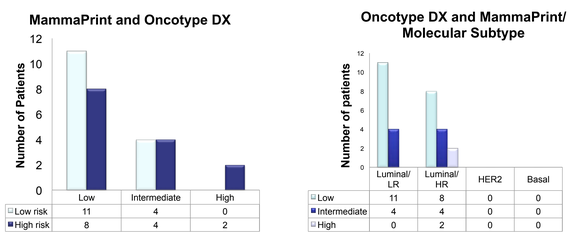
IHC/FISH vs TargetPrint







Oncotype DX vs MammaPrint and Molecular Subtype



Conclusions

-MammaPrint risk is not associated with stage at diagnosis, but High Risk MammaPrint is associated with high grade.

-When classified by MammaPrint and BluePrint, African-American women with stage I to III BC often present with High Risk disease by gene expression.

-Molecular subtyping confirms the biologic heterogeneity in triple negative, HER positive and hormone positive tumors and may allow for improved treatment selection.

-Determination of ER and HER2 by TargetPrint may offer additional biologic information.

-Oncotype RS and MammaPrint offered different prognostic information. Follow up will be needed to determine correlations with outcome.

References

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