Race and response to neoadjuvant chemotherapy according to MammaPrint risk

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BACKGROUND

African-American (AA) women with breast cancer have a less favorable prognosis, likely due to differences in tumor biology. The Neoadjuvant BReast Cancer Symphony Trial (NBRST, NCT01479101) was a prospective trial that has shown an association of MammaPrint/BluePrint (MP/BP) with a rate of pathologic Complete Response (pCR) of 2% pCR in Luminal A with 95% Distant Metastasis Free Interval at 3 yrs. Here, we determine the MP/BP risk distribution, the response to therapy, and outcome in AA and Caucasian (Cau) patients.

METHODS

NBRST enrolled 1,072 breast cancer pts in the US (June 2011 and December 2014). The current unplanned analysis compared clinicopathological characteristics, molecular risk assignment and outcome with neoadjuvant chemotherapy (NACT) in 150 AA and 748 Cau pts. Molecular subtyping groups were assessed by MP/BP as follows: Luminal A (MammaPrint Low Risk), Luminal B (MammaPrint High Risk), HER2 and Basal types.

Clinical Characteristics

	AA (150)	Cau (748)	Total (898)
Med age (range)	52.5 (22-77)	54 (18-89)	*0.021*
T1-2	94 (63%)	532 (71%)	
T3-4	56 (37%)	214 (29%)	0.127
TX	*0 (0%)*	*2 (<1%)*	
N0	39 (26%)	334 (45%)	
N1	90 (60%)	331 (44%)	
N2-3	17 (11%)	55 (7%)	*<0.001*
NX	*4 (3%)*	*28 (4%)*	
Grade 1	4 (3%)	61 (8%)	
Grade 2	40 (27%)	269 (36%)	
Grade 3	99 (66%)	397 (53%)	*0.002*
Grade unknown	*7 (5%)*	*21 (3%)*	
ER+	82 (55%)	496 (66%)	*0.007*
PgR+	71 (47%)	406 (54%)	0.120
HER2+	40 (27%)	219 (30%)	0.476
Triple neg	48 (32%)	153 (21%)	*0.003*
NCT +/- H	145 (97%)	681 (91%)	
NET +/- H	4 (3%)	61 (8%)	
NCT+ET +/- H	1 (<1%)	6 (1%)	0.059

MammaPrint all AA and Cau pts

MammaPrint distribution by AA vs Cau in all pts

AA (150) — Low Risk 7%, High Risk 93%
Cau (748) — Low Risk 19%, High Risk 81%
p-value *0.001*
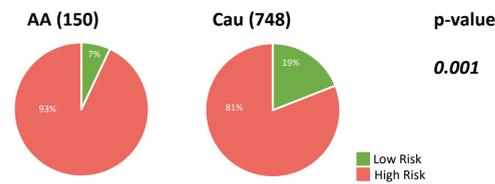
MammaPrint Low Risk in all patients

p=0.514

5 Year DM	n	events	% events	survival %		95% CI
African American	10	0	0.0%	1.000		
Caucasian	116	5	4.3%	0.926	0.859	0.993
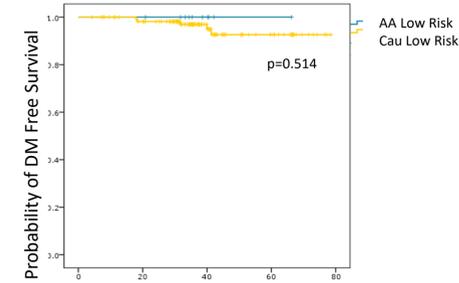
MammaPrint High Risk in all patients

p=0.137

5 Year DM	n	events	% events	survival %		95% CI
African American	107	18	16.8%	0.764	0.646	0.882
Caucasian	508	59	11.6%	0.836	0.789	0.883
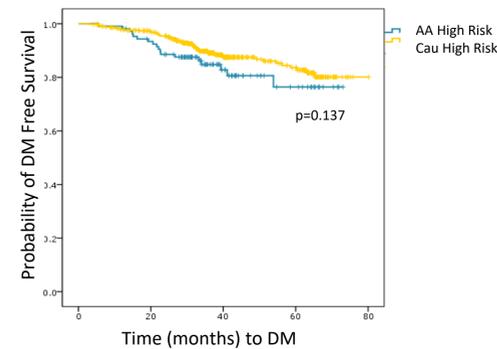
MammaPrint HR+/HER2- AA and Cau pts

MammaPrint distribution by AA vs Cau in HR+/HER2-

AA (n=50) — Low Risk 20%, High Risk 80%
Cau (n=305) — Low Risk 36%, High Risk 64%
p-value *0.035*
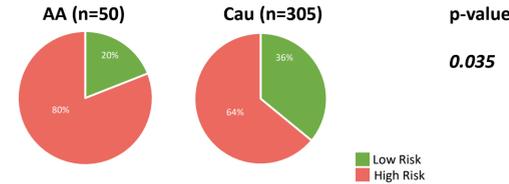
MammaPrint Low Risk in HR+/HER2- patients

p=0.534

5 Year DM	n	events	% events	survival %		95% CI
African American	8	0	0.0%	1.000		
Caucasian	102	5	4.9%	0.918	0.844	0.992
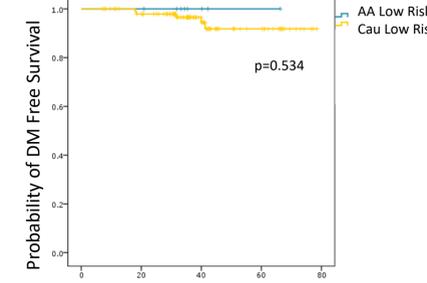
MammaPrint High Risk in HR+/HER2- patients

p=0.253

5 Year DM	n	events	% events	survival %		95% CI
African American	35	7	20.0%	0.780	0.631	0.929
Caucasian	191	28	14.7%	0.789	0.705	0.873
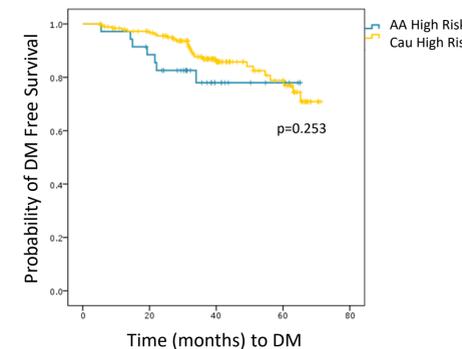
BluePrint

BluePrint distributions by AA vs Cau

AA (n=150) — Basal 46%, Luminal B-type 34%, Luminal A-type, HER2-type
Cau (n=748) — 34%, 32%, 19%, 15%

	AA	Cau	p-value
Basal	69 (46%)	252 (34%)	*0.0055*
Non-Basal	81 (54%)	496 (66%)	
Lum A	11 (7%)	139 (19%)	*0.0011*
Non-Lum A	139 (93%)	609 (81%)	
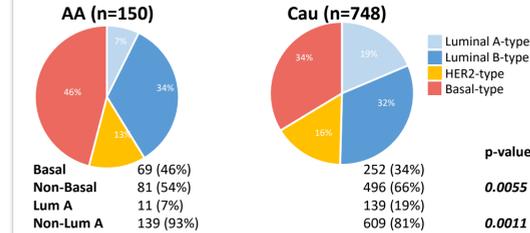
pCR rates in BluePrint Molecular Subgroups

| n = 10 | 100 | 49 | 218 | 19 | 116 | 67 | 252 | 145 | 686 |
| Lum A | | Lum B | | HER2 | | Basal | | Total | |

Lum A: 10% / 10%, p=0.497
Lum B: 10% / 6%, p=0.569
HER2: 89% / 62%, p=0.020
Basal: 40% / 37%, p=0.610
Total: 34% / 27%, p=0.085
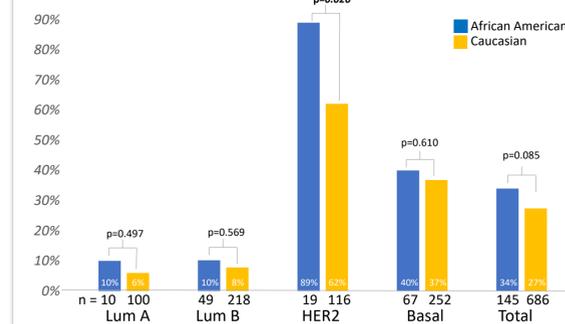
Uni-and multivariate analyses pCR rate

Univariate analyses	p-value	HR (95% CI)	Multivariate	p-value	HR (95% CI)
Race (AA vs Cau)	0.088	1.4 (0.95-2.0)		*0.012*	*1.9 (1.1-3.1)*
Age	0.241			0.466	
ER	<0.001			0.797	
PR	<0.001			0.022	
HER2	<0.001			0.028	
N-stage	0.005			0.019	
T-stage	<0.001			0.001	
Grade	<0.001			<0.001	
Histol (ILC, IDC)	0.001			0.935	
BP Molecular subtype	<0.001			<0.001	

MammaPrint in all pts

MP Low Risk
MP High Risk
p=0.007

For HR+/Her2- pts also sign (p=0.005).

| 5 Year DM	n	events	% events	survival %		95% CI
Low Risk Signature	126	5	4.0%	0.931	0.868	0.994
High Risk Signature	615	77	12.5%	0.823	0.780	0.866
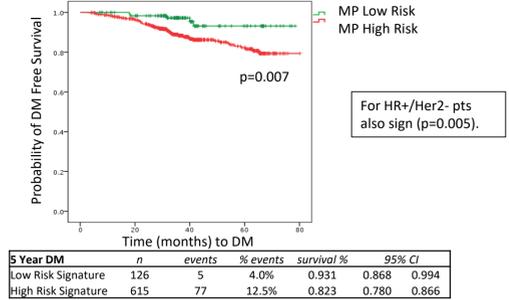
Other tests

TAILORx distributions and outcome
Albain et al, SABCS 2018
Distribution of risk is not different between AA and Cau in intermediate risk, although outcome of intermediate risk pts differs significantly. Risk distribution in 693 AA pts: 15% low, 68% intermediate and 17% high risk; in 8189 Cau pts: 17% low, 69% intermediate, 14% high risk. AA pts classified as intermediate risk had a 9 yr iDFS of 78.5% versus 83.9% for Cau pts (difference of 5.4%).

PAM50 distributions and outcome
Sun et al, SABCS 2017
Racial disparities reflected by RNA based subtyping test PAM50; distribution significantly different between AA (n=454) and Cau (n=439): 31% Lum A vs 50% and 35% Basal-like vs 18%. Outcome corresponds with assigned risk:

Cau — med/low risk
AA — med/low risk
Cau — high risk
AA — high risk
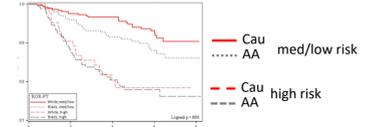
CONCLUSIONS

- AA pts were younger, and had a higher likelihood of having higher grade, ER-, LN+ tumors.
- AA pts were more often classified as Basal-type and less often classified as Luminal A-type compared with Cau pts by BluePrint.
- MP identified pts with Low Risk, irrespective of race (although numbers are small and longer FU is necessary).
- This study confirms that racial differences in gene expression contribute to the survival disparity observed between AA and Cau women diagnosed with breast cancer.
- MammaPrint is helpful to characterize the tumor's biology and select patients who will not benefit from chemotherapy independently of their race.