Clinical Implications for Patients with Early-stage Breast Cancer with Discordant Oncotype and MammaPrint Results

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BACKGROUND

Genomic tests provide critical information regarding risk of distant recurrence and inform physicians about optimal treatment plans by identifying patients who may safely forgo chemotherapy (CT) or adapt the duration of their endocrine therapy (ET) duration.

The PROMIS trial demonstrated the 70-gene risk of recurrence assay MammaPrint (MP) changed physician treatment plans among the Oncotype DX Recurrence Score (ODx RS) Intermediate group, using the pre-TAILORx range of RS 18-31.[1]

Similarly, NBRST demonstrated that use of the 80-gene signature BluePrint (BP) adds molecular subtyping which further identifies patients as ER+ Basal-Type or Luminal B-Type resulting in improved treatment planning and long-term survival.

In this analysis, we examined discordance among genomic tests and therapeutic implications for patients who received both a MP/BP and ODx RS.

METHODS

Patient Cohort: This analysis includes 722 patients from the ongoing FLEX study (NCT03053193), who received both MP/BP, and RS genomic assays.

Genomic Categorization: MP indicates CT benefit for MP High Risk and no CT benefit for MP Low Risk.[2,3] BluePrint (BP) classifies tumors into the following molecular subtypes: Luminal-, Basal-, and HER2-Type. ODx RS indicates a CT benefit for women aged ≤50 with RS16-100 and >50 with RS26-100.[4]

Clinical Impact Assessment: Clinical Impact was assessed by examining the standardized reports of ODx RS and MP results. See **Table 2** for clinical impact of genomic report discordance.

RESULTS

Figure 1. Scatterplot of MP Index and ODx Recurrence Score

Chemotherapy Benefit per MammaPrint | **No Chemotherapy Benefit per MammaPrint**

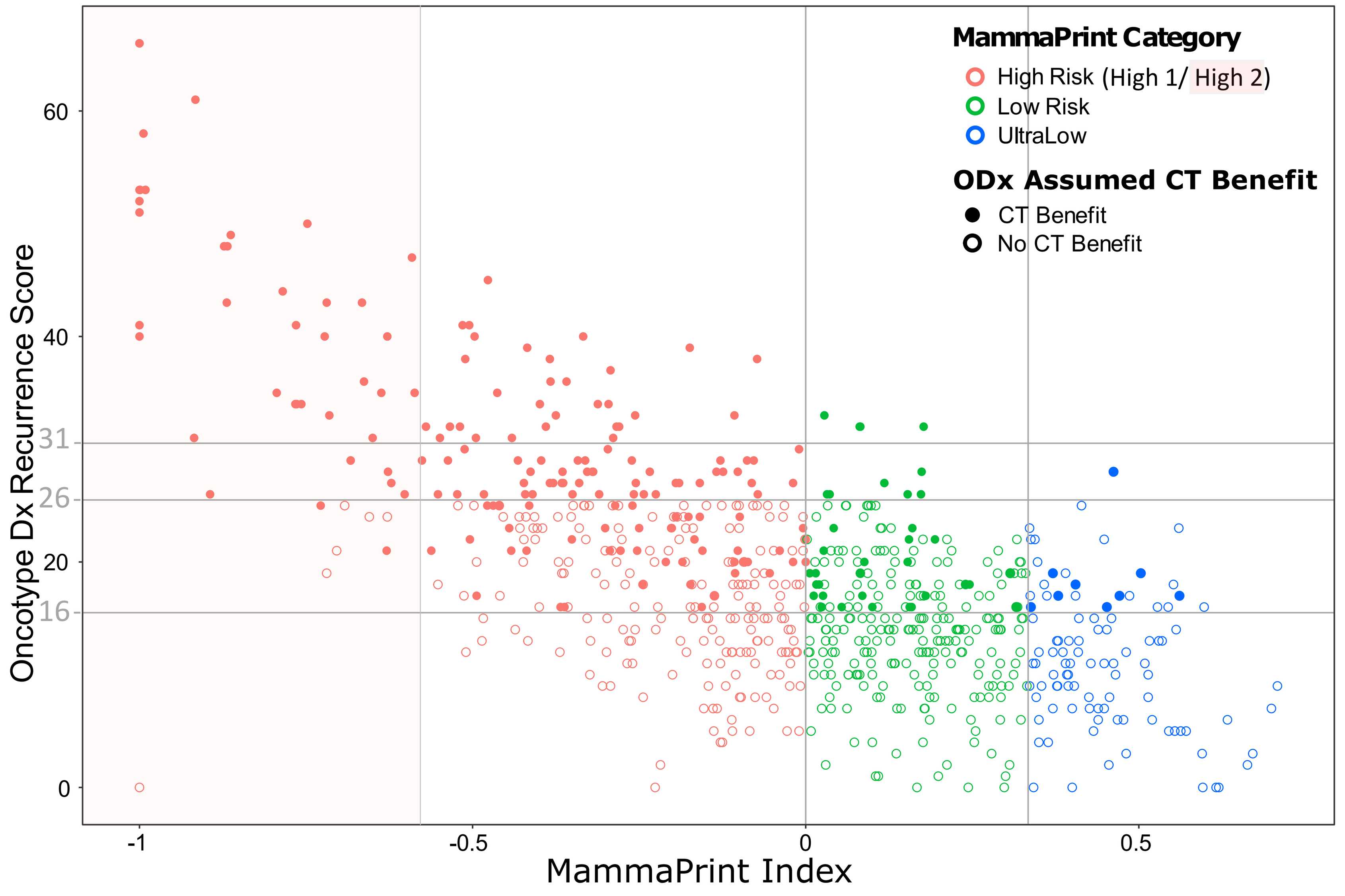
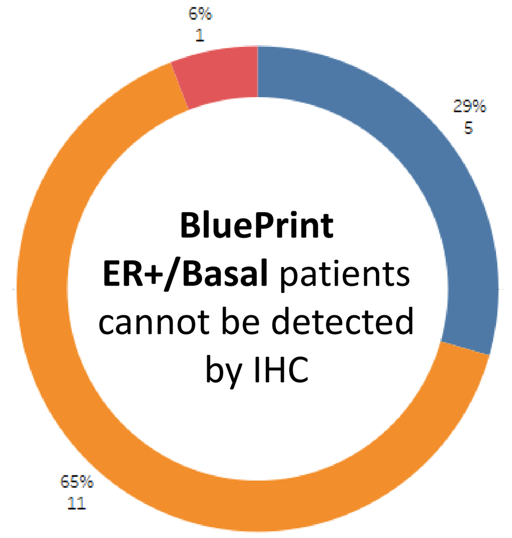


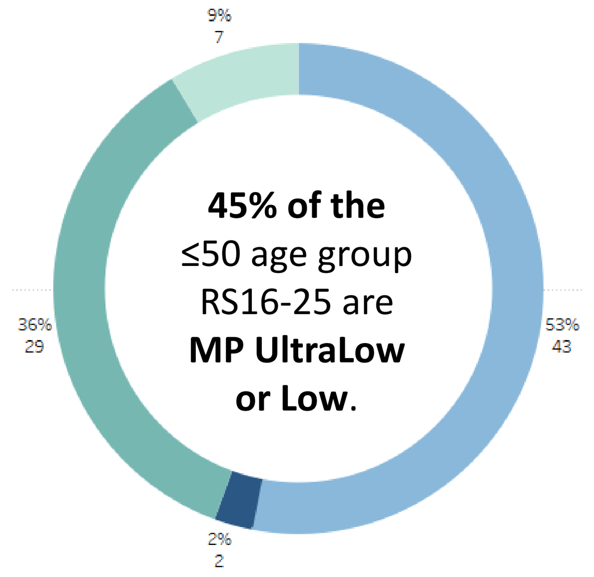
Table 1. Patient-Tumor Characteristics

	ODx no CT	ODx CT	P value
Number of Patients	516	206	
MammaPrint			
Low	320	46	<0.0001
High	196	161	
BluePrint			
Luminal A-Type	320	45	<0.0001
Luminal B-Type	195	144	
Basal-Type	1	16	
HER2-Type	0	1	
Age			
≤ 50	76	112	<0.0001
> 50	440	94	
Menopausal Status			
Pre/peri	76	88	<0.0001
Post	436	117	

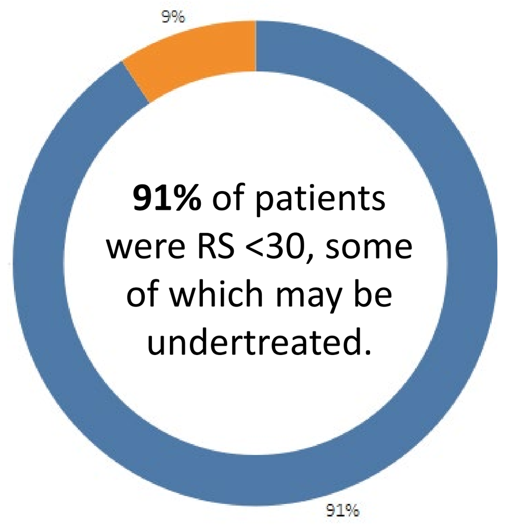
Figure 2. Clinical Impact of Discordance



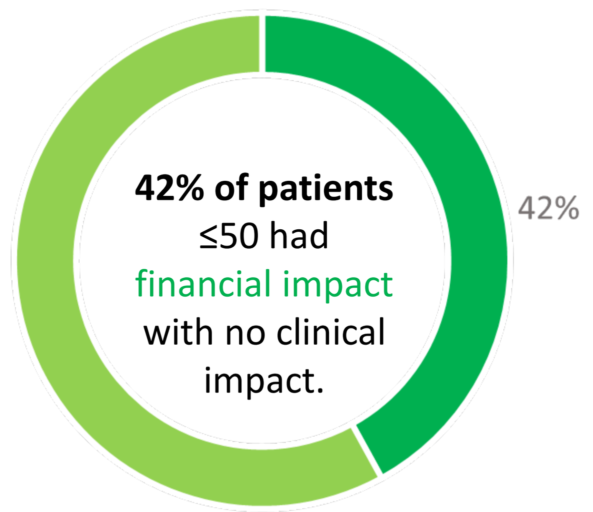
A. BluePrint identifies a subgroup of ER+ patients who have been previously shown to have unique treatment response and outcomes.[8] Colors denote treatment: CT, CT+ET, ET



B. MammaPrint can identify pre-menopausal patients who are candidates for safe CT de-escalation. Colors denote MP categories: Ultralow, Low, High 1, High 2



C. ODx prediction of chemo benefit (RS >30)[10] is restricted to 9% of analyzed population. Colors denote RS: RS0-30, RS31-100



D. Treatment guidance by RS was not followed in up to 42% of women ≤50 highlighting the financial toxicity of discordance.[12]

Table 2. Clinical Impact of Genomic Report Discordance

Clinical Impact	Percentage of Cohort	Age	RS	MP	BluePrint Luminal	BluePrint Basal	BluePrint HER2
Undertreatment	27%	≤50	RS0-15	MP High	24	0	0
		>50	RS0-25		171	1	0
Overtreatment	6%	≤50	RS16-100	MP Low	37	0	0
		>50	RS26-100		8	0	0
ET De-escalation	10%	≤50	RS0-15	MP UltraLow	6	0	0
		>50	RS0-25		69	0	0
BP Basal only: requires aggressive CT	2%	≤50	RS16-100	MP High	0	6	0
		>50	RS26-100		0	10	0

CONCLUSIONS

- Previous analyses show that BluePrint-identified ER+/Basal tumors have statistically improved DMFS when pCR is achieved.[8] These patients are only identifiable using genomics and require personalized treatment planning. (Figure 2A)
- Post-TAILORx there remains an unresolved intermediate in the pre-menopausal patient population in which there was a benefit of chemotherapy found in the ≤50 age group RS16-25.[11]
  - Based on this, the recommendation 1.3 in the ASCO 2022 Guidelines states that for patients "who are 50 years of age or younger with Oncotype DX recurrence score 16 to 25, the clinician may offer chemoendocrine therapy".[9]
  - In this cohort 11% (n=81) patients were premenopausal. 45% of these patients are MP UltraLow or Low.(Figure 2B)
  - >85% of these patients did not receive CT if they were MP Low, highlighting physician's desire to identify more pre-menopausal women who are candidates for safe CT de-escalation.[5,6,7]
  - Clinicians did not follow the guidance of the RS in up to 42% of women ≤50 years of age, highlighting the financial burden on the health ecosystem for a test not impacting treatment decisions vs cost-effectiveness of MP/BP to safely de-escalate in this subgroup.[5,6,7,12] (Figure 2D)
- The B-20 Trial reported, ODx is predictive of CT benefit for patients with a recurrence score >30.[10] This group only accounts for 9% of this analysis, suggestive of undertreatment for certain patient subsets. (Figure 2C)
- Observationally, 83% of MP High 2 patients were ≥ RS26 and 76% of MP High 1 were < RS26 (48% of MP High 1 were RS16-25).[10]
- Genomic discordance may result in undertreatment or overtreatment with chemotherapy. (Table 2)

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