Treatment recommendations in ER+ patients ≤ 50 years: comparison of the 21-gene assay and 70-gene signature in the PROMIS study

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Background

The PROMIS trial (NCT01617954) previously demonstrated that the MammaPrint 70-gene signature (70-GS) gives clinically actionable results for patients with an intermediate (18-30) recurrence score (RS) by the 21-gene assay (21-GA, Oncotype DX)[1], which can lead to ambiguous treatment guidance. Further adding to the uncertainty, results from Sparano et al., 2019[2] suggested an association between the 21-GA, patient age and clinical risk for patients ≤50 yrs with an Intermediate RS.

This subanalysis of the PROMIS dataset explores the potential impact that the 70-GS can have on clarifying adjuvant chemotherapy decisions for patients ≤ 50 yrs, a group left incompletely addressed by TAILORx.

Methods

MammaPrint (MP) risk of recurrence was determined for 840 ODx intermediate patients (RS 18-30) by standard diagnostic testing (Agendia, Irvine, CA).

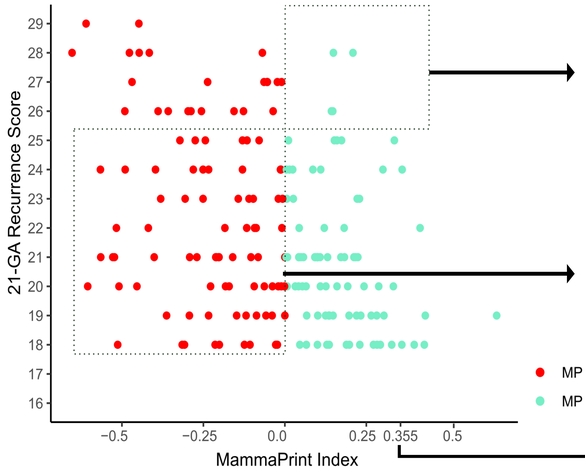
- Clinical risk (clin-low/clin-high) was assessed using the MINDACT, modified Adjuvant!Online Algorithm.[3]
- The MP High and Low Risk classification were subdivided by RS groups 18-20, 21-25, and 26-30 and by clinical risk stratification for patients ≤50 yrs (n=181).

MammaPrint Provides Results to Inform Treatment Decisions for Patients With an Intermediate RS

RS Group	Clinical Risk	MP Low Risk/n	% pts ≤ 50 that can potentially avoid CT based on MP
RS 18-20	Clin-low	27/45	60%
	Clin-high / (unknown)	15/26 (1)	56%
	Total	**42/72**	**58%**
RS 21-25	Clin-low	30/55	55%
	Clin-high / (unknown)	8/26 (1)	30%
	Total	**38/82**	**46%**
RS 26-30	Clin-low	3/16	19%
	Clin-high	1/11	9%
	Total	**4/27**	**15%**

56% of clin-high patients ≤50 with a RS 18-20 were found to be **Low Risk by MP.**

30% clin-high patients ≤50 with a RS 21-25 were found to be **Low Risk by MP.**

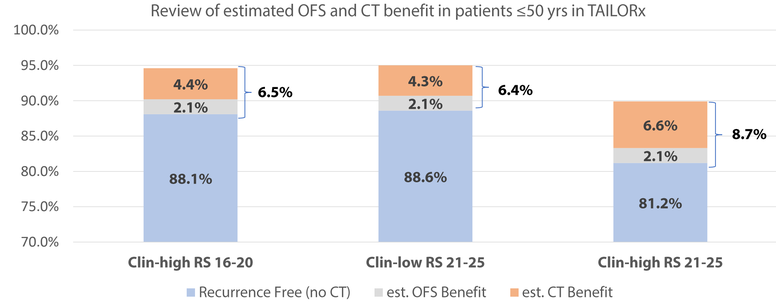


15% of patients ≤50 with a RS 26-30 were found to be MP Low Risk and may be potential candidates for de-escalation of adjuvant CT.

48% of patients ≤50 with RS 18-25 were MP High Risk.

13% of clin-high patients ≤50 with a RS 18-20 had a MP Ultralow Risk result. (MPI >0.355)

Can Incremental Survival Benefit Observed in Recent Trials be Attributed to Ovarian Function Suppression?



- **SOFT/TEXT trials report that a 1 - 5% improvement in 8-yr distant recurrence with ovarian function suppression (OFS) + Exemestane vs Tam alone was observed for women who did not receive prior CT, a benefit that was influenced by clinical risk.[4]** [A 2.1% average survival benefit was observed in pre-menopausal patients treated with an aromatase inhibitor versus tamoxifen + OFS.]
- Regarding the reported 6-9% survival benefit for patients ≤50 treated with CT in TAILORx, *Sparano et al, 2019*, stated that "it is possible that similar incremental benefits observed in younger women who received chemotherapy and had a recurrence score of 16 to 25 could be achieved with ovarian suppression and an aromatase inhibitor".[2] However, applying an estimated 2.1% average benefit from OFS across these RS groups results in a remaining difference of 4-6%, unaccounted for by OFS.
- ASCO Guidelines state that the subset of patients ≤50 yrs with a RS 16 to 25 may be offered chemo-endocrine therapy.[5]

Conclusions

- For most patients ≤50 with a RS 16-25, chemo-endocrine therapy is recommended as the preferred treatment. MammaPrint can identify more Low Risk patients ≤50 for whom chemotherapy may not be required.
- MammaPrint can identify up to 46% more patients ≤50 with a RS 21-25 as Low Risk.
- PROMIS & MINDACT demonstrate that MammaPrint provides clear results to inform treatment decisions in patients ≤50 yrs.

References

1. Tsai, JAMA Oncology 2018
2. Sparano, NEJM 2019
3. Cardoso, NEJM 2016
4. Pagani, JCO 2019
5. Andre, JCO 2019

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