Comparison of StemPrintER, a Novel Biology-based Genomic Predictor of Distant Recurrence in Breast Cancer, with Oncotype DX in the TransATAC cohort

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BACKGROUND:

- The StemPrintER Risk Score (SPRS) is an alternative genomic tool for early (0-5 years) and late (>5 years) recurrence risk prediction in ER+/HER2- breast cancer (BC) patients (Pece S. *et al.*, EBioMedicine 2019) (see also Abstract 1057).
- SPRS has the unique ability to profile the intrinsic "degree of stemness" of individual BCs, in contrast with most of the currently available genomic tools that interrogate the same tumor characteristics as standard clinical biomarkers, mostly proliferation and hormone receptor status.

OBJECTIVES:

- Independent validation of the prognostic value of SPRS in ER+/HER2- postmenopausal BC patients.
- Head-to-head comparison of the prognostic power of SPRS with Oncotype Dx risk score (RS) in ER+/HER2- postmenopausal BC patients

METHODS:

Study cohort: 818 postmenopausal ER+/HER2- BC patients from the Trans-ATAC cohort with negative (N0=629) or 1-3 positive (N1-3=189) lymph nodes, treated with anastrozole or tamoxifen for 5 years.

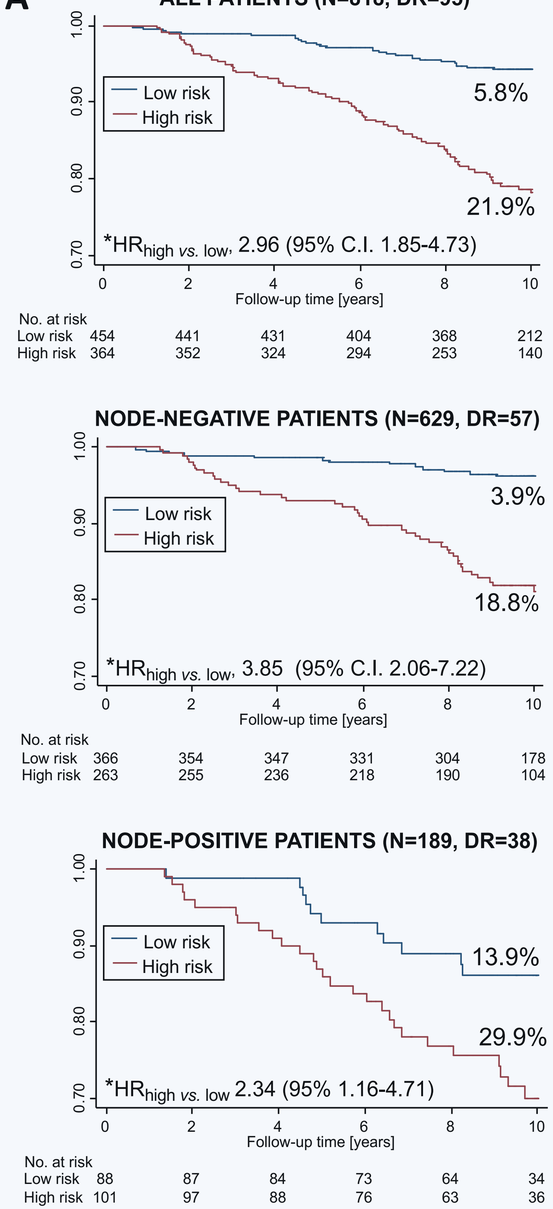
Primary endpoint: distant recurrence (DR, n=95 events in years 0-10).

Statistics: The likelihood χ2 (LRχ2) and Kaplan-Meier survival analyses were used to assess prognostic information provided by SPRS, Oncotype Dx risk score (RS) and the Clinical Treatment Score (CTS). Comparative analyses were made for DR risk over the 10-year follow-up, as well as in the early (0-5 years) or late (5-10 years) interval, according to nodal status.

RESULTS:

- SPRS significantly stratifies high *vs*. low risk groups when adjusted for clinical parameters as expressed by the CTS, identifying patients with a very low 10-year DR cumulative incidence among all patients, N0 and N1-3 patients (**FIG. A**)
- SPRS adds prognostic information on top of CTS in the overall period, and in early (0-5 years) and late (5-10 years) intervals, among all patients, as well as in N0 but not N1-3 patients (**FIG. B**)
- SPRS outperforms RS in 10-year DR risk prediction in all patients, as well as in N0 and N1-3 patients, and is superior to RS in adding prognostic information to CTS (**FIG. C**)
- SPRS significantly stratifies patients at high *vs*. low recurrence risk among low and intermediate, but not high, pre-specified RS groups (**FIG. D**).

A



*HR, multivariable hazard ratios after adjustment for CTS

B

	DISTANT RECURRENCE	HR (95% CI) (for change in 1SD)	P-value	*LR-χ^2/ ΔLR-χ^2	HR (95% CI) (for change in 1SD)	P-value	*LR-χ^2/ ΔLR-χ^2	HR (95% CI) (for change in 1SD)	P-value	*LR-χ^2/ ΔLR-χ^2
(0-10 years)		ALL PATIENTS (N=818, DR=95)			NODE-NEGATIVE (N=629, DR=57)			NODE-POSITIVE (N=189, DR=38)		
	SPRS	1.71 (1.42-2.07)	<0.0001	29.69	1.83 (1.44-2.33)	<0.0001	22.78	1.42 (1.04-1.93)	0.026	4.89
	CTS	2.13 (1.78-2.55)	<0.0001	63.20	2.31 (1.76-3.02)	<0.0001	33.89	1.90 (1.35-2.66)	<0.0001	14.16
	CTS+SPRS			12.74			10.11			2.59
(0-5 years)		ALL PATIENTS (N=818, DR=42)			NODE-NEGATIVE (N=629, DR=23)			NODE-POSITIVE (N=189, DR=19)		
	SPRS	1.73 (1.30-2.29)	<0.0001	13.59	1.92 (1.31-2.82)	<0.0001	10.65	1.39 (0.90-2.13)	0.138	2.17
	CTS	2.23 (1.71-2.92)	<0.0001	33.00	2.53 (1.68-3.81)	<0.0001	17.82	1.83 (1.14-2.94)	0.012	6.40
	CTS+SPRS			5.04			3.97			1.09
(5-10 years)		ALL PATIENTS (N=733, DR=53)			NODE-NEGATIVE (N=573, DR=34)			NODE-POSITIVE (N=160, DR=19)		
	SPRS	1.70 (1.32-2.19)	<0.0001	16.11	1.78 (1.30-2.43)	<0.0001	12.23	1.45 (0.94-2.23)	0.095	2.74
	CTS	2.04 (1.60-2.61)	<0.0001	30.43	2.16 (1.52-3.08)	<0.0001	16.49	1.97 (1.22-3.18)	0.006	7.80
	CTS+SPRS			7.69			6.04			1.54

SPRS is highly prognostic for distant recurrence and adds more prognostic information than Oncotype DX on top of standard clinicopathological parameters in ER+/HER2- postmenopausal BC patients.

C

	ALL PATIENTS (N=776, DR=94)			NODE-NEGATIVE (N=594, DR=56)			NODE-POSITIVE (N=182, DR=38)		
DISTANT RECURRENCE	HR (95% CI) (for change in 1SD)	P-value	*LR-χ^2/ ΔLR-χ^2	HR (95% CI) (for change in 1SD)	P-value	LR-χ^2/ ΔLR-χ^2	HR (95% CI) (for change in 1SD)	P-value	LR-χ^2/ ΔLR-χ^2
SPRS	1.79 (1.47-2.17)	<0.0001	33.36	1.97 (1.53-2.53)	<0.0001	26.33	1.42 (1.05-1.92)	0.021	5.23
OncotypeDX	1.52 (1.30-1.78)	<0.0001	22.14	1.58 (1.31-1.91)	<0.0001	18.01	1.40 (1.03-1.91)	0.034	4.11
CTS+SPRS			14.92			11.71			2.91
CTS+OncotypeDx			9.72			6.59			2.62

D

ALL PATIENTS		NODE-NEGATIVE		NODE-POSITIVE	
Oncotype DX RS (original cut-offs)	SPRS HR (95% CI)	Oncotype DX RS (original cut-offs)	SPRS HR (95% CI)	Oncotype DX RS (original cut-offs)	SPRS HR (95% CI)
Low (N=476)	1.84 (1.22-2.77)	Low (N=375)	1.87 (1.05-3.33)	Low (N=101)	1.51 (0.86-2.67)
Interm. (N=213)	1.56 (1.17-2.07)	Interm. (N=154)	1.89 (1.31-2.71)	Interm. (N=59)	1.14 (0.73-1.78)
High (N=87)	1.05 (0.65-1.70)	High (N=65)	0.87 (0.49-1.57)	High (N=22)	1.28 (0.55-2.94)

*LR-χ^2/ΔLR-χ^2 cut-off for statistical significance $\geq$ 3.84