Real-world clinical experience and outcomes in patients with early-stage breast cancer (EBC) treated according to the 21-gene recurrence score® (RS) result

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Evaluating the merits of a genomic assay includes measuring analytic and clinical validity, and establishing clinical utility—a property that is not consistently defined. One definition of clinical utility that has gained traction is "the balance of benefits and harms associated with the use of the test in practice" [*Genet Med*. 2015; doi:10.1038/gim.2015.173].
The 21-gene RS assay is the only assay clinically validated for both prognosis and prediction of chemotherapy (CT) benefit in patients with node-negative (N0) or node-positive (N+), ER+, HER2− EBC. The original clinical validation studies were prospectively designed using archived tissue from legacy trials that had long-term outcomes (NSABP B-14 and B-20, TransATAC, and SWOG 8814). With 10+ years of the RS assay in clinical use, we now have real-world, prospective outcomes for patients with N0 or N+ disease that meet the aforementioned definition of clinical utility.
Here we summarize the growing body of clinical evidence including the original validation studies, prospective outcomes-based trials, and analyses from two large, real-world registries in which patients were treated based on RS results: the US SEER and Clalit Health Services registries.
The US SEER registry is a population-based cancer surveillance program that covers 30% of the US population and includes 40,134 N0 and 4,691 N+ patients with RS results. The Clalit Health Services registry, from the largest HMO in Israel, has 2,028 N0 and micrometastatic (Nmi) patients who were uniformly tested and had complete treatment information. In the SEER and Clalit cohorts, the distribution of RS results were similar for N0/Nmi and N+ patients: 54% and 57% low (<18), 38% and 36% intermediate (18-30), and 8% and 7% high (≥31), respectively. 5-year outcomes by RS group show that patients with low RS results of any nodal status (N0/Nmi/N1-3) had similar outcomes (Table). Outcomes by RS group and age or grade were also similar for patients with low RS results of any nodal status.

5-y BC-specific Mortality (95% CI)

	SEER Registries				Clalit Registry	
	N0[a] (N=38,568)	Known CT use (% of N)	N+[b] (N=4,691)	Known CT use (% of N)	N0/Nmi[c] (N=2,028)	Known CT use (% of N)
RS <18	0.4% (0.3%-0.6%)	7%	1.0% (0.5%-2.0%)	23%	0.0% (0.0%-0.0%)	2%
RS 18-30	1.4% (1.1%-1.7%)	34%	2.3% (1.3%-4.1%)	47%	1.1% (0.5%-2.1%)	25%
RS ≥31	4.4% (3.4%-5.6%)	69%	14.3% (8.4%-23.8%)	75%	6.8% (4.1%-11.2%)	88%

a. Includes patients 40-84 years of age only (HR+, HER2−, nonmetastatic EBC). b. Includes Nmi and up to three positive nodes [N+(mi,1-3)]. c. Includes 1,815 (89%) N0 and 213 (11%) Nmi.

In summary, after 10+ years of clinical use, the 21-gene RS assay has now amassed a body of clinical evidence from >50,000 patients that confirms the original clinical validation results and supports its clinical utility. The assay identifies patients with low RS results who can be safely and effectively treated with hormonal therapy alone and spared the toxicity of CT exposure. In aggregate, these data support the clinical utility of the 21-gene RS assay and its value to physicians and patients by providing information based on individual tumor biology that they can use to tailor treatment.

Session: Poster Session 6: Prognostic and Predictive Factors: Prognostic and Predictive Factors - Other (7:30 AM-9:00 AM)
Date/Time: Saturday, December 10, 2016 - 7:30 am
Room: Hall 1

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