Low Recurrence Score by the Oncotype DX® Breast Cancer Assay Rarely Results in Recommendation for or Administration of Chemotherapy: A Pooled Analysis

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Abstract

Objective: To assess the impact of low recurrence scores (RSs) on the recommendation for and use of chemotherapy across multiple studies.
Methods: The Oncotype DX Breast Cancer Assay generates an RS that is prognostic and predictive of chemotherapy benefit in estrogen receptor–positive, lymph node–negative (ER+, LN-) early-stage breast cancer patients. Low RSs (< 18) have a low risk of distant recurrence at 10 years and little if any chemotherapy benefit. Several studies have addressed whether physicians will actually recommend no chemotherapy in patients with low RSs and, if so, whether chemotherapy will actually be withheld. Studies from Oratz et al, Liang et al, Erb et al, Ben-Baruch et al, and Lo et al[3-7] were pooled to examine the frequency of recommendation for chemotherapy and actual chemotherapy use among low RS patients.
Results: Of 725 patients total in these studies, 323 (44.7%) had low RSs. Of 190 patients with low RSs where the recommendation for or against chemotherapy was tabulated, 172 patients (91%) were advised not to have chemotherapy. Of 285 patients with low RSs where the actual use of chemotherapy was tabulated, 270 patients (95%) received no chemotherapy. (Some studies looked at both recommendation and use.)
Conclusion: A low RS provided actionable information for physicians that led to a recommendation for no chemotherapy or resulted in no chemotherapy in virtually all low RS patients. This has led to a reduction in chemotherapy use and could lead to reduced expenditures for pharmacy budgets as well.

Introduction and Background

- Oncologists face a complex decision-making process when considering the value and use of adjuvant treatment in early-stage breast cancer.
- The oncologist must evaluate the patient's risk for metastatic recurrence and the benefits and toxicity associated with treatment and communicate this in a fashion that is easily understood by the patient to aid in the shared treatment decision process.
- Oncologists have traditionally used clinicopathologic factors that include tumor size, hormone receptor status, tumor grade, and patient age to help estimate the risk of breast cancer recurrence.
- A more quantitative approach is needed for identifying individual risk for recurrence and benefits from therapy.
- The Oncotype DX Breast Cancer Assay generates a recurrence score (RS), based on the expression levels of 16 cancer-related genes and 5 reference genes, which is prognostic[1] and predictive[2] of chemotherapy benefit in estrogen receptor–positive, lymph node–negative (ER+, LN-) early-stage breast cancer patients. Patients with low RSs (< 18) have a low risk of distant recurrence at 10 years and little if any chemotherapy benefit.

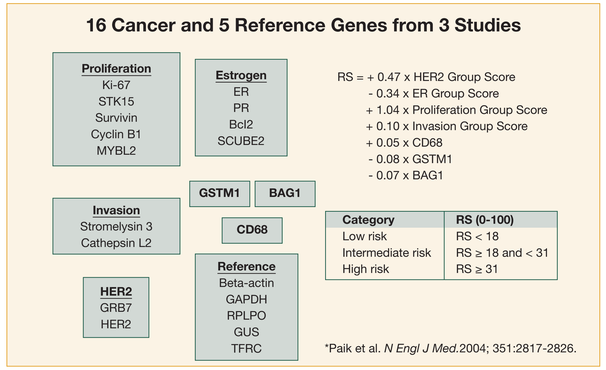

Figure 1. Oncotype DX 21-Gene RS Assay.

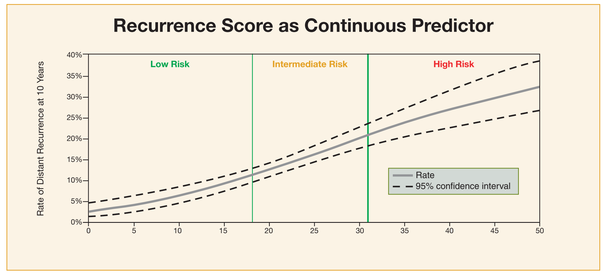

Figure 2. The RS Is a Continuous Predictor of the Risk of Distant Recurrence.

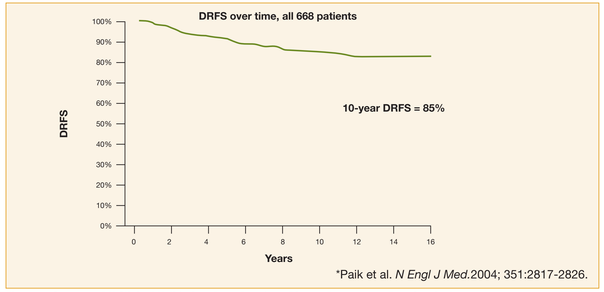

Figure 3. Oncotype DX Clinical Validation: B-14 Results—Distant Recurrence-Free Survival.

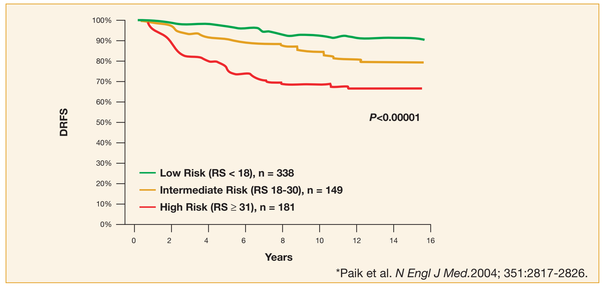

Figure 4. The RS Result Stratifies Patients by Their 10-Year DRFS.

Abbreviation: DRFS indicates distant recurrence-free survival.

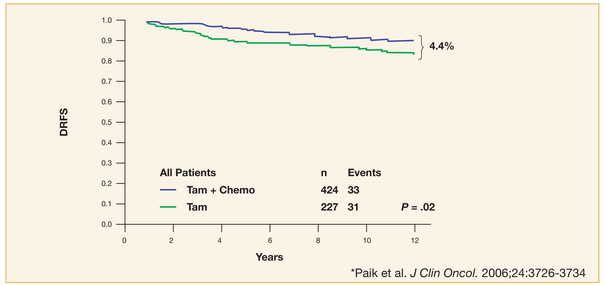

Figure 5. B-20 Results: Tam vs. Tam + Chemo, All 651 Patients.

Abbreviations: TAM indicates tamoxifen; DRFS indicates distant recurrence-free survival.

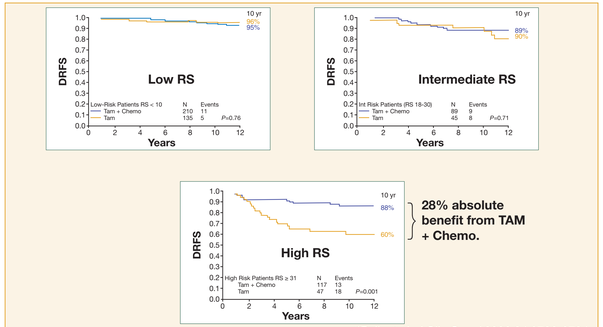

Figure 6. B-20 Results: Tam vs. Tam + Chemo.

Abbreviations: TAM indicates tamoxifen; DRFS indicates distant recurrence-free survival.

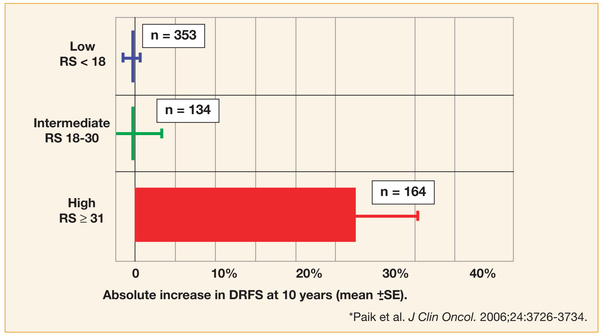

Figure 7. Patients with High RS Derive Significant Benefit from Chemotherapy (Prediction).

Abbreviation: DRFS indicates distant recurrence-free survival.

Study Objective

To assess the impact of RS results < 18 ("low RS") on the recommendations for and the use of chemotherapy (clinical utility) across multiple studies in both the academic and community settings.[3-7]

Methods

Several studies have addressed whether physicians will actually recommend no chemotherapy in patients with low RSs and, if so, whether chemotherapy will actually be withheld. Studies from Oratz et al, Liang et al, Erb et al, Ben-Baruch et al, and Lo et al[3-7] were pooled to examine the frequency of recommendation for chemotherapy and actual chemotherapy use among low RS patients.

Table 1. Study Groups

Study	No. of Patients	Low RS (%)	Intermediate RS (%)	High RS (%)
Oratz[3]	68	32 (47)	22 (32)	14 (21)
Liang[4]	260	120 (46)	93 (36)	47 (18)
Erb[5]	124	64 (52)	45 (36)	15 (12)
Ben-Baruch[6]	181	69 (38)	79 (44)	33 (18)
Lo[7]	89	38 (43)	42 (47)	9 (10)
Total	725	323 (44.7)	281 (38.9)	121 (16.4)

Table 2. Recommendations and Actual Treatment in Patients with Low RS

Study	Recommendation Against CTX (%)	Actual Treatment Without CTX (%)
Oratz[3]	24/32 (75)	28/32 (88)
Liang[4]	114/120 (95)	114/120 (95)
Erb[5]	NA	63/64 (98)
Ben-Baruch[6]	NA	65/69 (95)
Lo[7]	34/38 (90)	NA
TOTAL	172/190 (91)	270/285 (95)

Abbreviations: CTX indicates chemotherapy; NA indicates not available.

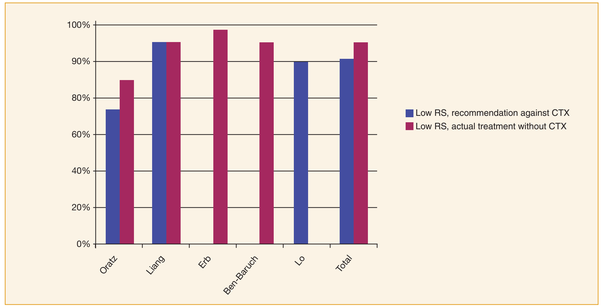

Figure 8. Recommendations and Actual Treatment in Patients with Low RS

Abbreviation: CTX indicates chemotherapy.

Conclusions

- A low RS provided actionable information for physicians that led to a recommendation for no chemotherapy given (95%) in virtually all low RS patients. Thus the assay is being used as intended in estrogen receptor–positive, lymph node–negative early-stage breast cancer.
- The Oncotype DX assay's ability to classify large groups of women with early-stage breast cancer as having low risk of distant recurrence for breast cancer and minimal if any benefit from chemotherapy could lead to a reduction in chemotherapy use and could lead to reduced expenditures for pharmacy budgets as well.
- One of the studies included in this pooled analysis (Lo et al) included a patient survey that indicated that the Oncotype DX assay also reduces decisional conflict and anxiety for early-stage breast cancer patients.
- The 2008 National Comprehensive Cancer Network guidelines have been updated to include the Oncotype DX assay as part of the treatment algorithm for early-stage breast cancer.[8]

References

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