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Gene Profiling: Does It Inform Decision Making in LN-positive and Neoadjuvant Rx Scenarios?

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Disclosures

Advisory Committee	Syndax Pharmaceuticals Inc, Taiho Oncology Inc
Contracted Research	Genentech BioOncology

Case presentation: Dr Peswani

60-year-old woman with poorly controlled DM and neuropathy

- Stage IIB, T2N1, node-positive, ER/PR-positive, HER2-negative breast cancer
- 3.5-cm mass that would require mastectomy; patient would prefer to preserve breast but avoid chemotherapy
- 21-gene Recurrence Score[®]: 19 (intermediate)



Case presentation: Dr Ibrahim

42-year-old premenopausal physician

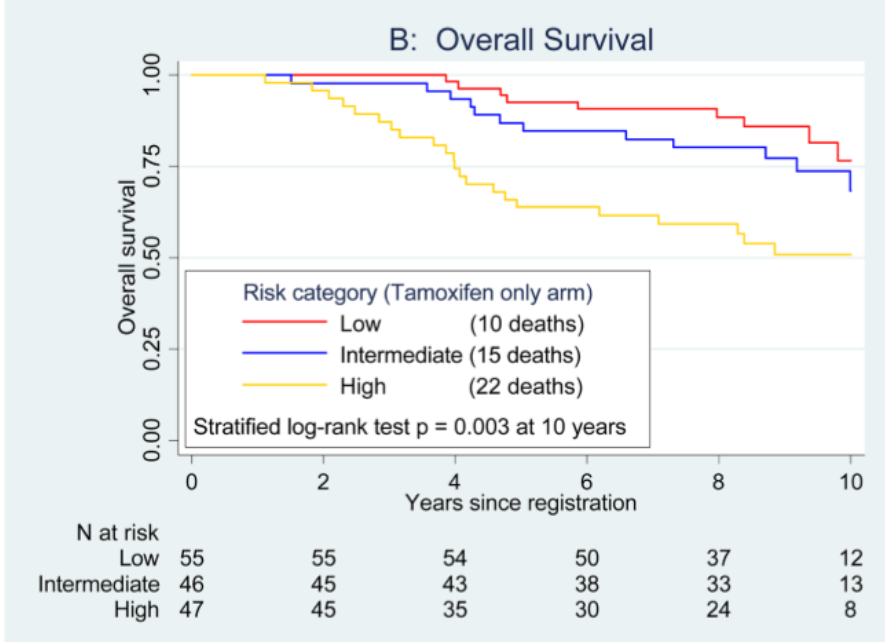
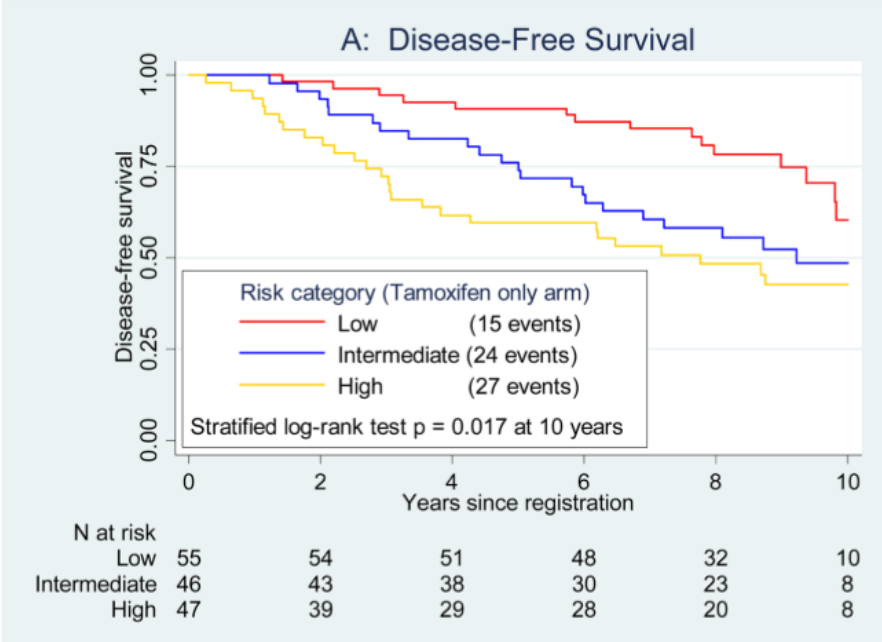
- 2012: 2.3-cm, ER-positive, HER2-negative IDC with 1/10 positive nodes; patient preferred not to have chemotherapy
- 21-gene Recurrence Score: 35
- Dose-dense AC → weekly paclitaxel followed by tamoxifen
- 2012-2017: Very bothersome tamoxifen-related side effects, considering stopping at 5 years



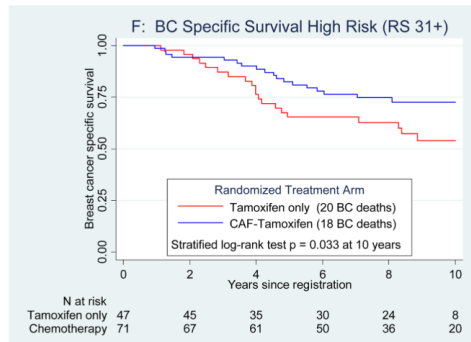
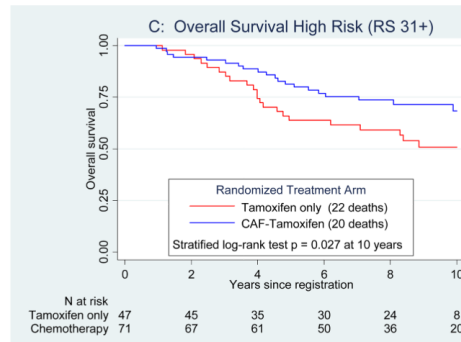
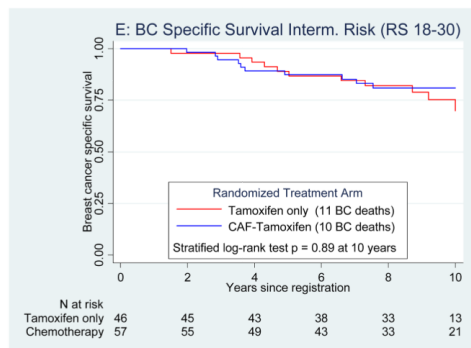
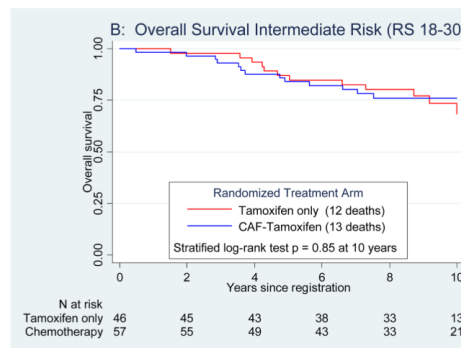
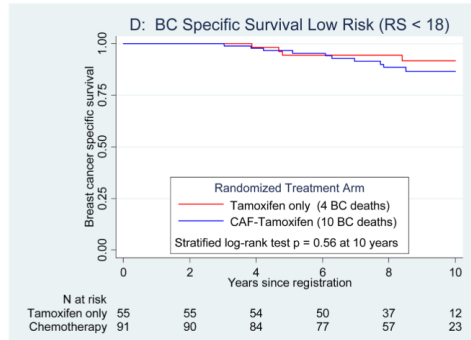
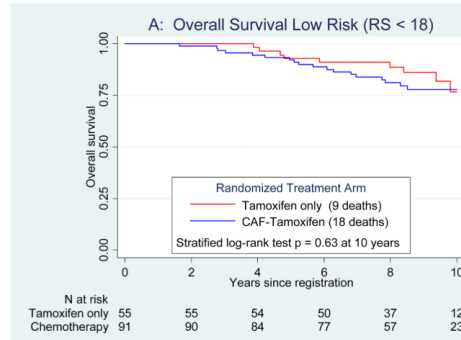
The Basic Question

In choosing adjuvant and neoadjuvant therapy for high-risk patients with ER-positive disease, does biology trump histopathology?

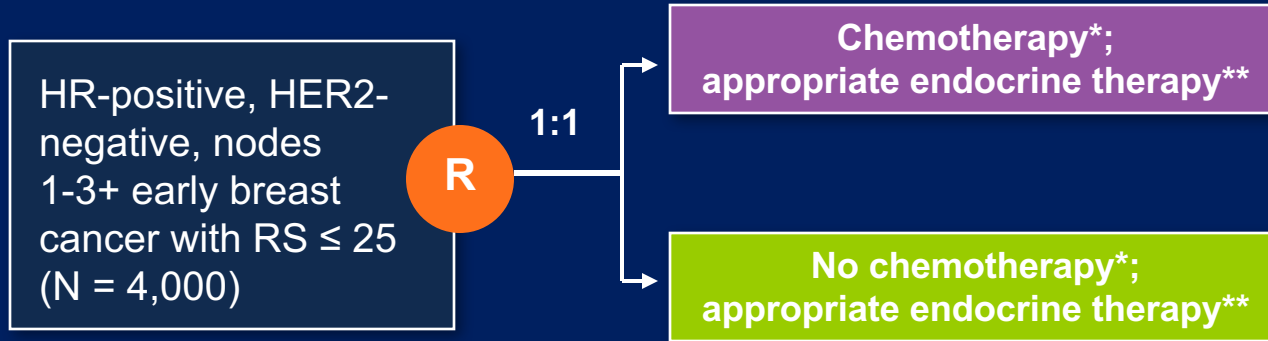
SWOG-8814: Recurrence Score in LN+ ER+ Disease



SWOG-8814: OS and BCSS by Recurrence Score +/- Chemotherapy



SWOG-S1007 (RxPONDER) Study Design



* Various 2nd- or 3rd-generation regimens (physician/patient choice)

** Various options, dependent on menopausal status (physician/patient choice)

Primary Objective

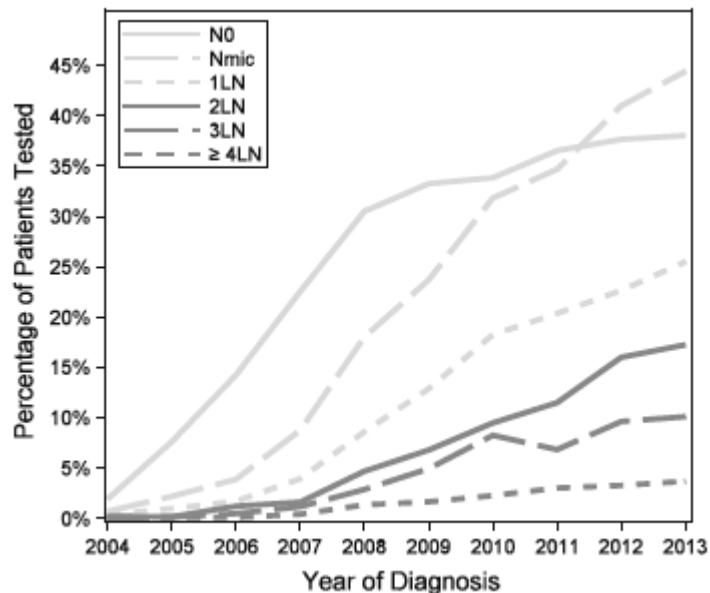
Determine the effect of chemo in patients with node-positive BC who do not have high RS by *Oncotype DX*

1. DFS for patients treated with chemo compared to no chemo and dependence on the magnitude of RS
2. Determine the optimal cut-point for recommending chemo or not

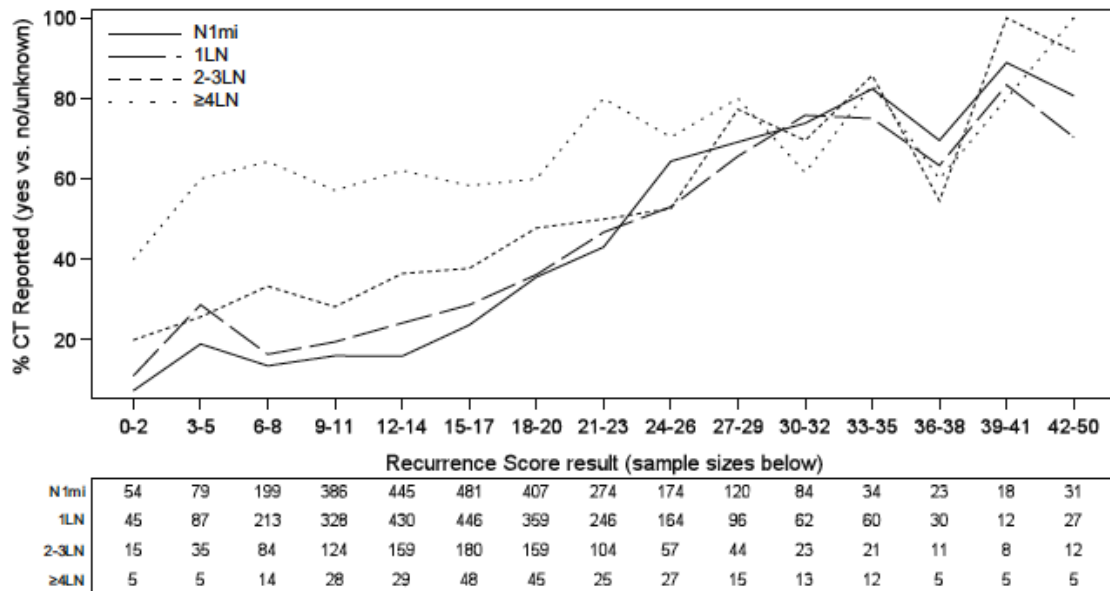
2016 ASCO
Guidelines:
Don't Use RS
in Patients with
LN-Positive
Disease

SEER Database: Recurrence Score Use at a Population Level

Recurrence Score Testing Over Time



ChemoRx Use by RS and Nodal Status



SEER Database: 5-Year BCSS by Nodal Status and Recurrence Score

# of positive lymph nodes	RS < 18 (N = 1644)		RS 18–30 (N = 2380)		RS ≥ 31 (N = 469)	
	N (%CT) ^a	5-year BCSS (95% CI)	N	5-year BCSS (95% CI)	N	5-year BCSS (95% CI)
Micrometastases	1644 (18%)	98.9 (97.4–99.6)	998 (47%)	99.1 (97.9–99.6)	178 (79%)	84 (74.1–90.4)
1	1549 (23%)	99.4 (98.4–99.8)	893 (47%)	95.9 (92.6–97.7)	178 (73%)	93.3 (85.2–97.0)
2	458 (31%)	97.1 (91.3–99.0)	268 (52%)	97.8 (91.4–99.4)	45 (82%)	87.0 (54.4–96.9)
3	139 (41%)	95.1 (87.0–98.2)	104 (54%)	87.2 (65.2–95.7)	29 (83%)	89.8 (63.5–97.5)
≥4	129 (59%)	92.8 (73.5–98.2)	117 (69%)	83.9 (69.5–91.9)	39 (77%)	65.4 (40.9–81.8)

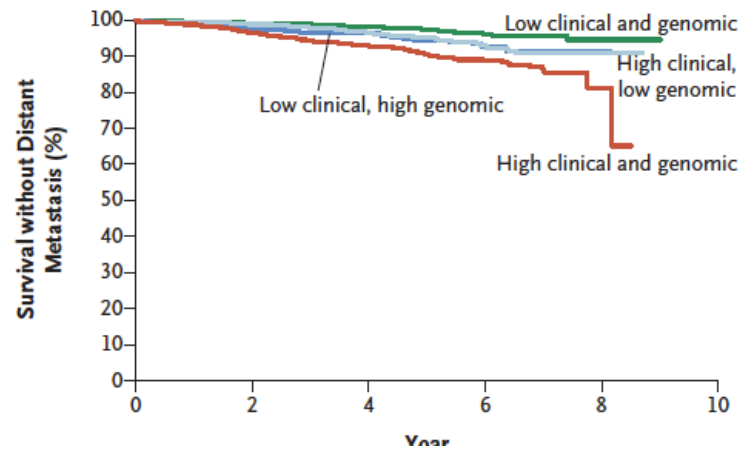
MINDACT: Low Genomic Risk Trumps High Clinical Risk

ASCO Biomarker Guidelines:

Recommendation 1.2.1 (update of 2016 recommendation 1.7):

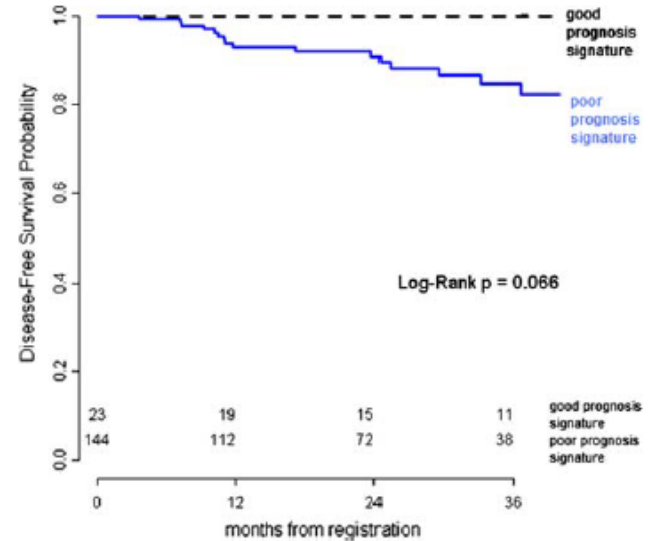
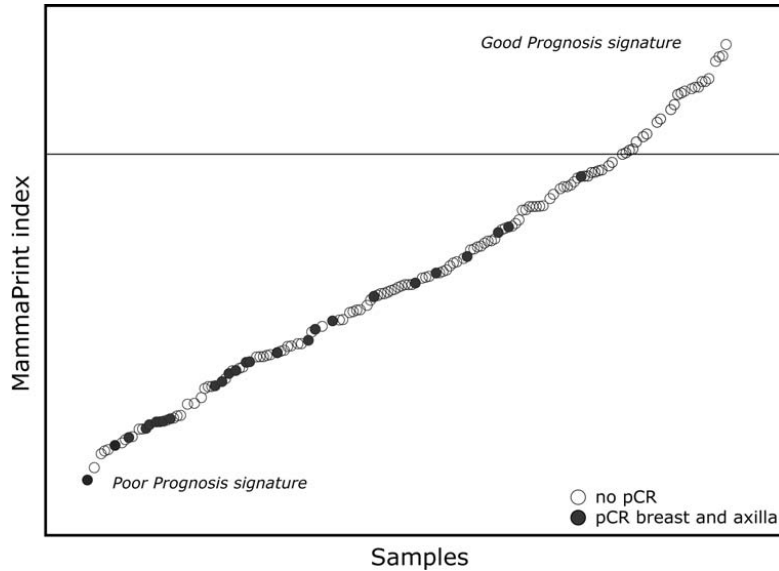
If a patient has **ER/PgR-positive, HER2-negative, node-positive**, breast cancer, the MammaPrint assay may be used in patients with one to three positive nodes and at **high clinical risk** per MINDACT categorization to inform decisions on withholding adjuvant systemic chemotherapy because of its ability to identify a good prognosis population with potentially limited chemotherapy benefit. However, such patients should be informed that a benefit of chemotherapy cannot be excluded, particularly in patients with more than one involved lymph node.

(Type: Evidence based; Evidence quality: High; Strength of recommendation: Moderate).

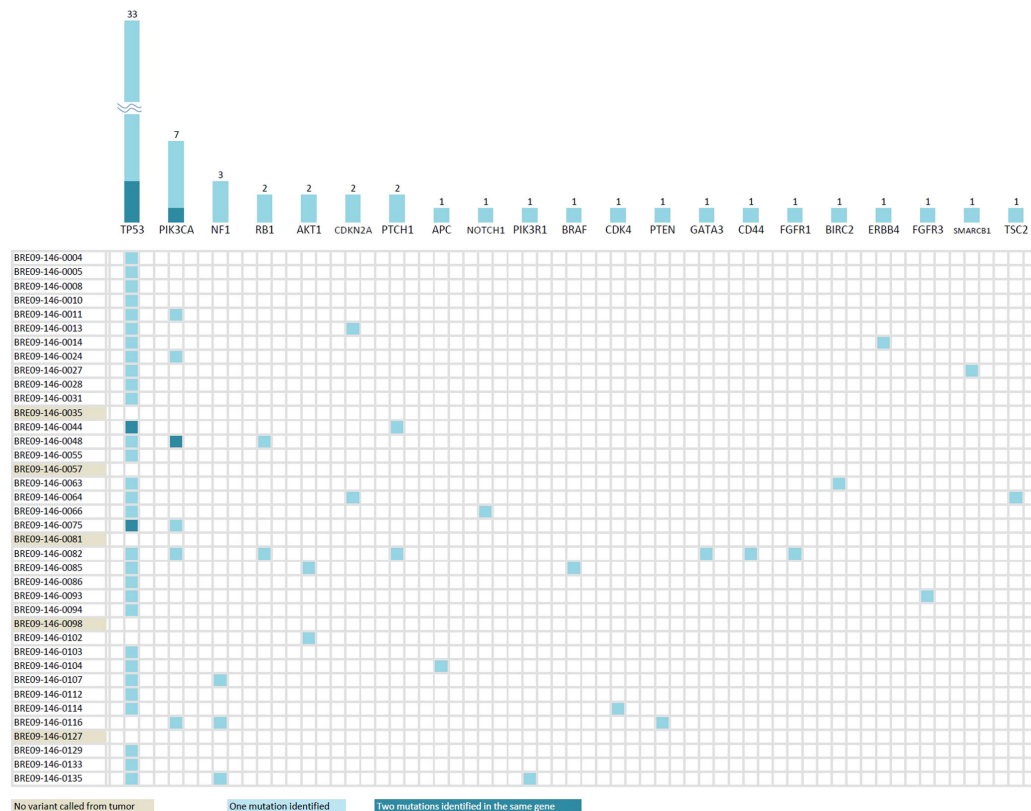
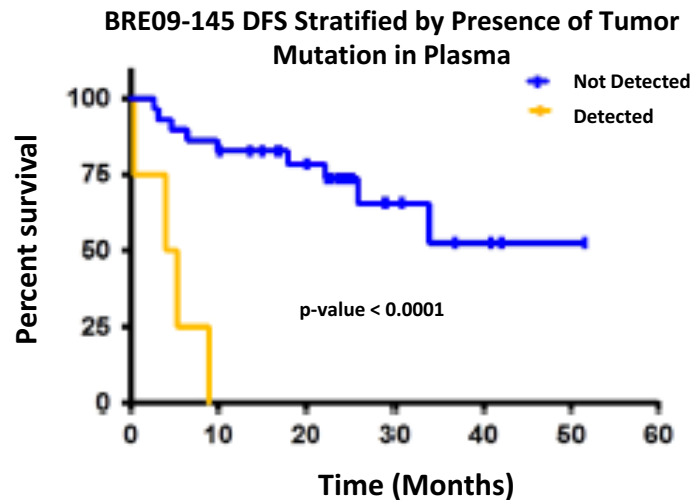


Cardoso, F et al. NEJM 2016

Gene Profiling and Neoadjuvant Rx: Divergent Results for pCR and DFS



The Next Frontier in Gene Profiling: ctDNA



Conclusions

- Gene profiling in patients with LN+, ER+ disease is similar to patients with LN-, ER+ disease
- Early data suggests that gene profiling is prognostic AND predictive
- Phase III trial ongoing, but docs have voted with their feet
- Gene profiling correlates with neoadjuvant pCR, BUT...
- Gene profiling of micrometastases will explode in the next few years

THANK YOU