Prognostic performance analysis of artificial intelligence test and 21-gene assay in premenopausal node-positive HR+ HER2- breast cancer patients

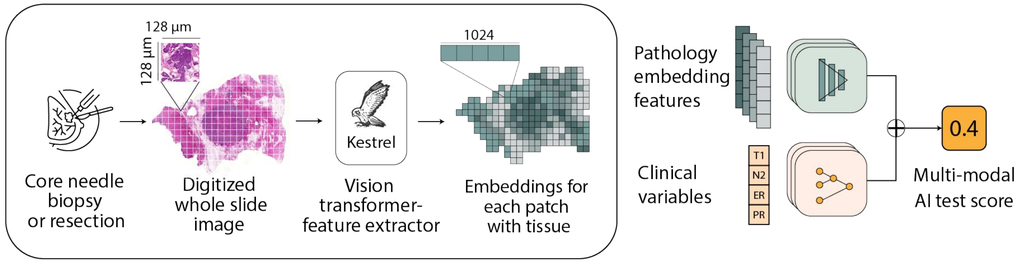
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Background

- The RxPONDER trial[1] was a landmark study demonstrating that Oncotype DX (a 21 gene assay) can help avoid unnecessary adjuvant chemotherapy in postmenopausal women with 1-3 positive nodes (N+) and an ODX recurrence score (RS) ≤25.
- However, node-positive premenopausal women with an RS ≤25 showed variable benefit to adjuvant chemotherapy.
- Therefore, current NCCN guidelines recommend Oncotype DX only as a consideration in this patient subgroup, leaving risk-adapted decision making unsolved and up to the discretion of their physician.

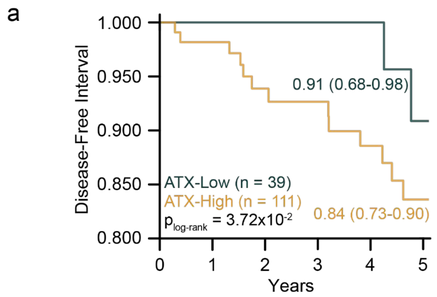
Methods

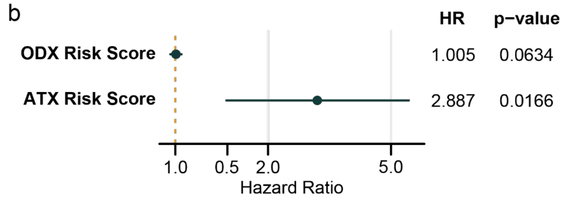


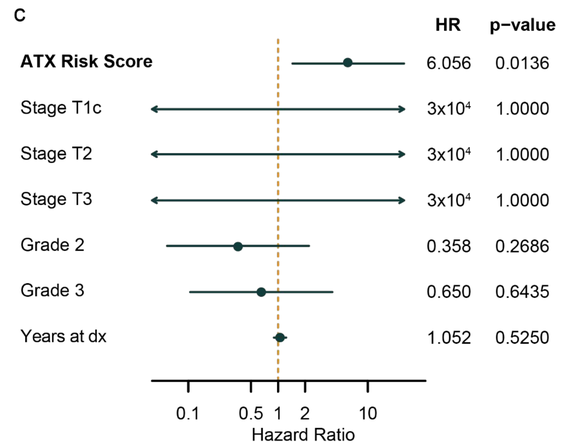
- ATX[2] is an artificial intelligence platform that integrates morphological features extracted from H&E-stained slides with clinical features to generate risk scores.
- We validate the prognostic accuracy of ATX recurrence score in premenopausal node-positive women.
- ATX risk scores were generated from 150 premenopausal HR+ HER2- patients.
  - Basel (n=32), Karmanos (n=11), Providence Health (n=48), and TCGA (n=59).
- 43 patients (Basel and Karmanos) had ODX recurrence scores available.
- Prognostic performance was assessed for disease-free interval using hazard ratio (HR per 0.1 increase in ATX score).
- Pooled scores were calculated using random-effects meta-analysis.

Dataset	n Total	n HR+ HER- Premenopausal	n HR+ HER- Premenopausal Recurrences
Providence	1687	48	6
TCGA	930	59	5
Basel	267	32	6
Karmanos	162	11	3

Results







a. ATX-high patients have significantly worse disease-free interval than ATX-low patients.
b. In a univariate model, ATX risk score is a significant predictor of DFI while Oncotype DX did not reach statistical significance.
c. In a multivariate model, after controlling for tumor stage, grade, and age at diagnosis, ATX risk score is the only variable that remains statistically significant ($p < 0.05$).

Conclusions

- ATX demonstrates promising independent prognostic performance in premenopausal node-positive breast cancer across diverse datasets.
- Larger studies are needed to confirm its efficacy and utility.

References

1. Kalinsky et al., 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. NEJM, 2021
2. Witowski et al., Multi-modal AI for comprehensive breast cancer prognostication. arxiv, 2024

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