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Artificial Intelligence-Based Histopathology Model Predicts Recurrence Risk in Older Patients with Early HR+/HER2− Breast Cancer: Results from the Basel University Hospital Cohort

Elena Diana Chiru[1], Lina Sojak[1], Jan Witowski[2], Ken Gary Zeng[2], Christian Kurzeder[3], Simone Muenst[4], Marcus Vetter[1]

[1] Cancer Center Baselland, Cantonal Hospital Basel-Land, Liestal, Switzerland [2] Ataraxis AI, New York, NY [3] Breast Care Center, Basel University Hospital, Basel, Switzerland [4] Institute for Pathology and Medical Genetics, Basel University Hospital, Basel, Switzerland

BACKGROUND & OBJECTIVES

Older pts with HR+/HER2 eBC face frequent uncertainty in treatment decisions, as tools like Oncotype DX (ODX) are less validated in this age group. Ataraxis Breast RISK (ATX) is a novel prognostic test that uses artificial intelligence to integrate morphological features from digitized H&E slides and clinical data to predict recurrence. The aim of this analysis was to assess ATX performance of a multimodal AI prognostic test in an elderly cohort and compare it with ODX.

METHODS

The primary analysis focused on identified 40 patients ≥70 years treated at Basel University Hospital (USB) in years 2010–2021. Additionally, we identified a group of 41 patients <50 years old for comparison. ATX scores were generated using archived samples of patients with available slides and follow-up data. The primary endpoint was disease-free interval (DFI). Harrell's concordance index (C-index) and hazard ratios (HR) were used to assess prognostic accuracy. In addition to results from the Basel cohort, we reference ATX results from a multi-institutional validation study reported previously.

RESULTS SUMMARY

- Among patients ≥70 years, ATX was prognostic of overall recurrence (HR 2.12), and had higher prognostic accuracy than ODX (C-index 0.79 vs. 0.55).
- ATX effectively distinguished high- vs low-risk subgroups
- ATX reclassified 77% of ODX-intermediate cases into low- and high-risk groups (HR: 1.61, p=0.393; C-index: 0.69)
- In 5 external cohorts of ≥70 y.o. patients, ATX had consistent performance (pooled C-index 0.74; HR 1.82).

RESULTS

ATX stratified Basel patients ≥70 years old into low-risk (n=9) and high-risk (n=31) groups. All patients in the low-risk group were recurrence-free. Meanwhile, the high-risk group had 9.6% recurrence rate at 5 years and 25.4% recurrence rate at 9 years of follow-up (Fig. 1).

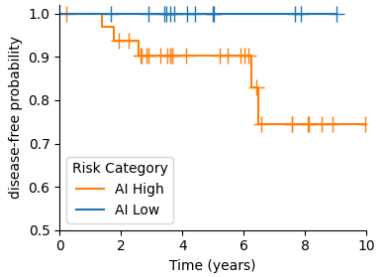


Fig 1. Kaplan-Meier curves for patients (≥70 years old, Basel patients only). Patients were classified into low- and high-risk groups per ATX score. The cut-off was predefined at 10% risk of 5-year overall recurrence.

The results on the Basel cohort were consistent with ATX results on other multi-institutional data, where HR+/HER2- patients ≥70 years old with high ATX scores had 28.3% 9-year recurrence rate vs. 6.1% 9-year recurrence rate in the low-risk group (Fig. 2). ATX was prognostic for overall recurrence in patients ≥70 years old with a pooled HR of 1.82 (1.51-2.20; Fig. 3) and a pooled C-index of 0.74 (0.70-0.81).

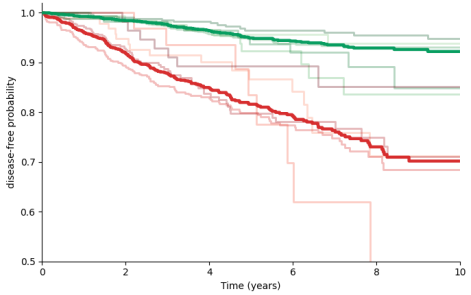


Fig 2 Kaplan-Meier curves for patients (≥70 years old) in all 5 external datasets. Green and red lines represent survival in low-ATX and high-ATX patient groups, respectively. Thicker lines represent pooled patients, and thinner, half-transparent lines represent recurrence-free probability in each dataset.

Dataset	N pts total	N pts ≥70 y.o.	Recurrences in ≥70 group	C-index (95% CI)	HR (95% CI)
Basel	269	40	5	0.79 (0.51-1.00)	2.12 (1.18-3.78)
Karmanos	162	20	4	0.72 (0.45-0.93)	1.93 (0.57-6.55)
UChicago	410	36	4	0.57 (0.12-0.88)	1.10 (0.29-4.21)
TCGA	930	157	4	0.70 (0.52-0.88)	1.64 (1.27-2.11)
Providence	1687	358	30	0.76 (0.68-0.83)	2.08 (1.53-2.82)

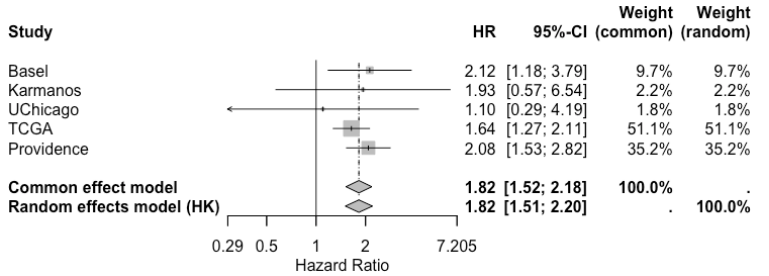


Fig 3. Meta-analysis of ATX performance in HR+/HER2- patients ≥70 years old, including Basel and four other independent cohorts.

CONCLUSION

ATX bridges a long-standing methodological gap in risk prediction for older HR+/HER2- breast cancer patients. By delivering robust and interpretable stratification, it enables more confident, evidence-based treatment decisions in this underserved population.

Presenter: Elena Diana Chiru, MD
elena-diana.chiru@ksbl.ch

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