Pathologist- and artificial intelligence-based TILs assessment in patients with early triple-negative breast cancer treated with neoadjuvant chemo-immunotherapy: real-world evidence from a nationwide cohort

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Introduction

- Neoadjuvant chemo-immunotherapy is the standard of care for patients with stage II-III triple negative breast cancer (TNBC)
- Real-world data on tumor-infiltrating lymphocytes (TILs) indicate a correlation of higher pre-treatment TILs levels with increased pathological complete response (pCR) rates
- Digital pathology and artificial intelligence (AI) tools could provide value towards a more standardized and objective TILs assessment and additional spatial insights

Aim

- To assess the performance and prognostic value of pathologist-based and AI/digital pathology-based TILs scoring methods

Methods

- Study population: nationwide cohort of patients with early TNBC treated with neoadjuvant chemo-immunotherapy according to the KEYNOTE-522 regimen, in 20 Swedish hospitals between 2022-2024
- TILs assessment on H&E-stained diagnostic biopsy tissue sections was performed:
  i) manually (sTILs), according to the International Immuno-Oncology Working Group guidelines and
  ii) digitally (AI-TILs = TILs/Stromal cells) using the deep learning-based scoring algorithm HoverNet
- Correlation with pCR was performed using univariate logistic regression model

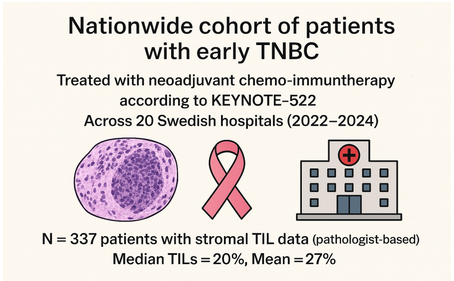


Figure 1. Overview of the RWD nationwide patient cohort

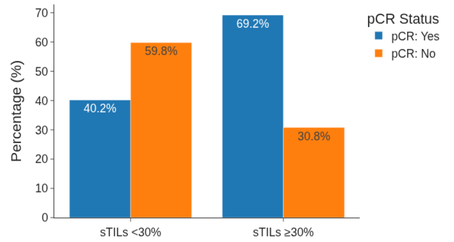


Figure 2. Distribution of pCR rates by stromal TILs category

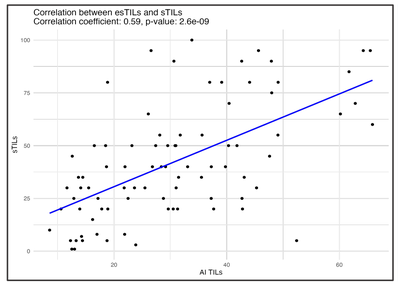


Figure 4. Correlation between AI- and pathologist-based TILs assessment (n= 84 with matched available TILs data). Spearman's rho= 0.59, p<0.0001

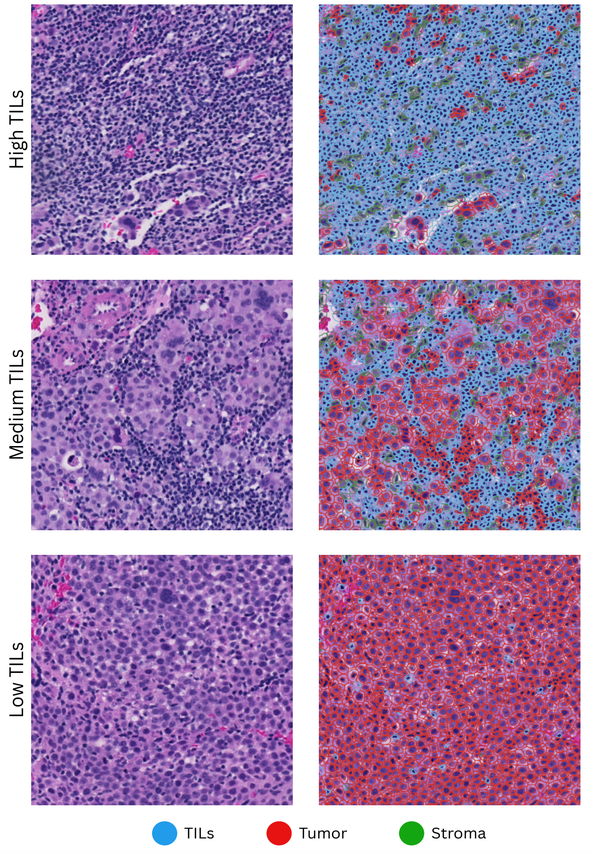


Figure 3. Representative H&E – stained tissue biopsies for different levels of pathologist-based (left column) and AI-based TILs (right column). AI-digital scoring (TILs/Stromal cells) using the HoverNet DL algorithm

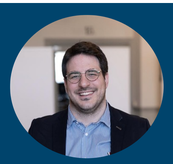
Results

- 337 patients were included in this nationwide cohort. 51.5% of the patients achieved pCR and 35% had RCB 2/3 (Fig. 1)
- Patients with baseline pathologist-based sTILs ≥30% were significantly associated with higher pCR rates and lower RCB score (chi-square test, p<0.0001) (Fig. 2).
- Both sTILs and AI-TILs were available for 84 patients (Fig. 3) and demonstrated a moderate correlation (rho= 0.59, p<0.0001) (Fig. 4)
- Both TILs variables (continuous) were significantly associated with increased pCR rates (OR=1.068, 95% CI: 1.04 1.11, p<0.001 for sTLs; OR=1.072, 95% CI: 1.03 -1.12, p<0.0001 for AI-based TILs).
- In patients with non-LPBC (sTILs <50%), high AI-TILs (cut-off: median) were associated with higher likelihood of achieving pCR compared to those with low AI-TILs (OR= 4.1; 95% CI: 1.3-14.1, p=0.018)

Conclusions

- Both pathologist- and AI-based TILs were predictive for pCR
- AI-TILs assessment could potentially contribute to a better response discrimination in patients with non-LPBC
- Additional validation is warranted

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References: 1. Zerdes I et al. NPJ Breast Cancer. 2025;11(1):23; 2. Bai Y et al. Clin Cancer Res 2021;27(20):5557-5565 ; 3. Vidal JM et al. EClinicalMedicine 2024;78:102928; 4. Steen S et al. 321P, ESMO 2025

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