# Artificial Intelligence-based spatial assessment of tumor-infiltrating lymphocytes and outcome in early HER2+ breast cancer: ancillary study of the phase III adjuvant ShortHER trial

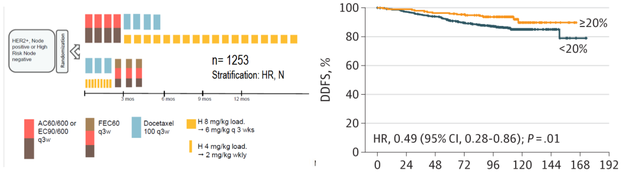
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## INTRODUCTION

We previously demonstrated the **prognostic role of tumor-infiltrating lymphocytes (TIL,manual score)** in the **ShortHER trial, a phase III randomized trial** testing de-escalated adjuvant chemotherapy and trastuzumab treatment for patients with **early HER2+ breast cancer (BC)** [Dieci, JAMA Oncol 2025].





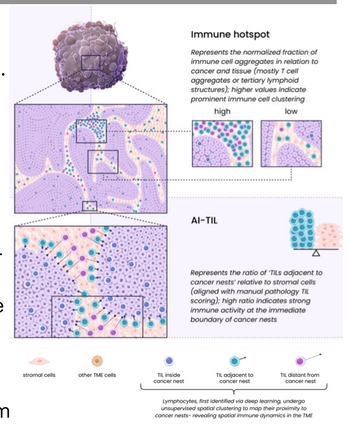


## OBJECTIVES

To assess the added prognostic value of **AI-based spatial TIL** metrics beyond manual TIL in **early HER2+ BC.**

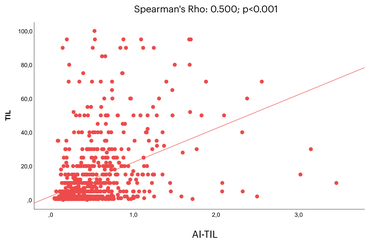
## METHODS and AI-PIPELINE

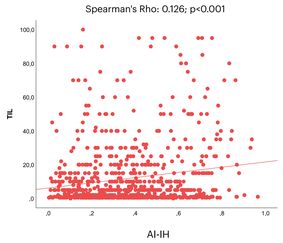
- **Study population**: n=848 patients enrolled in ShortHER trial; median-follow-up 9 years.
- **AI pipeline**: Zero-shot explainable AI (Case45) analyzing H&E slides.
- **AI metrics:**
  - **AI-TIL**
  - **AI-Immune hotspots (IH)**
- **Cut-offs:** Manual TIL ≥20%; AI-TIL and AI-IH ≥75th percentile.
- **Endpoint**: Distant disease-free survival (DDFS).
- **Cox-regression**: adj. for age, menoapusal status, stage, grade, hormone receptors, arm



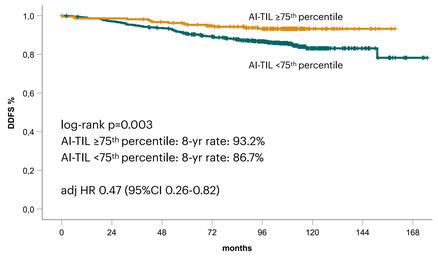

## RESULTS

### METRICS CORRELATION

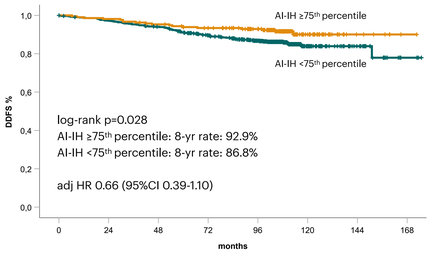


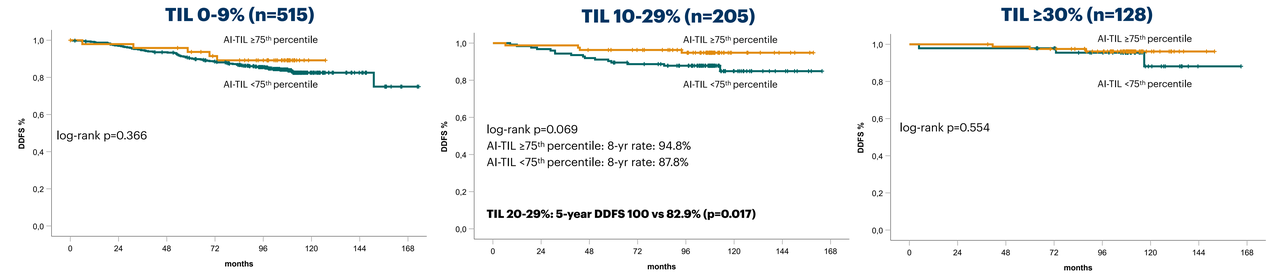

### PROGNOSTIC VALUE of AI-TIL



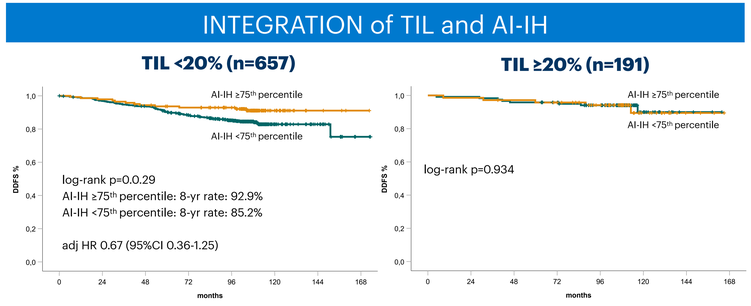

### PROGNOSTIC VALUE of AI-IH




### INTEGRATION of TIL and AI-TIL




### INTEGRATION of TIL and AI-IH




### MODEL PERFORMANCE

| Model | Likelihood ratio chi-square | P value |
|---|---|---|
| AI-TIL added to Model 1* | 5.61 | **0.018** |
| Manual TIL added to Model 2** | 4.17 | **0.041** |
| AI-IH added to Model 1* | 1.80 | 0.180 |
| AI-IH added to Model 2** | 3.26 | 0.071 |

***Model 1**: clinico-pathological factors + manual TIL
****Model 2**: clinico-pathological factors + AI-TIL

## CONCLUSIONS

AI-based spatial TIL metrics complement manual TILs scoring in refining prognostic stratification in early HER2+ breast cancer.

The added value of AI-based TIL metrics may be more relevant in case of intermediate manual TILs scores.

Funding:

Ref: Dieci MV, JAMA Oncol 2025; Dieci MV Ann Onc 2019; Conte PF et al. JCO 2023;

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