# PREDICTIVE MARKERS FOR PATHOLOGICAL COMPLETE RESPONSE TO NEOADJUVANT THERAPY IN EARLY-STAGE TRIPLE-NEGATIVE BREAST CANCER: A SINGLE-CENTER STUDY IN VIETNAM

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## INTRODUCTION

- Triple-negative breast cancer (TNBC) is an aggressive subtype with a poor prognosis.
- Neoadjuvant chemotherapy (NACT) is the standard of care for early-stage TNBC (eTNBC).
- Achieving a pathological complete response (pCR) after NACT is a strong surrogate marker for long-term survival, including improved disease-free survival (DFS) and overall survival (OS).
- The immune checkpoint inhibitor (ICI) pembrolizumab, combined with NACT, was approved in Vietnam in 2023 after demonstrating significantly improved pCR rates in clinical trials (e.g., KEYNOTE-522).
- However, high cost and lack of insurance coverage create significant barriers to access for most Vietnamese patients.
- Tumor-infiltrating lymphocytes (TILs) have emerged as a robust prognostic and predictive biomarker in TNBC. Higher baseline TILs are associated with higher pCR rates and better survival outcomes.
- **Objective**: To identify predictive factors, especially the role of TILs, for pCR in Vietnamese eTNBC patients treated with neoadjuvant pembrolizumab and chemotherapy.

## METHODS AND MATERIALS

- **Study Design**: A prospective, single-arm, single-center study conducted at Vietnam National Cancer Hospital (K Hospital) from December 2023 to May 2025.
- **Patient Population**: 49 female patients (age ≥ 18) with newly diagnosed, unilateral, non-metastatic (Stage II-III) eTNBC. Key inclusion criteria included ECOG 0-1 and adequate organ function.
- **Treatment Regimen**: Patients received neoadjuvant pembrolizumab combined with chemotherapy (Paclitaxel + Carboplatin followed by Doxorubicin + Cyclophosphamide, TC-AC).
- **Assessments**:
  - **TILs**: Evaluated on pre-treatment H&E-stained slides by two independent pathologists according to the International TILs Working Group guidelines.
  - **pCR**: Assessed on surgical specimens post-NACT. pCR was defined as the absence of residual invasive carcinoma in both the breast and axillary lymph nodes (ypT0/is ypN0).
  - **Statistical Analysis**: Patient characteristics were described using medians (IQR) and percentages. Univariate and multivariate logistic regression models were used to identify independent predictors of pCR. A p-value < 0.05 was considered significant. ROC curve analysis was used to determine optimal TILs cut-off values.

## RESULTS

**Table 1. Baseline Patient Characteristics (N=49)**

| Characteristic | Category | N (%) or Median (IQR) |
|---|---|---|
| **Age (years)** | Median (IQR) | 48.9 (44-55) |
| **Tumor Size (cm)** | Median (IQR) | 3.5 (2.5-4.5) |
| **T Stage** | T1-T2 | 41 (83.7%) |
| | T3-T4 | 8 (16.3%) |
| **N Stage** | N0 | 11 (22.4%) |
| | N+ | 38 (77.6%) |
| **Clinical Stage** | Stage II | 29 (59.2%) |
| | Stage III | 19 (38.8%) |
| **Ki67 (%)** | Median (IQR) | 70 (50-80) |
| **HER2 Status** | HER2-Negative (0) | 33 (67.3%) |
| | HER2-Low (1+/2+) | 16 (32.7%) |
| **TILs (%)** | Median (IQR) | **35 (20-50)** |

**Table 2. Predictive Performance of TILs Cut-offs for pCR**

| TILs Cut-off | Sensitivity | Specificity | Accuracy |
|---|---|---|---|
| **≥ 30%** | 78,80% | 81,30% | 79,96% |
| **≥ 50%** | 100,00% | 55,60% | 67,30% |

The ≥ 30% cut-off provided the most balanced predictive performance for pCR.

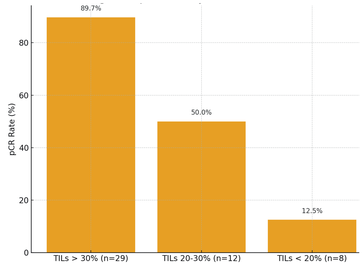



**Figure 1. pCR Rate by Baseline TILs Strata**

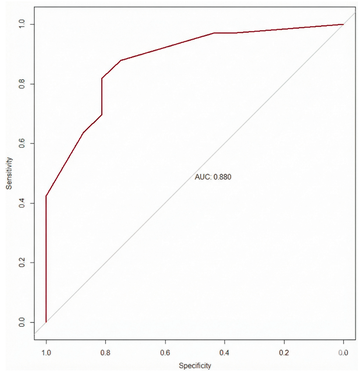



**Figure 1: ROC analysis of the prognostic role of TILs in predicting the likelihood of complete response**

- The **overall pCR rate** for the cohort was **67.3%** (33 out of 49 patients).
- In the multivariate analysis, **baseline TILs percentage** (as a continuous variable) was the only independent predictor of pCR (Odds Ratio [OR]: 1.14; 95% Confidence Interval [CI]: 1.06–1.27; p=0.003).
- Patients with HER2-low tumors had a lower pCR rate compared to HER2-negative patients (univariate p=0.049)

## DISCUSSION

- The pCR rate of 67.3% in this Vietnamese cohort is consistent with the landmark KEYNOTE-522 trial (64.8%), supporting the efficacy of the pembrolizumab-chemotherapy regimen in our clinical setting.
- Our study confirms that baseline TILs are a strong and independent predictor of pCR (OR 1.14, p=0.003), aligning with large international pooled analyses.
- The dramatic increase in pCR rates from 12.5% (in TILs <20%) to 89.7% (in TILs >30%) underscores the critical role of a pre-existing anti-tumor immune response in mediating the efficacy of immune checkpoint inhibitors.
- The 30% TILs cut-off demonstrates a strong balance of **sensitivity (78.8%) and specificity (81.3%)**, suggesting it is a practical and clinically relevant threshold for predicting response, as recommended by the International TILs Working Group.
- **Limitations:** This study is limited by a small sample size (n=49), a single-center design, and short follow-up duration, which precludes analysis of DFS or OS outcomes.

## CONCLUSION

- **Baseline TILs and HER2 expression status** are significant predictive factors for pCR in eTNBC patients receiving neoadjuvant pembrolizumab and chemotherapy.
- TILs are an independent, robust biomarker, with a **≥ 30% threshold** offering a practical tool to predict treatment response.
- Identifying such predictive tools is critical for optimizing patient selection and managing resources in developing countries like Vietnam, where access to novel therapies is limited.

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**Conflict of Interest Declaration**

The authors declare that there are no financial or personal conflicts of interest related to this study.

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