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Prediction of pathologic complete response to chemoimmunotherapy in triple-negative breast cancer using tumor-infiltrating lymphocytes: exploiting cutoff values

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Objective: Triple-negative breast cancer (TNBC) prognosis is significantly influenced by tumor-infiltrating lymphocytes (TILs), but the lack of validated cutoff values limits their clinical applicability. This study aimed to assess TILs as predictors of pathologic complete response (pCR) within the Neo-Real study, a multicenter, real-world data investigation on neoadjuvant pembrolizumab plus chemotherapy (P+CT) for TNBC. **Methodology:** TILs were evaluated using the standardized methodology of the International TILs Working Group. Logistic regression and receiver operating characteristic (ROC) curve analysis were performed to evaluate the predictive ability of TILs and multivariable models for pCR. **Results:** The analysis included 128 patients. The pCR and results of ROC curve analysis for each TIL's cutoff were as follows: 10%: pCR of 39% for TILs <10% vs. 69% for TILs ≥10% (AUC 0.635, accuracy 66.7%, sensitivity 78%, specificity 50%); 30%: pCR of 52.2% for TILs <30% vs. 78.8% for TILs ≥30% (AUC 0.608, accuracy 56.2%, sensitivity 35.6%, specificity 86%); 50%: pCR of 55.4% for TILs <50% vs 87.5% for TILs ≥50% (AUC 0.575, accuracy 50.4%, sensitivity 19.1%, specificity 96%). A cutoff of 10% demonstrated the highest accuracy for pCR, while high specificity was observed at a cutoff of 50%. The probability of residual disease if TILs ≥50% is considerably low. A multivariable logistic regression model, using TILs (≥10% vs. <10%), Ki67 (≥50% vs. < 50%), and tumor stage (III vs. II), exhibited the highest AUC (0.688) for predicting pCR. **Conclusion:** Our study underscores the predictive value of TILs for pCR following neoadjuvant P+CT for TNBC. Further enhancement of TILs' predictive potential may be achieved through multivariable models. The cutoff value of ≥50% identified patients with a very high probability of pCR. The results reinforce TILs' use as a biomarker for treatment de-escalation, especially for TILs ≥50%.

Keywords: triple-negative breast neoplasm; immunotherapy; tumor infiltrating lymphocytes.