Can high TILs compensate for incomplete neoadjuvant pembrolizumab in early TNBC? Insights from the PETRHA cohort

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Background

- Tumor-infiltrating lymphocytes (TILs) are a predictive and prognostic biomarker in early triple-negative breast cancer (TNBC), linked to higher pathologic complete response (pCR) following chemo-immunotherapy.
- In real-world settings, pembrolizumab is often discontinued early due to access or toxicity issues.
- Prior PETRHA data showed incomplete pembrolizuma correlates with lower pCR.
- Whether TILs can offset incomplete immunotherapy exposure remains unclear.

Methods

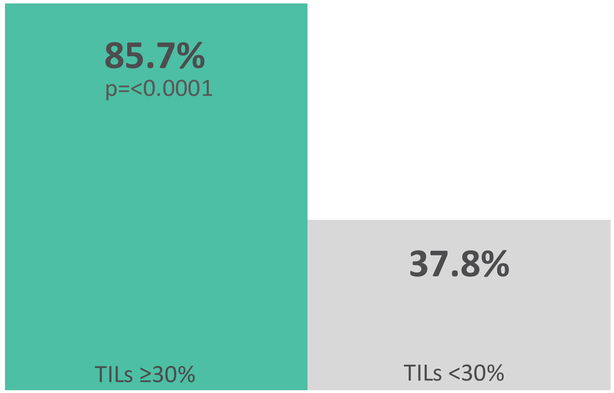
304 patients (PETRHA cohort)
→ TILs were evaluated on pretreatment core biopsies by local pathologists and categorized using two predefined thresholds (>20% and >30%).
→ 111 with TILs data
→ Compared by pembrolizumab completion
→ pCR (ypT0/is ypN0) as primary outcome

Associations between TIL levels, pembrolizumab completion, and pCR were evaluated using chi-square or Fisher's exact tests, and logistic regression was used to estimate odds ratios (OR) with 95% confidence intervals.

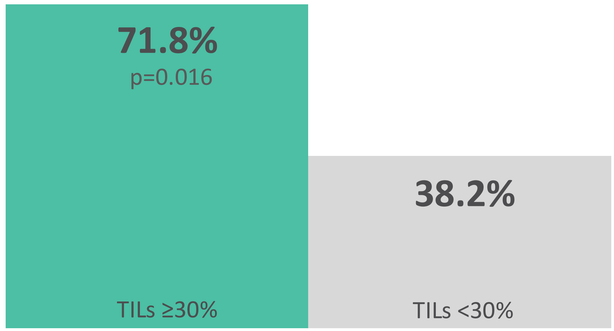
Results

- 59 patients (53.2%) had TILs <20% and 52 (46.8%) had TILs ≥20%, while 70 (63.1%) had TILs <30% and 41 (36.9%) had TILs >30%.
- Thirty-eight (34.2%) received an incomplete number of neoadjuvant pembrolizumab cycles, while 73 (65.8%) completed the regimen.

Higher baseline TILs (>30%) showed higher pCR rates, independent of pembrolizumab completion



pCR distribution by TILs level in patients who completed pembrolizumab (≥8 cycles for q3w and ≥ 4 cycles for q6w)
In ≥ 20% cut-off: 71.8% vs. 38.2%, p=0.004)



pCR distribution by TILs level in patients with incomplete pembrolizumab (<8 cycles for q3w and <4 cycles for q6w)

- In a multivariable logistic regression model TILs >30% were the strongest independent predictor of pCR (OR 12.74, p=0.001).
- Completion of neoadjuvant chemotherapy was also independently associated with higher pCR (OR 4.95, p=0.045).

Conclusion

High baseline TILs (>30%) were associated with higher pCR rates, even among patients who did not complete neoadjuvant pembrolizumab. The best outcomes were observed in those with both high TILs and full treatment completion (pCR 85.7%), suggesting a synergistic effect between immune activation and immunotherapy exposure. These findings indicate that robust immune infiltration may partially compensate for reduced pembrolizumab administration.

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