The Relationship Between Tumor-Infiltrating Lymphocytes (TILs), Pathologic Complete Response, and Event-Free Survival in Patients with Early-Stage Triple-Negative Breast Cancer Treated with KEYNOTE-522 regimen in a Real-World Scenario

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Introduction

Tumor-infiltrating lymphocytes (TILs) are established prognostic and predictive biomarkers in early-stage triple-negative breast cancer (eTNBC). The addition of pembrolizumab to neoadjuvant chemotherapy (NAC) has demonstrated improved outcomes in this setting (KEYNOTE-522 trial). The role of TIL levels in this context needs to be further explored.

Methods

- The Neo-Real / GBECAM-0123 study is a retrospective multicenter cohort including patients with stage II-III TNBC treated with pembrolizumab plus NAC across institutions in Brazil and Argentina since 2020.
- Baseline stromal TILs were assessed on pre-treatment biopsies according to international guidelines and categorized as: <30%, 30-49%, or ≥50%.
- Associations with pCR and event-free survival (EFS) were evaluated using logistic and Cox regression models, respectively.

Results

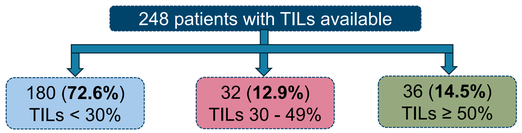


Table 1. Patients' characteristics, N (%)

	TILs < 30% (N=180)	TILs 30 - 49% (N=32)	TILs ≥ 50% (36)	P-value
Age, median (range)	45 (21 – 80)	42 (24 – 74)	41 (27 – 68)	0.110
Histology Ductal Special type	 165 (91.7%) 15 (7.3%)	 31 (96.9%) 1 (3.1%)	 34 (94.4%) 2 (5.6%)	0.975
Premenopausal	22 (44%)	12 (50%)		
Ki67 index ≥ 50%	125 (70.2%)	31 (96.9%)	28 (77.8%)	**0.002**
Grade 1-2 3	 47 (26.4%) 131 (73.6%)	 2 (6.2%) 30 (93.7%)	 4 (11.8%) 30 (88.2%)	**0.012**
Clinical T status T1 T2 T3 T4	 16 (8.9%) 112 (62.6%) 37 (20.7%) 14 (7.8%)	 3 (9.4%) 23 (71.9%) 5 (15.6%) 14 (7.8%)	 5 (13.9%) 26 (72.2%) 4 (11.1%) 1 (2.8%)	0.642
Clinical Nodal status N0 N1 N2 N3	 85 (47.7%) 58 (32.6%) 20 (11.2%) 15 (8.4%)	 14 (43.7%) 13 (40.6%) 3 (9.4%) 2 (6.2%)	 19 (52.8%) 12 (33.3%) 4 (11.1%) 1 (2.8%)	0.933
Stage II III	 119 (68%) 56 (32%)	 24 (77.4%) 7 (22.6%)	 27 (79.4%) 7 (20.6%)	0.321
BRCA Mutated Wild-type/ Unknown	 16 (8.9%) 164 (91.1%)	 7 (21.9%) 25 (78.1%)	 4 (11.1%) 32 (88.9%)	0.109
AC schedule Every 3 weeks Dose-dense	 77 (43.3%) 101 (56.7%)	 10 (32.3%) 21 (67.7%)	 13 (37.1%) 22 (62.9%)	0.477

Figure 1. Pathologic complete response (pCR) according to TILs levels and Ki67 index. Nearly all pts with both high TILs and high Ki-67 achieved pCR.

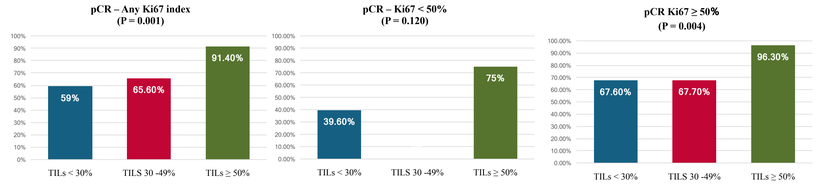


Table 2. Multivariable logistic regression of factors associated with pCR

Variable		OR	95% CI	P-value
TILs	< 30%	*reference*		
	30 – 49%	0.84	0.35 – 2.00	0.700
	≥ 50%	6.96	1.88 – 25.65	**0.004**
Grade 3 (vs 1-2)		1.09	0.50 – 2.38	0.817
Stage III (vs II)		0.60	0.30 – 1.17	0.138
Ki67 ≥ 50% (vs < 50%)		9.06	1.54 – 53.27	**0.015**
Pembrolizumab < 6 cycles (vs ≥ 6 cycles)		0.51	0.23 – 1.13	0.099

Table 3. Multivariable Cox regression of factors associated with EFS

Variable		OR	95% CI	P-value
TILs	< 30%	*reference*		
	30 – 49%	0.65	0.14 – 2.82	0.566
	≥ 50%	0.97	0.21 – 4.49	0.977
Stage III (vs II)		3.68	1.58 – 8.53	**0.002**
Patologic complete response (vs residual disease)		0.20	0.07 – 0.54	**0.002**

Figure 2. EFS according to TILs levels among patients with pCR. 2-year EFS was 97.0% in TILs < 30%, 95.2% in TILs 30-49%, and 93.2% in TILs ≥50%.

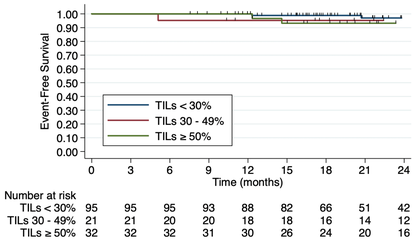
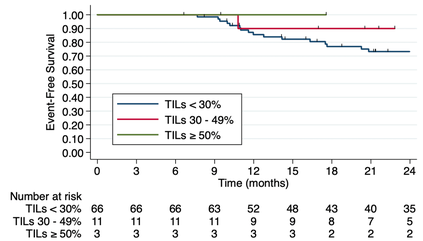


Figure 3. EFS according to TILs levels among patients with residual disease: 2-year EFS was 73.3% in TILs < 30%, 90% in TILs 30-50%, and 100% in TILs ≥50%.



CONCLUSIONS

In this real-world cohort of patients with eTNBC treated with the KEYNOTE-522 regimen, high baseline TILs and Ki-67 index were strongly associated with higher pCR rates. These findings support the role of TILs as a relevant biomarker for treatment response. Long-term outcomes were primarily driven by pathologic response and disease stage, underscoring the importance of achieving pCR.

References

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2. de Jong VM, et al. Journal of Clinical Oncology 2022;40:2361-2374.

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