

Supplementary Information

Supplementary Table 1 Cox Prognostic Models for TILs as continuous variable (10% of increment) for all cohort

All Cohort (n=110)	<u>Progression-Free Survival</u>			<u>Overall Survival</u>		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
sTILs (continuous)	0.80	0.62-1.03	0.085	0.81	0.56-1.16	0.252
sTILs (continuous)*	0.79	0.61-1.04	0.094	0.84	0.58-1.21	0.351

*Adjusted for age, visceral disease, hormonal receptor status, site of metastasis

Cox proportional hazard models for TILs analyzed as a continuous variable (10% increment) in the entire cohort (n=110). Results are shown for both PFS and OS. The unadjusted model for PFS shows a trend towards improved outcomes with increasing TIL levels, though this was not statistically significant (HR = 0.80, 95% CI: 0.62-1.03, p=0.085). Adjusting for age, visceral disease, hormone receptor status, and site of metastasis did not substantially alter the results (HR = 0.79, 95% CI: 0.61-1.04, p=0.094). Similar findings were observed for OS, with HR = 0.81 (95% CI: 0.56-1.16, p=0.252) in the unadjusted model and HR = 0.84 (95% CI: 0.58-1.21, p=0.351) in the adjusted model.

Supplementary Table 2 Cox Prognostic Models for TILs as continuous variable (10% of increment) for the cohort of patients whose TILs were evaluated at the metastatic site.

Metastatic site Cohort (n=57)	<u>Progression-Free Survival</u>			<u>Overall Survival</u>		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
sTILs (continuous)	0.62	0.38-1.02	0.061	0.45	0.20-0.99	0.045
sTILs (continuous)*	0.57	0.32-0.98	0.045	0.44	0.17-1.18	0.104

*Adjusted for age at diagnosis, visceral disease, hormonal receptor status, and site of metastasis

Cox proportional hazard models for TILs as a continuous variable (10% increment) in the cohort of patients whose TILs were evaluated at the metastatic site (n=57). A non-significant association between increasing TILs and PFS was observed (HR = 0.62, 95% CI: 0.38-1.02, p=0.061), while in the adjusted model higher TILs values were significantly associated with PFS, suggesting a potential prognostic role of TILs in patients with metastasis (HR = 0.57, 95% CI: 0.32-0.98, p=0.045). Higher TILs were significantly associated with better OS in univariate model (HR = 0.45, 95% CI: 0.20-0.99, p=0.045): when controlling for clinical variables we found a similar trend but did not reach statistical significance (HR = 0.44, 95% CI: 0.17-1.18, p=0.104).

Abbreviations: BC, breast cancer; CI: confidence interval; HR: hormone receptor; PFS: progression-free survival; OS, overall survival, TILs: tumor-infiltrating lymphocytes