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BREAST CANCER, EARLY STAGE

186O Tumor-infiltrating lymphocytes (TILs) as an independent prognostic factor for early HER2+ breast cancer patients treated with adjuvant chemotherapy and trastuzumab in the randomized shortHER trial

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Background: TILs are an established prognostic factor for triple negative breast cancer. We investigated the prognostic role of TILs for HER2+ early breast cancer patients enrolled in the prospective ShortHER trial.

Methods: The ShortHER study randomized 1254 patients with HER2+ early breast cancer to receive 9 weeks vs 1 year of adjuvant trastuzumab combined with chemotherapy (Conte, ASCO 2017). TILs were assessed for 855 cases on centralized HES slides according to recommendations (Salgado, Ann Oncol 2015). Metastasis-free survival (MFS) was calculated from randomization to distant disease recurrence or death. Median follow up was 72 months.

Results: Median TILs was 5% (Q1-Q3 1%-15%). Higher TILs were associated with hormone receptor-negative status ($p < 0.001$) and age <60 years ($p = 0.008$). There was no association with stage and PIK3CA mutation. Increased TILs were associated with better MFS (HR 0.69, 95%CI 0.54-0.88 for each 10% TILs increment, $p = 0.003$). 5-yrs MFS rates were 91%, 94% and 100% for TILs<20%, TILs > =20% & <50% and TILs > =50% ($p = 0.013$). Multivariable cox models confirmed TILs as independent prognostic factor (Table).

Table: 186O

MULTIVARIATE COX MODELS FOR MFS

Factors	All patients		Hormone Receptor neg		Hormone Receptor pos	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
TILs 10% increase	0.67 (0.52-0.86)	0.001	0.72 (0.53-0.97)	0.031	0.57 (0.36-0.91)	0.017
HR pos vs neg	0.63 (0.39-1.00)	0.049	-	-	-	-
Stage I-II vs III	0.31 (0.20-0.50)	<0.001	0.27 (0.13-0.59)	0.001	0.33 (0.19-0.60)	<0.001
Age >60 vs < 60	1.02 (0.65-1.60)	0.936	1.44 (0.69-3.02)	0.337	0.82 (0.45-1.47)	0.501

The association between 10% TILs increments and MFS was significant in the short (HR 0.49, 95%CI 0.29-0.82, $p = 0.006$) but not in the long arm (HR 0.84, 95%CI 0.65-1.10, $p = 0.212$). Patients with TILs <20% benefitted from long treatment (HR 0.76, 95%CI 0.60-0.97, $p = 0.024$), whereas for patients with TILs > =20% the HR favored the short arm (HR 2.79, 95%CI 0.98-7.96, $p = 0.055$; 8 events only). Interaction test

showed p = 0.064 (arm*10% TILs increase) and p = 0.019 (arm*TILs binary variable with 20% cutoff).

Conclusions: TILs are an independent prognostic factor for HER2+ early breast cancer patients treated with adjuvant chemotherapy and trastuzumab. Integration of TILs in prognostic algorithms can help refining risk stratification and guiding therapeutic de-escalation.

Clinical trial identification: EudraCT 2007-004326-25 Start date: 2007-11-15.

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