244P Immune infiltrate composition across intrinsic subtypes in hormone receptor (HR)+/HER2- early breast cancer (BC) enrolled in the prospective LETLOB trial

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Background: In HR+/HER2- early BC, high tumour infiltrating lymphocytes (TIL) levels predict higher pathological complete response to neoadjuvant chemotherapy, but are associated with shorter overall survival (Denkert, Lancet Oncol 2018). HR+/HER2- BC is a biologically heterogeneous disease, encompassing all BC molecular intrinsic subtypes, with different clinical behaviour (Cejalvo, CTR 2018). Little is known concerning the distribution of TIL levels and immune infiltrate composition across intrinsic subtypes in HR+/HER2- BC.

Methods: Gene-expression data (Affymetrix platform) from pre-treatment frozen core-biopsies was available from 66 postmenopausal patients with HR+/HER2- early BC from the LETLOB trial (neoadjuvant letrozole+/-lapatinib) (Guarneri, JCO 2014). Intrinsic subtype was assigned using a research-based PAM50 subtype predictor. Relative leukocyte fractions were calculated using CIBERSORT (Newman, Nature Methods 2015), a deconvolution method based on RNA gene-expression signatures. Pre-treatment stromal TILs were assessed on centralized HES slides according to recommendations (Salgado, Ann Oncol 2015).

Results: Intrinsic subtype distribution was as follows: basal 18% (N = 12), HER2-enriched 8% (N = 5), Luminal A 39% (N = 25), Luminal B 36% (N = 24). Non-luminal subtypes (HER2-enriched and Basal) had significantly higher baseline TIL levels than luminal subtypes (median (range): 7 (0-100) and 2 (0-35), respectively; $p = 0.038$). Non-luminal subtypes also presented higher fractions of CD4 memory activated T-cells ($p = 0.018$), γδ T-cells ($p = 0.010$) and M1 macrophages ($p = 0.001$) and lower fractions of T-regulatory cells ($p = 0.002$) than luminal subtypes.

Conclusions: In HR+/HER2- early BC, non-luminal subtypes show higher TIL levels and a more pro-inflammatory anti-tumour immune infiltrate composition. This immune heterogeneity across intrinsic subtypes should be considered when analysing the complex prognostic role of TILs in HR+/HER2- early BC.

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