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Neutrophil-to-lymphocyte and lymphocyte-to-monocyte ratios in breast cancer

<u>L. Gerratana</u><sup>1</sup>, D. Basile<sup>1</sup>, S. Zago<sup>2</sup>, M.G. Vitale<sup>1</sup>, G. Pelizzari<sup>1</sup>, M. Bonotto<sup>1</sup>, C. Bozza<sup>1</sup>, M. Bartoletti<sup>1</sup>, V. Fanotto<sup>1</sup>, C. Lisanti<sup>1</sup>, M. Cinausero<sup>1</sup>, S. Barban<sup>1</sup>, M. Lera<sup>1</sup>, I. Venuti<sup>1</sup>, M. Mansutti<sup>3</sup>, A.M. Minisini<sup>3</sup>, G. Fasola<sup>3</sup>, F. Curcio<sup>2</sup>

<sup>1</sup>School of Medical Oncology, Department of Medicine, University of Udine, Udine, Italy, <sup>2</sup>Clinical Pathology Institute, University Hospital of Udine, Udine, Italy, <sup>3</sup>Department of Oncology, University Hospital of Udine, Udine, Italy

Background: Immunity plays a pivotal role in cancer progression and prognosis. A high neutrophil-to-lymphocite ratio (NLR) or a low lymphocyte-to-monocyte ratio (LMR) are respectively associated with systemic inflammation and immune suppression and have been associated with a poor outcome. Aim of this study is to further investigate the interaction between the immune system and breast cancer (BC) through the NLR and LMR.

Methods: This retrospective study analyzed a consecutive cohort of 657 patients (pts) with a diagnosis of pT1 BC, without restrictions regarding lymph node status (T1BC), or metastatic BC (MBC) treated between 2004 and 2017 at the Department of Oncology of Udine (Italy). Differences in terms of NLR and LMR among the two cohorts and between clinico-pathological characteristics in the T1BC subgroup were explored through the Kruskal-Wallis test. The prognostic impact in terms of OS in the  $T1BC\ population\ was\ investigated\ through\ uni-\ and\ multivariate\ Cox\ regression.$ 

Results: Both NLR and LMR were significantly different between the T1BC and the MBC cohorts. In particular, pts with T1BC had a higher median LMR (3.9 vs 2.9; P=0.0001) and lower NLR (2 vs 2.7; P=0.0001). After stratification according to molecular profile, T1BC and MBC cohorts of Luminal B-like subtype were significantly different in terms of both LMR (4.2 vs 3; P = 0.0001) and NLR (2 vs 2.5; P = 0.0001). In triple negative subtype, the difference between TB1C and MBC was observed for NLR (1.9 vs 3.2; P = 0.0272) only. On the other hand, no differences between TB1C and MBC were highlighted for the other subtypes. When focusing on the clinicopathological characteristics of the T1BC cohort, LMR was associated with progesterone receptor (PR) expression (P = 0.0261) and marginally with the estrogen receptor (ER) expression, while NLR with tumor diameter (P = 0.0240) and marginally with grading. Furthermore, among T1BC pts, NLR had no prognostic impact in terms of OS, while LMR was associated with a better outcome also when corrected for ER, PR and HER2 status (HR 0.44, 95%CI 0.28 - 0.71, P = 0.001).

Conclusions: These results suggest a role for systemic inflammation and immunesuppression in breast cancer, especially in the triple negative and luminal B-like

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