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Tumour infiltrating lymphocytes in early breast cancer: High levels of CD3, CD8 cells and Immunoscore® are associated with pathological CR and time to progression in patients undergoing neo-adjuvant chemotherapy

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Background

The presence of high levels of tumour infiltrating lymphocytes (TILs) has been associated with better prognosis in early triple-negative breast cancer (TNBC). The Immunoscore® (IS) is a prognostic tool, which categorizes the densities of spatially positioned CD3 and CD8 cells in both invasive margins (IM) and the center of the tumor (CT), yielding a five-tiered classification (0–4). High IS values have been reported to predict improved outcomes in colorectal cancer.

Methods

We performed the IS in 103 breast cancer (BC) patients (pts) who previously received neo-adjuvant anthracycline and taxane +/- trastuzumab based chemotherapy TNBC=53, Luminal=32, HER2+=18. Pre-treatment tumor samples were immune-stained for CD3 and CD8 T-cell markers. Quantitative analysis of the immune cells was carried out using a computer-assisted image analysis in different tumour locations.

Results

The pathological complete response (pCR) rate of the entire cohort was 44%. On univariate analysis, factors associated with higher pCR included tumor size ($p<0.005$), nodal status ($p<0.069$), ER ($p<0.000$), PR ($p<0.000$), molecular subtype (TNBC=62%, HER2+=50% and Luminal A+B=9%, $p<0.000$), Ki67 (>40=56% vs. 15-39=40% vs. <15=0%, $p<0.000$) and Stage ($p<0.028$). T-cell density subsets (CD3, CD8, in the CT and IM) as well as the IS were significantly higher in TNBC vs. non-TNBC pts. A high density of CD3 (> than 800mm^2) and CD8 (> than 400mm^2) positive T-cells in the CT was associated with higher pCR (CD3 CT: 60% vs. 25%, $p=0.000$ and CD8 CT: 64% vs. 27%, $p=0.000$). Analysis of CD3 (> than 1400mm$^{2)}$ (CD3 IM: 63% vs. 19%, $p=0.00$) and CD8 in the IM (> than 500mm^2) was also significant for an association with pCR (CD8 IM:63% vs. 15%, $p=0.000$). High IS (3+4= 63%) vs. intermediate (2=35%) vs. low (0+1=24%) was significantly associated with pCR ($p=0.006$). In a logistic regression model Ki-67 ($p<0.005$) and IS ($p<0.021$) and molecular subtype ($p<0.010$) retained significance. DFS: At 3 years 94% of IS high pts did not relapse compared to 80% IS intermediate or low pts ($p<0.07$).

Conclusions

This study shows a significant prognostic and potentially predictive role for the IS in BC pts, particularly in TNBC.

Clinical trial identification

Ruby Project.

Legal entity responsible for the study

The authors.

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Disclosure

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