Background: Characterization of the immune phenotype of tumors during progression could aid in developing patient-tailored therapy strategies. Here, we sought to identify differences in immune markers comparing paired tumors from primary and metastatic sites from the GEICAM/2009-03 (ConvertHER) study.

Methods: Matched primary and metastases were analyzed by immunohistochemistry as described by Herbst et al., 2014 for PDL1 expression. The nanostring gene expression platform was used to profile and identify differences in the expression of 805 immune-related genes. Significant features (p-value <0.05) were assessed for functional enrichment of KEGG pathways and GO terms.

Results: Out of 44 pairs analyzed for PDL1, 29 (65%) were ER+/HER2-, 3 (7%) ER-/HER2+, 6 (14%) ER-/HER2+ and 6 (14%) ER+/HER2- (TN). PDL1 expression (1%) was observed in the immune cell (IC) compartment in 11 (1%) ER+/HER2+, 4 (33%) ER-/HER2-, 2 (33%) ER-/HER2- and 11 (22%) TN samples. No significant differences were observed between primary and metastases. Out of 60 pairs analyzed by nanostring, the most, (40, 67%) were ER+/HER2+, 5 (8%) ER+/HER2+, 7 (12%) ER+/HER2+ and 8 (13%) TN. In the global population, we found that 162 genes were differentially expressed (fold-change >2) between primaries and metastasis. For the ER+/HER2+ subgroup, expression of 98 genes significantly differs in metastasis compare to primaries. No clear changes in pre-specified immune signatures were observed, possibly due to the high tumor heterogeneity, different treatments and small sample size. Interestingly, analyses of pre-specified gene signatures suggest that metastases have decreased Notch pathway, innate inflammation and TGFβ-activated fibroblasts signatures. Moreover, GO-enriched signature analyses suggest that B cell differentiation and type 1 IFN pathway are also reduced in metastases both in the global population and in ER+/HER2- tumors, thus suggesting a decreased immune defense during progression.

Conclusions: Our analysis failed to identify novel immune biomarkers of BC metastasis. However, these data point out that tumors could relax the immune system response during progression.

Clinical trial identification: NCT01377363.

Legal entity responsible for the study: GEICAM Spanish Breast Group.
Funding: Genentech Inc.
Disclosure: L. Molinero, H. Koeppen: Employee of Genentech. All authors have declared no conflicts of interest.