breast cancer, metastatic

**GENOMIC AND IMMUNE CHARACTERIZATION OF METASTATIC BREAST CANCER (MBC): AND ANCILLARY STUDY OF THE SAFIR01 & MOSCATO TRIALS**

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**Aim:** So far, little is known about immune and genomic landscape in metastatic breast cancer (mBC).

**Methods:** Patients were retrospectively identified from SAFIR01 and MOSCATO studies that performed molecular screening from a biopsy of a metastatic lesion. Whole exome sequencing (WES) was performed using Hi-Seq technology. Coverage was 50x and 100x for normal and tumoral tissue respectively. Bioinformatic analyses reported mutations and copy number alterations. Immune characterisation was determined by the presence of intratumoral and stromal TILs with PD1 and PDL1 expression assessed by IHC (internal protocol, Medimmune). We correlated tumor characteristics and immune and genomics data.

**Results:** 280 samples were stained for immune analyses. Using a 50% cut-off, few tumors presented intratumoral (n = 3/244, 1%) and stromal (n = 11/244, 5%) TILs. This rate was significantly higher in HER2+ tumors (stromal TIL, 16%; p = 0.0002). Positivity for PD1 (n = 14/252, 5%) and PDL1 (n = 7/255, 3%) were rare, compared to reported in other tumor types. A trend towards higher PDL1 was observed in HER2+ mBC (8.3%; p = 0.0653). Ninety-three samples were analysed for WES with 17 genes found mutated in >3 samples (p < 0.05). Except for PIK3CA, p53 and AKT1, these genes were mutated in <2% of samples in TCGA analyses of primary tumors and include NAV3 (n = 5), FRAS1 (n = 7), PI4KA (n = 5), PALB2 (n = 4), SCAPER (n = 4), PRKCB (n = 4), CACNA1S (n = 4), TSC1 (n = 4), GALC (n = 4), NAP1L1 (n = 4), PHACTR3 (n = 4). When analysing genes specifically mutated in metastases, an enrichment in pathways involved in MAPK (FDR = 0.0035), ER signalling (0.0004), lipids metabolism (0.0001) and GNRH signalling (FDR = 0.00018) was observed

**Conclusions:** This is the first study that assesses both immune and genomic landscapes in mBC. We observed that mBC dramatically differs from primary tumors, and is enriched in genes potentially involved in resistance mechanisms (ESR1, TSC1) or migration process (FRAS1, SCAPER). TILs, PD1, PDL1 are at very low frequency in metastatic lesions, except for Her2 ++ mBC. Our results suggest that other immune suppressor networks are involved in mBC. Therefore, CD73, CD39 and FoxP3 are being analysed and will be presented.

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