1520 First report of AURORA, the breast international group (BIG) molecular screening initiative for metastatic breast cancer (MBC) patients (pts)

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Background: MBC remains an incurable disease and the second cause of cancer mortality for women worldwide. While evidence supports molecular evolution of the disease during its life cycle, few molecular profiling studies provide comprehensive longitudinal molecular and clinical data.

Methods: AURORA is a European multicenter program enrolling MBC pts at first diagnosis or after 1 line of therapy for MBC. Central targeted gene sequencing (TGS) is performed on DNA extracted from primary tumor, a metastatic biopsy, whole blood and circulating tumor DNA (ctDNA) extracted from baseline plasma. From the paired tissue samples, RNA-seq and copy number variation analysis (CNV) are performed in batches. Fresh frozen metastatic biopsies, baseline and sequential plasma and serum samples are biobanked for future research. Up to 100 pts with "bone-only" disease are allowed without a bone biopsy. Pathology, clinical and follow-up data are collected, and pathology slides are scanned at high resolution. A report with the TGS data is annotated by a molecular advisory board (MAB) and provided to the treating physician.

Results: Curated molecular results are available for 381 pts recruited up to November 2017. Pathological subtype distribution is: 232 HR+/HER2-, 69 HER2+, 77 triple-negative (TNBC), 3 N/A. In addition to the whole MBC population, analysis has focused on relevant categories of clinical interest: de novo and bone-only MBC, endocrine resistance, pts treated with targeted agents (mTOR, CDK4/6, HER2 inhibitors), chemo-resistant TNBC and BC with late relapse. Clinically-relevant molecular categories were defined based on annotated aberrations: putative mechanisms of resistance alterations (ESR1, FGFR1, RB1), activating drivers (ERBB2, PIK3CA, AKT1), somatic and germline alterations in DNA damage repair genes (homologous recombination, mismatch repair). We report on subtype switching from primary BC to MBC, on molecular signatures, on genes and pathways disrupted in several of these categories, and on the added value of ctDNA profiling.

Conclusions: Analysis of data from the AURORA program sheds light on the molecular makeup of several clinically-relevant MBC categories.

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