https://doi.org/10.29289/259453942022V32S2006

MULTIGENE GERMLINE NGS TESTING IN TRIPLE-NEGATIVE BREAST CANCER (TNBC)

Rafael Canfield Brianese[1], Karina Miranda Santiago[1], Giovana Tardin Torrezan[1], Marina de Brot[2], José Claudio Casali da Rocha[3], Fabiana Baroni Alves Makdissi[4], Dirce Maria Carraro[1]

[1]A.C. Camargo Cancer Center, Laboratory of Clinical and Functional Genomics – São Paulo (SP), Brazil.
[2]A.C. Camargo Cancer Center, Pathology Department – São Paulo (SP), Brazil.
[3]A.C. Camargo Cancer Center, Oncogenetics Department – São Paulo (SP), Brazil.
[4]A.C. Camargo Cancer Center, Breast Surgery Department – São Paulo (SP), Brazil.

Objective: Triple-negative breast cancer (TNBC) is a breast cancer subtype strongly associated with BRCA1 germline mutations that are involved in homologous recombination DNA repair deficiency (HRD). Tumors with HRD may benefit from DNA-damage-inducing agents and PARP inhibitors. We aim to characterize germline mutations in HRD-related genes in TNBC and associate them with clinical data. **Methods:** TNBC patients (n=117) attending the A.C.Camargo Cancer Center had genetic testing performed by NGS (26–127 cancer predisposition gene panels) in leukocyte/saliva DNA. When possible, germline variants were screened in tumor DNA for loss-of-heterozygosity (LOH). **Results:** All patients were screened for germline variants: 26% (30/117) were Hereditary HRR-related, 21% BRCA1, 2% BRCA2, 2% PALB2, and 1% RAD51. For women diagnosed at a young age (<40 years), this rate increases to 38% (20/52), 31% BRCA1, 4% BRCA2, 2% PALB2, and 1% RAD51. In addition, 37% of cases presented variants of uncertain significance (VUS). LOH analysis showed that 100% (6/6) of pathogenic variants had LOH, while only 30% of VUS had LOH. Interestingly, for two cases with concurrent pathogenic and VUS, only the pathogenic variant exhibits LOH. Additionally, 47% (7/15) of the VUS with LOH were in HRR-related genes. **Conclusion:** The majority of germline variants in TNBC are in the BRCA1 gene, but other HRR-related genes also contribute to HRD. LOH analysis may help classify VUS regarding pathogenicity.

Keywords: Triple-negative breast cancer. Germline mutation. Loss of heterozygosity.