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1044 – Screening for the brazilian founder variant p.Arg337His in the tp53 gene and its co-segregation with XAF1-E134* in breast cancer patients treated by the unified health system in the midwest of Brazil

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Introduction: Breast cancer is the most common neoplasm among women worldwide, with 5% to 10% of cases associated with hereditary predisposition. Li-Fraumeni syndrome, caused by germline variants in the TP53 gene, stands out for its high risk of multiple and early-onset neoplasms. In Brazil, the founder variant p.Arg337His (R337H) has substantial epidemiological relevance and has been associated with breast cancer. Evidence suggests that the R337H variant occurs in linkage disequilibrium with the XAF1-E134* variant, with both being co-inherited within the same haplotype, which may contribute to modulating tumor risk and aggressiveness.

Objective: This study aimed to investigate the frequency of the R337H variant and evaluate its co-segregation with XAF1-E134* in patients diagnosed with breast cancer.

Methods: A total of 129 patients treated in the Unified Health System and referred to the Human Genetics Center of the Federal University of Goiás, according to the 2025 National Comprehensive Cancer Network (NCCN) criteria, were included. After obtaining informed consent, peripheral blood was collected for DNA extraction, followed by next-generation sequencing using a breast cancer-associated genetic panel. In patients who tested positive for R337H, genotyping of the XAF1-E134* variant was performed.

Results: Among the patients analyzed, seven (5.4%) were positive for R337H, and all showed co-segregation with XAF1-E134*. Ages ranged from 33 to 67 years (mean 45.3 years), with a predominance of cases under 45 years of age (57.1%). Multiple neoplasms were also observed in some patients, including lung tumors and one case of metachronous contralateral breast cancer diagnosed seven years later, reinforcing a pattern of greater clinical complexity.

Conclusion: The findings reinforce the relevance of genetic screening in breast cancer, especially in populations with a high frequency of the R337H variant, and suggest that the R337H-XAF1-E134* haplotype may contribute to more aggressive phenotypes.

Ethics: Approved by the Research Ethics Committees of Hospital das Clínicas, Federal University of Goiás (CAAE 50626315.6.0000.5078) and the Association for Cancer Control in Goiás (CAAE 50626315.6.3001.0031).

Keywords: breast neoplasms; Li-Fraumeni syndrome; tumor suppressor protein p53; genetic predisposition to disease.