

PRESENTATION: ORAL PRESENTATION (FAST PRESENTATION)

<https://doi.org/10.29289/259453942025V36S11189>

1189 – Prevalence of li-fraumeni syndrome in breast cancer patients in central Brazil

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Introduction: Pathogenic variants in the TP53 gene are among the most frequently associated genetic alterations in human malignancies and are the main cause of Li-Fraumeni syndrome. This syndrome is linked to multiple cancer types, with breast cancer being the most prevalent. The p.R337H variant shows high frequency in Southern and Southeastern Brazil, being observed in approximately 8% of breast cancer patients. However, its prevalence in the Central-West region remains poorly understood.

Objective: To describe the prevalence of TP53 variants in patients with a clinical profile consistent with Hereditary Breast and Ovarian Cancer syndrome (HBOC) in Central Brazil.

Methods: A total of 390 patients meeting clinical criteria for HBOC and negative for BRCA1 and BRCA2 variants were analyzed. Genetic analysis was performed using next-generation sequencing, with copy number variations confirmed by multiplex ligation-dependent probe amplification (MLPA).

Results: Among patients, 17 (4.36%) carried germline variants in TP53. The identified variants included missense variants p.Arg248Gln (1 case), p.Arg337His (12 cases), p.Arg337Cys (1 case), and p.Pro152Leu (2 cases), as well as a deletion spanning exons 2–11 (E2–11). This extensive deletion, confirmed by MLPA, compromises nearly the entire TP53 gene and is described here for the first time. The p.Arg337His variant accounted for 3.08% (12/390) of the cohort.

Conclusion: These findings support the hypothesis that the p.R337H founder variant originated in Southern Brazil and spread to the Southeast. In the Central-West region, a greater diversity of TP53 variants was observed, including rare variants and a novel large deletion. These results highlight the importance of comprehensive TP53 analysis, beyond targeted screening for p.R337H, and support its inclusion alongside BRCA1 and BRCA2 testing in high-risk HBOC patients. Furthermore, this study emphasizes the importance of identifying families with Li-Fraumeni syndrome, enabling appropriate genetic counseling, risk assessment, and early surveillance strategies.

Ethics: Research Ethics Committee Approval (CAAE 50626315.6.3001.0031; Approval No. 4.093.502), Association for Cancer Control in Goiás (ACCG).

Funding: National Council for Scientific and Technological Development (CNPq), Grant No. 380157/2024-1; Research Support Foundation of the State of Goiás (FAPEG), Research Program for the Unified Health System (PPSUS) 2017 Call, Grant No. 201710267001232.

Keywords: breast cancer; TP53; Li-Fraumeni syndrome; pR337H.