

<https://doi.org/10.29289/259453942024V34S1016>

Enrichment of intestinal bifidobacterium genus is associated with residual disease among patients with early-stage HER2+ breast cancer (BC) following neoadjuvant chemotherapy (NACT)

Ludmila Thommen Teles^{1,2}, Vitor Heidrich^{1,3}, Rosângela Vieira de Andrade⁴, Maria Sueli Soares Felipe⁴, Melissa Lole Da Cas Vita⁵, Thiago David Alves Pinto⁶, Anamaria Aranha Camargo^{1,3}, Romualdo Barroso de Sousa^{1,2}

¹Instituto Sírio-Libanês de Ensino e Pesquisa, Health Science Graduate Program.

²DASA Oncology, Brasília Hospital.

³Hospital Sírio-Libanês, Molecular Oncology Center.

⁴Universidade Católica de Brasília, Graduate Program in Genomic Sciences and Biotechnology.

⁵Hospital Sírio-Libanês.

⁶Universidade de Brasília, Health Science Graduate Program.

Objective: The objective of this study was to characterize the gut microbiome (GM) of patients with early-stage breast cancer (eBC) who underwent NACT and to evaluate its association with clinicopathological factors and outcomes.

Methodology: This was a prospective study conducted at two Brazilian Institutions. Fecal samples were collected at the baseline and prior to surgery. The GM was analyzed by 16S rRNA amplicon sequencing to characterize the alpha (InvSimpson indexes) and beta (weighted UniFrac distance) diversity, as well as the taxonomic composition. **Results:** Among the 55 female patients included, the median age was 49 years, 56% had stage III disease, and 23% had used antibiotics in the prior 2 months before starting NACT. Regarding the immunohistochemical profile, 34.5% (n=19) of patients had estrogen receptor-positive (ER+)/HER2-negative BC, 20% (n=11) had HER2-positive disease, and 45.5% (n=25) were triple-negative. All patients with ER+ had KI 67 >14%. There was no significant difference in alpha or beta-diversity between patients with or without pathological complete response, nor within clinical pathologic factors. The taxonomic profiling of fecal samples revealed that Lachnospiraceae at family and Blautia at genus levels were the most abundant taxon, and longitudinal samples collected during NACT showed no significant changes in GM composition. We found an enrichment for Clostridia sp. among patients who did not use antibiotics ($p < 0.05$, $p\text{FDR} \leq 0.25$). Notably, we found a higher abundance of Bifidobacterium genus ($p < 0.05$, $p\text{FDR} \leq 0.25$) in baseline samples from patients with HER2+ tumors who presented residual disease following NACT. **Conclusion:** This pilot study demonstrates the feasibility of GM sequencing in patients with eBC. We identified a significant association between the relative abundance of intestinal Bifidobacterium genus response to NACT among patients with HER2+ tumors. If validated, these results can help tailor the preoperative systemic treatment of patients with HER2+ eBC.

Keywords: breast cancer; neoadjuvant chemotherapy; gut microbiota.