https://doi.org/10.29289/259453942025V35S1006

Innovative platform for chemoresistance: advancing functional precision medicine in breast cancer

Martina Lichtenfels[1], Antônio Luiz Frasson[2], Julia Caroline Marcolin[1], Heloisa Rezende[3], Camila Alves da Silva[1], Alessandra Borba Anton de Souza[2], Caroline Brunetto de Farias[1], José Luiz Pedrini[4]

[1]Ziel Biosciences – Porto Alegre (RS), Brazil.
[2]Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Centro de Oncologia – Porto Alegre (RS), Brazil.
[3]Hospital HINJA – Volta Redonda (RJ), Brazil.
[4]Grupo Hospitalar Conceição, Centro da Mama – Porto Alegre (RS), Brazil.

Objective: To validate a novel in vitro chemoresistance platform by assessing the chemoresistance profiles of naïve-treatment breast cancer and residual tumors after neoadjuvant chemotherapy. **Methods:** Patients with primary invasive breast cancer (naïve-treatment) and residual disease after neoadjuvant chemotherapy were included. Tumor samples were obtained and cultured on the chemoresistance platform with several cytotoxic drugs used for breast cancer treatment. After 72 hours, cell viability was evaluated, with resistance categorized as low, intermediate, and high. **Results:** Samples from 70 patients with primary breast cancer and 27 with residual disease after neoadjuvant chemotherapy were tested using the chemoresistance platform. Patients undergoing upfront surgery exhibited significantly favorable clinicopathological characteristics and prognosis, such as older age, smaller tumors, negative axillary lymph node, and luminal subtype, compared to those with residual disease who presented younger age, larger tumors, positive axillary lymph node, and more triple-negative breast cancer. The chemoresistance platform revealed distinct resistance patterns, with tumors showing higher resistance to taxanes than to anthracyclines and cyclophosphamide ($p<0.05$). Residual disease after neoadjuvant chemotherapy exhibited significantly higher resistance to docetaxel, paclitaxel, doxorubicin, and cyclophosphamide than primary tumors, possibly indicating the acquisition of resistance during treatment. High resistance in residual disease after neoadjuvant chemotherapy correlated with a worse prognosis, with 8% experiencing local recurrence, 24% developing metastasis ($p=0.0001$), and 12% dying from disease progression ($p=0.0500$). Overall survival was 98.5% in the primary tumor group and 88% in the residual disease after neoadjuvant chemotherapy group. **Conclusion:** The chemoresistance platform effectively identified drug resistance patterns based on tumor characteristics, demonstrating the potential of functional precision medicine to personalize and improve breast cancer treatment by avoiding inefficient drugs, particularly in the context of treatment de-escalation.

Keywords: breast neoplasms; drug resistance; precision medicine.