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Intrinsic chemoresistance in luminal breast neoplasms: efficacy from an innovative *in vitro* chemoresistance platform

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Objective: The aim of this study was to validate an *in vitro* chemoresistance platform, BioversoÒ, to predict the responsiveness of luminal tumors to cytotoxic and target therapy drugs. **Methodology:** Patients with estrogen receptor (ER)-positive HER2-negative breast cancer (BC) who underwent upfront surgery were included. Fresh tumor samples were collected during surgery and dissociated to obtain the tumor cells. The tumor cells were cultured in the BioversoÒ with the drugs, and after 72h, cell viability was evaluated. The test result is defined as low, medium, and high resistance. **Results:** Samples from 31 patients diagnosed with ER+/HER- undergoing upfront surgery were tested in the BioversoÒ. A total of 18 (58%) patients presented luminal A tumors and 13 (42%) luminal B. A majority (83.8%) underwent breast-conserving surgery and sentinel lymph node biopsy (80%). The tumor staging revealed 61.2% T1, followed by 35.5% T2 and 3.3% T3 categories. Invasive ductal carcinoma was predominant (90%), with histologic grading of 23.4% grade 1, 63.3% grade 2, and 13.3% grade 3. Adjuvant chemotherapy, predominantly ACT regimen, was administered to 38.7% of the cohort. Over a median follow-up of 13 months, no recurrence was observed. The chemoresistance platform demonstrated higher rates of high resistance to taxanes (63.3% docetaxel and 70.9% paclitaxel), platin-based drugs (60% carboplatin and 46.4% cisplatin), and mTOR inhibitors (60% everolimus) compared with anthracyclines (22.6% doxorubicin and 25.8% epirubicin), cyclophosphamide (14.8%), and PARP inhibitors (36.8% Olaparib). The high resistance to taxanes, platin drugs, and everolimus corroborates existing literature, and the data regarding olaparib invite consideration for personalized treatment based on tumor biomarker profiling. **Conclusion:** The preliminary finding highlighted the capability of BioversoÒ to delineate distinct resistance patterns to both cytotoxic drugs and target therapies in luminal BC and suggest the potential influence of intrinsic tumor resistance in the differential response to BC treatments.

Keywords: breast neoplasms; drug therapy; taxanes; anthracyclines; drug resistance.