

**Chemosensitivity (CS) of patient (pt) breast cancer (BrCa) cells in vitro: correlation with prior chemotherapy (CT) and implications for personalized treatment planning**

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*Abstract:*

**Background:**

A predictive BrCa chemosensitivity assay will facilitate individualized treatment. Unlike older assays, the Microculture Kinetic (MiCK) assay measures active apoptosis. In order to determine the in vitro CS of pt BrCa cells, we tested pt tumor cells (tc) in vitro using the MiCK assay.

**Methods:**

Tumor excisions or biopsies were sent to a central laboratory, prepared using our previously described MiCK technology (Lab Invest 74: 557, 1996) and tc apoptosis was measured over 48 hours with various drugs. In vitro results were compared to clinical status. CS was measured in kinetic units of apoptosis (KU) with inactive <1.0, low CS 1.0-2.59, moderate CS 2.6-4.2, and high CS >4.2. Physicians (MDs) decided on CT without knowledge of MiCK results.

**Results:**

**57 pts were evaluable for MiCK results. CS to drugs for tc from pts with no prior CT was: paclitaxel (P) mean 1.2 KU, cyclophosphamide as 4-hydroxycyclophosphamide (4HC) 2.7, doxorubicin (Dox) 1.8, epirubicin (Epi) 2.1, docetaxel (Doc) 2.0, vinorelbine 0.9, gemcitabine (Gem) 0.7, liposomal D 1.4, carboplatin (Carbo) 1.7, cisplatin (Cis) 2.0, and topotecan 1.2. Combinations tested in some pts showed Carbo-P 2.6 KU and Cis-Gem 2.7. These results were compared to CS of tc from pts with prior CT. CS for pts with prior CT were P 1.8 KU, Doc 1.7, Dox 1.9, Epi 2.9, 4HC 1.1, and Vin 1.2. Although there was no difference between the CS of BrCa cells with or without prior CT for Dox or Epi, CS for 4HC was statistically significantly reduced after prior CT ( $p < 0.0003$ ). Overall, Doc had higher CS than P ( $p < 0.004$ ), Epi higher than Dox ( $p < 0.0001$ ), and 4HC higher than P ( $p < 0.0001$ ) or Carbo ( $p = 0.03$ ). However, in individual pts, P was higher or equal to Doc in 5/18 (28%), Dox higher or equal to Epi in 9/36 (25%), and P higher or equal to 4HC in 5/32 (16%).**

**Conclusions:**

**This indicates that the MiCK assay may be used to evaluate CS of BrCa cells from individual pts. After prior CT, BrCa cells show altered CS profiles, with persistent CS to Dox or Epi but reduced CS to 4HC. These data may be useful to MDs in selecting CT for individual pts. MiCK may also be useful in developing new drugs and new combination therapies.**

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