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Can we increase response rate (RR) and overall survival (OS) by individualizing chemotherapy in ovarian cancer (OC) –the role of new chemotherapy (CT) induced apoptosis assay

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Background: In order to develop an assay to improve OS of OC pts, we tested pt tumor cells (TC) using a novel CT-induced in vitro apoptotic assay (the Microculture Kinetic [MiCK] assay). This was a prospective blinded trial in which physicians selected CT without knowledge of MiCK assay results.

Methods: TC obtained at surgery were prepared and cultured with drugs as previously described (Lab Invest 74: 557, 1996). TC apoptosis from single drugs or combination regimens was measured over 48 hours. Assay results were compared to OS and RR following CT. The assay results were measured as kinetic units of apoptosis (KU) with $> \text{or} = 1.7$ KU defined highly active vs less active < 1.7 KU. The best CT was defined as apoptosis > 0.57 KU (> 1 measurement s.d.) higher than other drugs.

Results: A total 128 pts were evaluable for MiCK results. Combination paclitaxel (Pac) + carboplatin (C) gave significantly more apoptosis 2.6 KU vs single agent Pac 1.8 KU or C 1.4 KU ($p < 0.0001$). However, single drug Pac or C was more effective than Pac+C in 28% and was equal to Pac+C in 9% of pts. In 46% of pts, another drug or combination produced more apoptosis compared to Pac+C. When comparing CT for all stages, OS was significantly better at 24 months in 92% pts who received best CT vs only 76% in pts who received a non-best assay predicted CT ($p = 0.01$). There was a significantly higher overall RR 82% in pts who received the best CT in the assay vs 54% in pts who received a non-best assay predicted CT ($p = 0.04$). In stage 3 or 4 (54/90) OC pts treated with highly active CT by assay had a significantly increased OS (94% alive at 24 mo) compared those with less active CT (77% alive; $p = 0.02$). The hazard ratio for death in pts receiving highly active CT was 0.17 (95% CI 0.03-0.92). The CR, PR, SD, and nonrelapse rate was 85% for pts with highly active CT, compared to 57% for those pts receiving less active CT ($p = 0.03$).

Conclusions: The drug induced apoptosis MiCK assay is useful in predicting which CT will result in increased OS and increased RR in this study. This assay can help oncologists to select the best CT for individual pts. This assay may help develop new CT regimens and select responsive pts.

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