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In vitro chemosensitivity (CS) testing in endometrial carcinoma (ECa) of single and combination chemotherapy (CT) using the novel microculture kinetic (MiCK) apoptosis assay: Implications for ECa treatment (Rx)

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Background:

The in vitro apoptosis MiCK assay has been used to predict single or combination CT response in ovarian cancer patients (pts). The feasibility of MiCK in ECa was addressed in an exploratory, prospective trial.

Methods:

With Internal Review Board approval, ECa tumor cells from staging hysterectomies were sent to a central laboratory. Single cell suspensions of viable ECa cells were created. 100,000-500,000 cells were plated in individual wells. Single and combination regimens were tested: doxorubicin (D), cisplatin (C), and paclitaxel (P) [control arm for the current Gynecologic Oncology Group (GOG) ECa phase III trial], the combination of carboplatin (Ca) and P, versus single agent testing with P, Ca, D, C, ifosfamide (I), and vincristine (V) [all active CT in GOG trials]. Apoptosis was measured continuously over 48 hours (Lab Invest 74: 557-570, 1996). CS response was considered high when > 4.0 KU (kinetic units of apoptosis) and not sensitive when < 1.0 KU.

Results:

Fifteen of nineteen pts were evaluable by the MiCK assay. The highest mean CS of 4.3 KU was noted in the triple combination of C+D+P with a lower mean CS of 3.4 for Ca+P.

KU Values for ECa Panel of Agents

Rank	Regimen	n	Mean	Max
1.	C+D+P	7	4.3	6.6
2.	Ca+P	8	3.4	5.4
3.	P	13	3.1	6.0
4.	C	12	2.9	9.3
5.	I	14	2.5	9.9
6.	D	13	1.9	4.3
7.	Ca	9	1.8	5.1
8.	V	7	1.0	3.5

Combination CT had higher CS than single drug CT. However, in 25% of pts a single drug had higher CS than the combination CT. C+D+P CS was higher than single agent D. (p=0.02).

Conclusions:

Using the above panel of agents simulating clinical dose regimens, the novel MiCK assay was successfully employed as an in vitro CS test for ECa response. CS results were compatible with GOG trial findings. Although most pts are best treated with combination CT, 25% of pts might be treated with single agent CT selected by the MiCK assay. It appears to have high activity as a single agent. The MiCK assay may be useful both for future new drug testing and individualizing ECa pts CT management.

