

CLIA ID # 99D1030993

CAP ID # 7186701

Patient : Patient X.
 Date of birth : 03/12/1943
 Specimen ID : HP11-2239
 Specimen type : omentum

Collected : 04/27/2011
 Received : 04/28/2011
 Physician : Chad Hamilton
 Institution : Walter Reed Army Medical Center

Clinical

68-year-old female with a diagnosis of uterine cancer endometrioid grade 3 stage 1A, since 03/2009, currently in relapse. No prior chemotherapy.

Recommendation

Based on the results of the MiCK assay the combination of Cytoxan with doxorubicin is the best chemotherapy regimen for the patient. Velcade, as a single drug, would be a good alternative.

MiCK Assay Results

Drug tested	Max. Resp. (KU)	Resp. level	Drug tested	Max. Resp. (KU)	Resp. level
4HC(cytoxan)+Doxorubicin	5.2	Sensitive	Taxol	2.2	Low to moderate
Velcade	4.6	Moderate	Irinotecan	1.8	Low
Doxorubicin	4.0		Vinorelbine	1.8	
Cisplatin	4.0		Carboplatin+Taxotere	1.8	
Gleevec(imatinib)	3.7		4HI(ifosfamide)+Taxol	1.8	
Sunitinib	3.7		Etoposide	1.6	
Melphalan	3.4		Vincristine	1.6	
Carboplatin+Taxol	3.4		Carboplatin	1.5	
Dactinomycin	3.4		Alimta	1.2	
4HI(ifosfamide)	3.1		Caelyx(Doxil)	0.9	
Cisplatin+Gemcitabine	3.1		Carboplatin+Gemcitabine	0.9	
Cisplatin+Taxotere	2.8	5-Fluorouracil	0.6	Nonsensitive	
Oxaliplatin	2.5	Gemcitabine	0.6		
4HC(cytoxan)	2.5	Low to moderate	Hexamethylmelamine		0.3
Taxotere	2.5		Abraxane		0.3
Topotecan	2.2		Sorafenib		0.0

Interpretation

Recurrent endometrial carcinoma, omental biopsy:

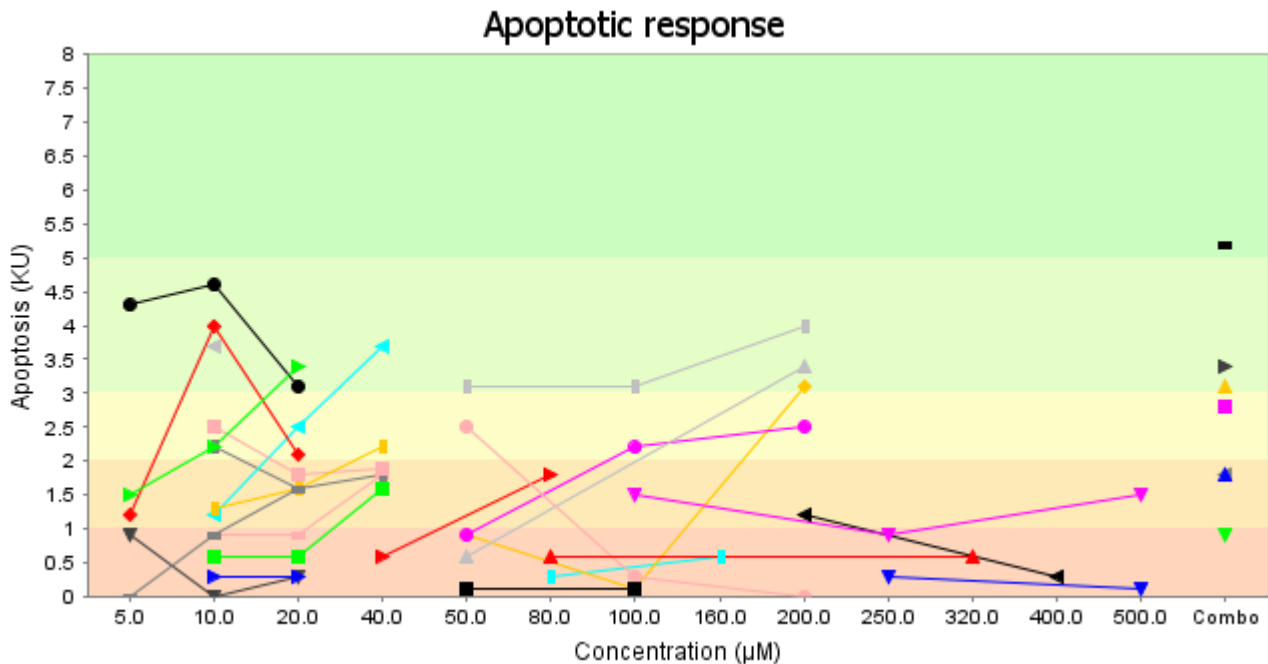
1. A population of cytologically malignant epithelial cells is present.
2. In the MiCK assay the tumor was most sensitive to the drug combination of Cytoxan with doxorubicin giving 5.2 KU, the single drug Velcade was nearly as effective giving 4.6KU of apoptosis.
3. The extent of the response was consistent with a moderate level of sensitivity to these drugs.
4. The responses to the additional drugs and combinations listed in the Table and Graph were consistent with lower levels of effectiveness.
5. The Table and Graph below show all drugs tested with their associated KU values.

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Legend: ND: data not displayed NS: not sensitive			
4HC(cytoxan)+Doxorubicin	5.2	Cisplatin+Taxotere	2.8
Velcade	4.6	Oxaliplatin	2.5
Doxorubicin	4.0	4HC(cytoxan)	2.5
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4HI(ifosfamide)	3.1	4HI(ifosfamide)+ Taxol	1.8
Cisplatin+Gemcitabine	3.1	Etoposide	1.6
		Vincristine	1.6
		Carboplatin	1.5
		Alimta	1.2
		Caelyx(Doxil)	0.9
		Carboplatin+Gemcitabine	0.9
		5-Fluorouracil	0.6
		Gemcitabine	0.6
		Hexamethylmelamine	0.3
		Abraxane	0.3
		Sorafenib	0.0

Comments

Viable malignant cells collected from the specimen were tested for their sensitivity to multiple single drugs and drug combination at three concentrations each.

Cytoxan and ifosfamide require hepatic metabolic transformation to their active metabolites, 4HC and 4 HI, respectively. For the assay the active metabolites were used.

The MiCK assay identifies chemotherapy drugs that are most effective in killing tumor cells by apoptosis and

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quantitates the level of effectiveness using our kinetic units, KUs. In this study the drug combination of Cytoxan with doxorubicin gave the highest level of apoptosis followed closely by the single drug Velcade, giving 5.2 and 4.6 KUs respectively. Responses between 3.0 and 5.0 KUs are considered to be in the moderate range. At least a partial clinical response should be expected with drugs in this range of effectiveness. The other drugs and combinations delivered lower levels of apoptosis.

All tested chemotherapy drugs induced apoptosis in an appropriate cell control.

Microscopic/Immunophenotypic studies

The Pap stained cytospin preparation of the cells contains a poorly differentiated tumor of loosely adherent cells occurring as single cells and small clusters. There is prominent anisocytosis of the cells. Most cells have abundant cytoplasm, vacuoles are seen in occasional cells. The N/C ratio is clearly elevated although most cells have abundant cytoplasm. Nuclei are large, single, and hyperchromatic with occasional nucleoli being noted. The tumor is strongly CK positive and ~25% of the cells are KI-67 positive, which is a high fraction.

Attending Pathologist

Medical Director

DiaTech Oncology, LLC

Electronically signed on 07-07-2011

The pathologist's signature on this report indicates that the case was personally reviewed and the findings confirmed by the attending pathologist. This test was performed at DiaTech Clinical Pathology Laboratory. This laboratory is certified under CAP and CLIA-88 and is qualified to perform high complexity clinical testings. The MiCK assay measures drug induced apoptosis and its performance characteristics were determined at Vanderbilt University and at DiaTech Oncology. Clinical use of the MiCK assay is based on a statistically significant increase in CR rate and overall survival of AML patients whose treatment protocol included a drug to which the patient's tumor cells were sensitive in the assay. When used with solid tumors, the MiCK assay is expected to identify drugs most effective in killing patient's tumor cells by apoptosis. This test has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such approval was not required.

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