

CLIA ID # 99D1030993

CAP ID # 7186701

Patient : Patient X
 Date of birth : 04/14/1946
 Specimen ID : HP10-2520
 Specimen type : Fluid

Collected : 08/04/2010
 Received : 08/05/2010
 Physician : Dr. X
 Institution : Hospital X

Clinical

64-year-old female with a diagnosis of breast cancer since 02/2009, currently in relapse. Previous treatment with taxotere, carboplatin, herceptin.

Recommendation

Based on the results of the MiCK assay cisplatin is the clear single agent of choice. Although not tested in combination with cisplatin, taxotere, vinorelbine, and vinblastine also demonstrated significant activity and could possibly be used in combination with cisplatin with an potential synergistic effect.

MiCK Assay Results

Drug tested	Max. Resp. (KU)	Resp. level
Cisplatin	5.3	Sensitive
Vinblastine	4.25	Moderate
Vinorelbine	4.25	
Taxotere	4.25	
Taxol	2.91	Low to Moderate
Mitoxantrone	2.67	
Abraxane	2.39	
Ixabepilone	2.15	
4HC(cytoxan)	2.15	
Doxorubicin	2.15	Low
5DFUR	1.86	
Epirubicin	1.86	
Carboplatin	1.34	
Gemcitabine	1.34	Nonsensitive
Etoposide	0.0	
5-Fluorouracil	0.0	
Methotrexate	0.0	

Interpretation

Recurrent breast carcinoma, pleural effusion:

1. A population of cells with morphological and immunophenotypic features of an epithelial malignancy is present.
2. In the MiCK assay, the patient’s tumor cells were most sensitive to the single drug cisplatin, giving 5.3KU of apoptosis.
3. Based on the MICK assay the extent of the response was consistent with high sensitivity of the tumor to this single agent.

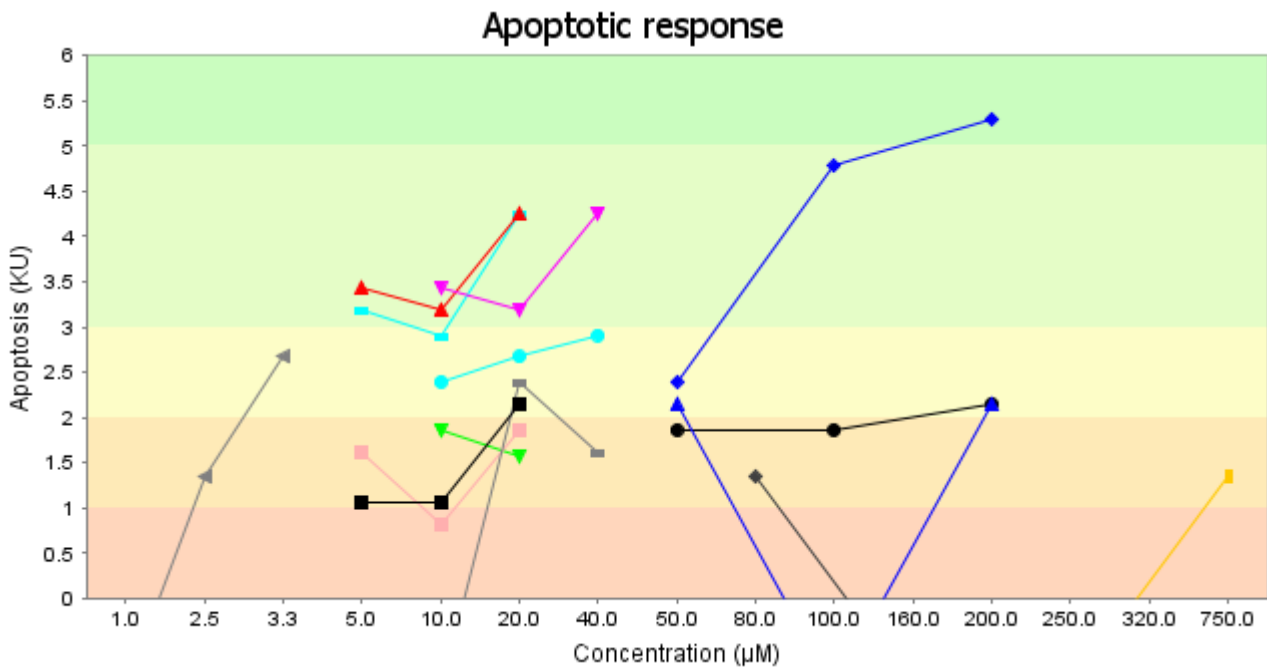
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- Responses to other reagents were consistent with lower sensitivity to these reagents.
- The table and graph below show all reagents tested, their concentrations, and the MICK assay results.



Legend:		NS: data not shown	
◆ Cisplatin	5.3	▬ Abraxane	2.39
▬ Vinblastine	4.25	● Ixabepilone	2.15
▲ Vinorelbine	4.25	▲ 4HC(cytoxan)	2.15
▼ Taxotere	4.25	■ Doxorubicin	2.15
● Taxol	2.91	▼ 5DFUR	1.86
▲ Mitoxantrone	2.67	▬ Epirubicin	1.86
		◆ Carboplatin	1.34
		◆ Gemcitabine	1.34
		▲ Etoposide	0.0
		▬ 5-Fluorouracil	0.0
		▲ Methotrexate	0.0

Comments

Viable neoplastic cells collected from the specimen were tested for their sensitivity to multiple single drugs at three concentrations. Of note, the alkylating agent cytoxan requires hepatic metabolic transformation to the active metabolite, 4HC, and therefore cannot be tested directly invitro. For the MICK assay the active metabolite, 4HC, was used. The MICK assay identifies chemotherapy reagents that are most effective in killing malignant cells by inducing apoptosis, it specifically identifies and quantitates apoptotic cells. In this study, cisplatin was most effective in inducing apoptosis causing 5.3KU maximal response which is consistent with high sensitivity of the tumor cells to this reagent. Of note, a response of greater than 5.0KU is consistent with a high drug sensitivity and has previously been associated with a complete clinical response to chemotherapy. Additionally the single drugs Taxotere, vinorelbine, and

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vinblastine gave moderate levels of apoptosis. Other tested reagents induced lower levels of apoptosis. All tested chemotherapy reagents induced apoptosis in appropriate control cell lines.

Microscopic/Immunophenotypic studies

The H&E stained cytospin preparations of the fluid contain a near pure population after purification of single malignant cells of moderate size. Most cells have abundant basophilic cytoplasm. Binucleate cells are frequent. Nuclear chromatin is dense with irregular distribution. A single prominent nucleolus is generally present. The tumor is strongly positive for pan cytokeratin. Ki67 is positive in 10-15% of the cells. ER receptors are positive in <3% of the tumor cells. All ICCs are interpreted in light of appropriate controls. The final viability of the cells is 100%.

The report was faxed to Dr. X's office on 01-05-2010.

Attending pathologist
DiaTech Oncology, LLC
514-389-5372 office

Electronically signed on 01/05/2010

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.

DiaTech Oncology, 740 Dr. Penfield Ave. Suite 4200, Montreal, Quebec, Canada www.diatech-oncology.com