

CLIA ID # 99D1030993

CAP ID # 7186701

Patient : Patient X

Collected : 10/15/2008

Date of birth : 12/20/1951

Received : 10/16/2008

Specimen ID : HP08-2474

Physician : Anastasios Raptis

Specimen type : Right chest wall nodule

Institution : University of Pittsburgh

Clinical

56-year-old female with a diagnosis of stage IV leiomyosarcoma since more than 8 years, now in relapse. Previous chemotherapy with Gemcitabine+Taxotere resulting in complete response, most recent on 09/17/2008 with ET-743.

Recommendation

Based on the result of the MiCK assay Cytoxan, ifosfamide, daunorubicin and doxorubicin either singly or in combination, would be the most advantageous to the patient. If used in combination a synergistic response with a greater degree of apoptosis might reasonably be expected (although not specifically tested that way).

MiCK Assay Results

Drug tested	Max. Resp. (KU)	Resp. level
4HC(cytoxan)	4.7	Moderate
4HI(ifosfamide)	3.9	
Daunorubicin	3.8	
Taxol	3.3	
Doxorubicin	3.3	
Cisplatin	1.5	Low
Epirubicin	0.9	Nonsensitive
Gleevec(imatinib)	0.9	
Caelyx(Doxil)	0.9	
Oxaliplatin	0.0	
Carboplatin	0.0	
Vincristine	0.0	
Vnbl	0.0	
Methotrexate	0.0	
Etoposide	0.0	
Dactinomycin	0.0	

Interpretation

Recurrent leiomyosarcoma tissue biopsy:

- 1.
2. A population of cells with morphologic and immunocytochemical features of a leiomyosarcoma is present.
3. In the MICK assay the tumor cells were most sensitive to Cytoxan (4HC)and nearly as sensitive to ifosfamide(4HI). Doxorubicin, daunorubicin, and taxol also showed significant, but lower activity.
4. In the MICK assay the extent of the response was consistent with a moderate sensitivity of the tumor cells to these agents. Please see the Comment section for further detail.

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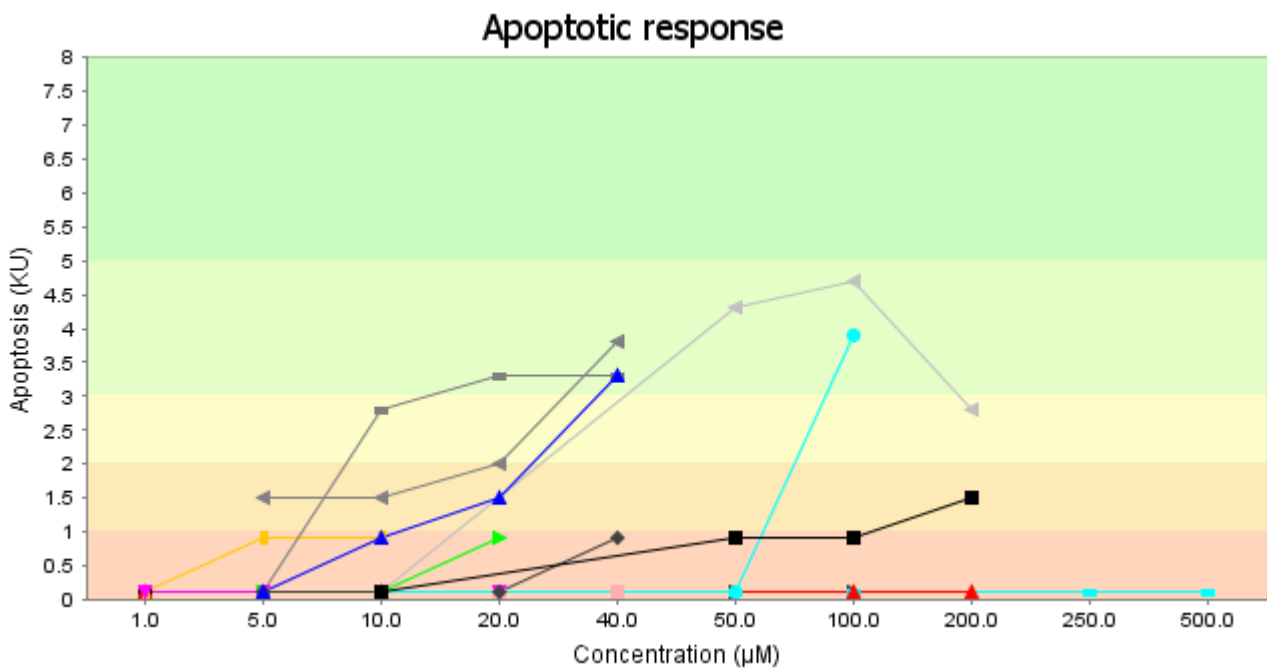
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5. Responses to the other tested reagents were consistent with lower sensitivity of the tumor cells to these reagents.
 6. The Table and Graph below show all tested reagents, concentrations, and the MICK assay results.



Legend:		ND: data not displayed	NS: not sensitive
← 4HC(cytoxan)	4.7	✚ Epirubicin	0.9
● 4HI(ifosfamide)	3.9	➤ Gleevec(imatinib)	0.9
← Daunorubicin	3.8	◆ Caelyx(Doxil)	0.9
■ Taxol	3.3	➤ Oxaliplatin	0.0
▲ Doxorubicin	3.3	■ Carboplatin	0.0
■ Cisplatin	1.5	◆ Vincristine	0.0
		● Vnbl	0.0
		▲ Methotrexate	0.0
		■ Etoposide	0.0
		▼ Dactinomycin	0.0

Comments

Viable neoplastic cells collected from the specimen were tested for their sensitivity to multiple single agents at multiple concentrations of these agents. Of note, the alkylating agents cyclophosphamide and ifosfamide require hepatic metabolic transformation to their active metabolite, 4HC and 4HI respectively and therefore cannot be tested directly in vitro. For the MICK assay their active metabolites, 4HC and 4HI respectively, were 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, cytoxan(4HC) and ifosphamide(4HI)

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were most effective in inducing apoptosis causing 4.7 and 3.9KU maximal response respectively which is consistent with moderate sensitivity of the tumor cells to these reagents. Of note, responses from 3.0 to 5.0 are consistent with a moderate drug sensitivity and have previously been associated with a partial clinical response to chemotherapy. Other tested reagents induced lower levels of apoptosis.

All tested chemotherapy reagents induced apoptosis in appropriate control cell lines.

Microscopic/Immunophenotypic studies

Cytospin preparations of the tumor contain a pleomorphic tumor cell population which is predominately mononuclear but does have binucleate and multinucleate cells. Cytoplasm is generally abundant but occasional cells with a very high N/C ratio are present. Nuclear chromatin is distinctly coarse, nucleoli are not noted. The tumor is strongly positive for vimentin and desmin and also is negative for pancytokeratin. Ki67 has a high positive fraction.

Attending pathologist

Medical Director

DiaTech Oncology, LLC

Electronically signed on 10-11-2011

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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