

CLIA ID # 99D1030993

CAP ID # 7186701

Patient : Patient X

Collected : 08/15/2011

Date of birth : 08/25/1948

Received : 08/16/2011

Specimen ID : HP11-2369

Physician : Eric Feldman

Specimen type : Whole blood

Institution : New York Presbyterian

Clinical

62-year-old female with a diagnosis of AML.

Recommendation

Based on the results of the MiCK assay there are several drugs/drug combinations that are likely to be very successful with the patient. Any single drug or drug combination inducing greater than 5.0KUs is considered to be highly effective and likely to be successful. The patient's blasts responded to many drugs and drug combinations with KUs well in excess of 5.0KUs so there is a wide range of options available for the chemotherapy regimen.

Since we had so many cells to work with we tested all typical AML drug regimen plus a number of "off label" drugs not typically used for AML.

Of significant note for the patient's therapy is that the addition of cytarabine adds little positive effect in the drug duets. For instance with idarubicin and cytarabine there was a KU value of 12.7, but with idarubicin alone the measured KUs was 12.6KUs. Essentially the cytarabine added nothing but increased toxicity.

If the patient cannot tolerate the high toxicity of many of these drugs, Cytosan gave 7.2KUs of apoptosis, not as high as some of the other drugs but still highly effective.

If there are any questions about the results or report I would be happy to speak with you about them. Direct office line is 514 398 5372.

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MiCK Assay Results

Drug tested	Max. Resp. (KU)	Resp. level	Drug tested	Max. Resp. (KU)	Resp. level
Vidaza	13.7	Sensitive	Mercaptopurine+Methotrexate+V...	4.5	Moderate
4HC(cytosan)+Fludarabine	13.1		Methotrexate+Vincristine	4.1	
4HI(ifosfamide)	12.9		Mitoxantrone	3.4	
Cytarabine+Idarubicin	12.7		Mitoxantrone+Etoposide	3.3	
Doxorubicin	12.6		Etoposide	3.1	
Idarubicin	12.6		Cytarabine+Mitoxantrone	2.6	
Daunorubicin	12.3		Gleevec(imatinib)	2.4	
Cytarabine+Oxaliplatin+Fludara...	11.5		Cytarabine	1.9	
Cytarabine+Daunorubicin	11.2		Methotrexate	1.7	
Oxaliplatin	10.4		Cytarabine+Fludarabine	1.5	
Cytarabine+Vidaza	9.4		Cytarabine+Decitabine	0.0	
Velcade	9.2		Fludarabine+Etoposide	0.0	
Bendamustine	9.0		Chlorambucil	0.0	
Cytarabine+Velcade	8.6		ArsenicO3	0.0	
4HC(cytosan)+Doxorubicin+Vinc...	8.5		Hydroxyurea	0.0	
4HC(cytosan)	7.2		Mercaptopurine	0.0	
Cytarabine+Etoposide	6.7		Vincristine	0.0	
Thioguanine	5.5		Fludarabine	0.0	
		Decitabine	0.0		

Interpretation

Acute myelogenous leukemia, peripheral blood:

1. A population of cells with morphological and immunologic features of acute myelomonocytic leukemia is present.
2. In the MiCK assay, the patient's tumor cells were highly sensitive to multiple single drugs and drug combination, giving KU values greater than 5.0 of apoptosis. Any drug or drug combination giving a KU value greater than 5.0KUs is considered to be highly effective and there were several drugs/ combinations that were.
3. Based on the MiCK assay the extent of the response was consistent with high sensitivity of the tumor to these drugs/combinations.
4. Responses to other reagents were consistent with lower sensitivity to these reagents.
5. The Table and Graph below show all reagents tested, their concentrations, and the MiCK assay results.

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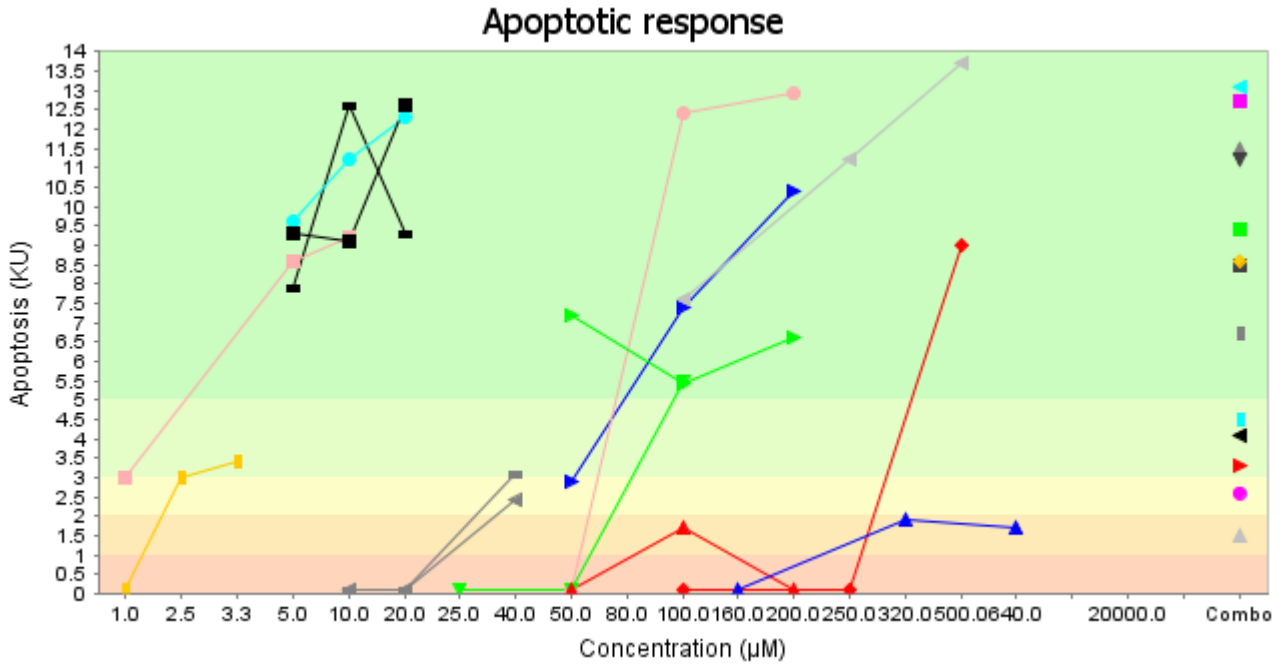
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Legend:		ND: data not displayed	NS: not sensitive
◀ Vidaza	13.7	▶ 4HC(cytoxan)	7.2 ND ArsenicO3 0.0
◀ 4HI(ifosfamide)	12.9	▶ Thioguanine	5.5 ND Hydroxyurea 0.0
◀ Doxorubicin	12.6	▶ Mitoxantrone	3.4 ND Mercaptopurine 0.0
◀ Idarubicin	12.6	▶ Etoposide	3.1 ND Vincristine 0.0
◀ Daunorubicin	12.3	▶ Gleevec(imatinib)	2.4 ND Fludarabine 0.0
▶ Oxaliplatin	10.4	▶ Cytarabine	1.9 ND Decitabine 0.0
◀ Velcade	9.2	▶ Methotrexate	1.7
▶ Bendamustine	9.0	ND Chlorambucil	0.0
▶ 4HC(cytoxan)+Fludarabine	13.1	▶ Mercaptopurine+Methotrexate+Vincristine	4.5
▶ Cytarabine+Idarubicin	12.7	▶ Methotrexate+Vincristine	4.1
▶ Cytarabine+Oxaliplatin+Fludarabine	11.5	▶ Mitoxantrone+Etoposide	3.3
▶ Cytarabine+Daunorubicin	11.2	▶ Cytarabine+Mitoxantrone	2.6
▶ Cytarabine+Vidaza	9.4	▶ Cytarabine+Fludarabine	1.5
▶ Cytarabine+Velcade	8.6	NS Cytarabine+Decitabine	0.0
▶ 4HC(cytoxan)+Doxorubicin+Vincristine	8.5	NS Fludarabine+Etoposide	0.0
▶ Cytarabine+Etoposide	6.7		

Comments

Since we were able to isolate a large number of blasts/blast equivalents from the peripheral blood we were able to test all of the typical AML drug regimens as well as non typical drugs. Fortunately, the blasts were unusually

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susceptible to the chemotherapy drugs, typical and atypical. So there are several options available for the patient's chemotherapy regimen.

The Microculture Kinetic (MiCK) assay is a "second generation" of chemosensitivity assays that is now available. Unlike the 1st generation assays (resistance assays) the MiCK assay is able to tell the treating oncologist which drug(s) are effective with an 82% PPV and which ones are not with a 100% NPV. These figures are derived from a soon to be published, recently completed study on AML done at the University of Pittsburgh and Vanderbilt University.

Microscopic/Immunophenotypic studies

The Wright stained peripheral blood smear contains circulating blasts and immature monocytoid cells. Auer rods are not identified. Cytologic features are clearly monocytoid. Flow cytometric studies indicate that the blasts are HLA-DR, CD33, CD14, CD34, CD38, and CD117 positive.

The report was faxed to Dr Feldman's office and emailed to Ms Jane Stanley on 8-17-2011.

Attending pathologist

Medical Director

DiaTech Oncology, LLC

Electronically signed on 08-18-2011

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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