

CLIA ID # 99D1030993

CAP ID # 7186701

Patient : Patient X
 Date of birth : 10/09/1935
 Specimen ID : HP07-2597
 Specimen type : Lymph node
 Center

Collected : 11/28/2010
 Received : 11/29/2010
 Physician : Dr. X
 Institution : Central Florida Regional Medical

Clinical

76-year-old male with a diagnosis of non-Hodgkin lymphoma since 12/2008. Prior chemotherapy included Rituxan, Adriamycin, Cytoxan, VCR and Prednisone.

Recommendation

Based on the results of this study, Velcade should be included in the treatment protocol if clinically indicated. The combination of Velcade/epirubicin is also reasonable to consider.

MiCK Assay Results

Drug tested	Max. Resp. (KU)	Resp. level
Velcade	5.8	Sensitive
Epirubicin	4.3	Moderate
Doxorubicin	2.9	Low to moderate
Fludarabine	2.5	
4HC(cytoxan)	2.0	
Vincristine	2.0	Low
Dexamethasone	1.9	
Mitoxantrone	1.9	
Caelyx(Doxil)	1.6	
pentostatin	1.3	
Melphalan	1.2	
Etoposide	1.2	
Cladribine	1.2	Nonsensitive
Idarubicin	0.6	

Interpretation

Lymph node, site not specified, biopsy:

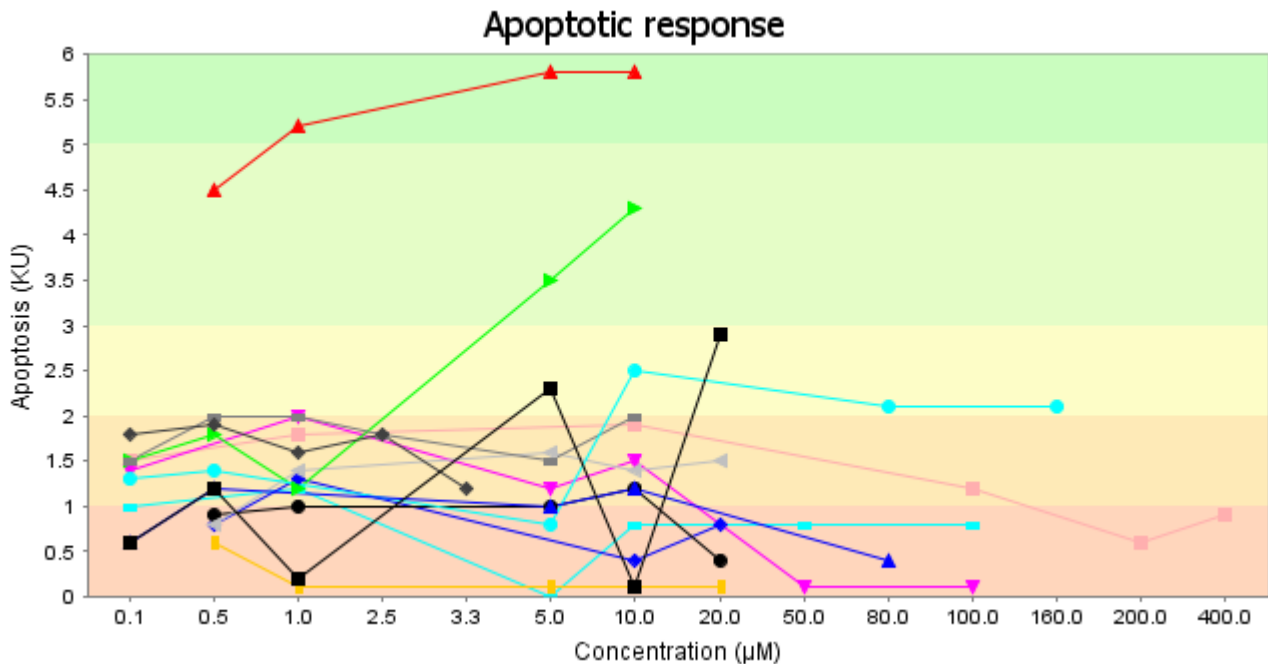
1. Population of abnormal kappa light chain-restricted CD5-positive B lymphocytes identified (see comment).
2. In the MiCK assay, the patient's tumor cells were most sensitive to Velcade (see comment).
3. Responses to other tested agents were consistent with a lower sensitivity of the patient's neoplastic cells to these compounds (see comment).

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Legend: ND: data not displayed NS: not sensitive			
▲ Velcade	5.8	■ Vincristine	2.0
▲ Epirubicin	4.3	■ Dexamethasone	1.9
■ Doxorubicin	2.9	■ Mitoxantrone	1.9
● Fludarabine	2.5	■ Caelyx(Doxil)	1.8
▼ 4HC(cytosan)	2.0	● pentostatin	1.3
■ Melphalan	1.2	■ Etoposide	1.2
■ Idarubicin	0.8	■ Cladribine	1.2

Comments

Viable neoplastic cells collected from the specimen were tested for their sensitivity to multiple doses of cladribine(2CDA), Cytosan(4HC), dexamethasone, Doxil, doxorubicin, epirubicin, fludarabine, mitoxantrone, pentostatin, Velcade, vincristine and etoposide(VP16) as single agents. Of note, alkylating agent cyclofosamide requires metabolic transformation by hepatocytes and, thus, cannot be tested in vitro. Synthetic active metabolite of cyclofosamide (4HC) was used in this study.

The MiCK assay identifies drugs that are most effective in killing patient's tumor cells by apoptosis. The extent of drug induced apoptosis is measured in Kinetic Units. In this study, Velcade was the most effective inducer of apoptosis causing 5.8 KU maximal response. Of note, responses from 3 to 5 KU are consistent with a moderate drug sensitivity

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of tumor cells and have been previously seen in cancer patients with partial clinical response to chemotherapy. However, for non-Hodgkin's lymphoma patients, statistical correlation between the extent of Velcade induced apoptosis and treatment outcome has not been established. A table in the "Interpretation" section shows maximal apoptotic responses achieved with each agent.

All tested agents induced apoptosis in a control cell line.

Microscopic/Immunophenotypic studies

Wright-Giemsa stained preparations of the disaggregated tissue show a mixture of intermediate to large-sized atypical lymphocytes with irregular nuclear contours, variably abundant light blue cytoplasm, and occasional nucleoli. Flow cytometry studies detected an abnormal kappa light chain-restricted B cell population co-expressing intermediate CD5, bright CD23, low CD20, and showing no significant FMC7 expression. The immunophenotype of the B cells is most consistent with B-cell SLL/CLL. However, increased cell size suggests progression to a higher grade neoplasm. By flow cytometry, specimen contains 99% lymphocytes. Abnormal kappa light chainrestricted B cells account for 98.5% of the total lymphocytes.

Attending pathologist
Medical Director
DiaTech Oncology, LLC

Electronically signed on 11-29-2011

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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