Haematologica. 2009 Nov;94(11):1569-80.

# Loss of HLA-DR expression and immunoblastic morphology predict adverse outcome in diffuse large B-cell lymphoma - analyses of cases from two prospective randomized clinical trials.

Bernd HW, Ziepert M, Thorns C, Klapper W, Wacker HH, Hummel M, Stein H, Hansmann ML, Ott G, Rosenwald A, Müller-Hermelink HK, Barth TF, Möller P, Cogliatti SB, Pfreundschuh M, Schmitz N, Trümper L, Höller S, Löffler M, Feller AC; German High Grade Non-Hodgkin's Lymphoma Study Group (DSHNHL).

**Source**

Institute of Pathology, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160 D-23538 Lübeck, Germany. bernd@patho.uni-lue-beck.de

**Abstract**

**BACKGROUND:** Research on prognostically relevant immunohistochemical markers in diffuse large B-cell lymphomas has mostly been performed on retrospectively collected clinical data. This is also true for immunohistochemical classifiers that are thought to reflect the cell-of-origin subclassification of gene expression studies. In order to obtain deeper insight into the heterogeneous prognosis of diffuse large B-cell lymphomas and to validate a previously published immunohistochemical classifier, we analyzed data from a large set of cases from prospective clinical trials with long-term follow-up.

**DESIGN AND METHODS:** We performed morphological and extensive immunohistochemical analyses in 414 cases of diffuse large B-cell lymphoma from two prospective randomized clinical trials (NHL-B1/B2, Germany). Classification into germinal center and non-germinal center subtypes of B-cell lymphoma was based on the expression pattern of CD10, BCL6, and IRF4. Multivariate analyses were performed adjusting for the factors in the International Prognostic Index.

**RESULTS:** Analyzing 20 different epitopes on tissue microarrays, expression of HLA-DR, presence of CD23(+) follicular dendritic cell meshworks, and monotypic light chain expression emerged as International Prognostic Index-independent markers of superior overall survival. Immunoblastic morphology was found to be related to poor event-free survival. The non-germinal center subtype, according to the three-epitope classifier (CD10, BCL6, and IRF4) did not have prognostic relevance when adjusted for International Prognostic Index factors (relative risk=1.2, p=0.328 for overall survival; and relative risk=1.1, p=0.644 for event-free survival).

**CONCLUSIONS:** The previously reported International Prognostic Index-independent prognostic value of stratification into germinal center/non-germinal center B-cell lymphoma using the expression pattern of CD10, BCL6, and IRF4 was not reproducible in our series. However, other markers and the morphological subtype appear to be of prognostic value.

PMID: 19880780 [PubMed - indexed for MEDLINE] PMCID: PMC2770968

Free Article: http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/19880780/?tool=pubmed