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MYC status in concert with BCL2 and BCL6 expression predicts outcome in diffuse large B-cell lymphoma.

Horn H, Ziepert M, Becher C, Barth TF, Bernd HW, Feller AC, Klapper W, Hummel M, Stein H, Hansmann ML, Schmelter C, Möller P, Cogliatti S, Pfreundschuh M, Schmitz N, Trümper L, Siebert R, Loeffler M, Rosenwald A, Ott G; German High-Grade Non-Hodgkin Lymphoma Study Group.

Author information

Department of Clinical Pathology, Robert-Bosch-Krankenhaus and Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany.

Abstract

MYC rearrangements occur in 5% to 10% of diffuse large B-cell lymphomas (DLBCL) and confer an increased risk to cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (CHOP) and rituximab (R)-CHOP treated patients. We investigated the prognostic relevance of MYC-, BCL2- and BCL6-rearrangements and protein expression in a prospective randomized trial. Paraffin-embedded tumor samples from 442 de novo DLBCL treated within the RICOVER study of the German High-Grade Non-Hodgkin Lymphoma Study Group (DSHNHL) were investigated using immunohistochemistry and fluorescence in situ hybridization (FISH) to detect protein expression and breaks of MYC, BCL2, and BCL6. Rearrangements of MYC, BCL2, and BCL6 were detected in 8.8%, 13.5%, and 28.7%, respectively. Protein overexpression of MYC (>40%) was encountered in 31.8% of tumors; 79.6% and 82.8% of tumors expressed BCL2 and BCL6, respectively. MYC translocations, MYChigh, BCL2high, and BCL6low protein expressions were associated with inferior survival. In multivariate Cox regression modeling, protein expression patterns of MYC, BCL2 and BCL6, and MYC rearrangements were predictive of outcome and provided prognostic information independent of the International Prognostic Index (IPI) for overall survival and event-free survival. A combined immunohistochemical or FISH/immunohistochemical score predicts outcome in DLBCL patients independent of the IPI and identifies a subset of 15% of patients with dismal prognosis in the high-risk IPI group following treatment with R-CHOP. Registered at http://www.cancer.gov/clinicaltrials: RICOVER trial of the DSHNHL is NCT 00052936.

Comment in

MYC, BCL2, BCL6 in DLBCL: impact for clinics in the future? [Blood. 2013]

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