Different biological risk factors in young poor-prognosis and elderly patients with diffuse large B-cell lymphoma

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Prognostically relevant risk factors in patients with diffuse large B-cell lymphoma (DLBCL) have predominantly been evaluated in elderly populations. We tested whether previously described risk factors are also valid in younger, poor-prognosis DLBCL patients. Paraffin-embedded samples from 112 patients with de novo DLBCL, enrolled in the R-MegaCHOEP trial of the German High Grade Non-Hodgkin Lymphoma Study Group (DSHNHL) were investigated using immunohistochemistry (MYC, FOXP1, LMO2, GCET1, CD5, CD10, BCL2, BCL6, IRF4/MUM1) and fluorescence in situ hybridization (MYC, BCL2, BCL6). MYC, BCL2 and BCL6 breaks occurred in 14, 21 and 31%, respectively. In the majority of cases, MYC was simultaneously rearranged with BCL2 and/or BCL6. The adverse impact of MYC rearrangements was confirmed, but the sole presence of BCL2 breaks emerged as a novel prognostic marker associated with inferior overall survival (OS) (P=0.002). Combined overexpression of MYC and BCL2 showed only limited association with inferior OS. All immunohistochemical cell of origin classifiers applied failed to predict survival time. DLBCL tumors with significant proportion of immunoblastic and/or immunoblastic-plasmacytoid cells had inferior OS, independently from from BCL2 break. Younger, poor-prognosis DLBCL patients, therefore, display different biological risk factors compared with an elderly population, with BCL2 translocations emerging as a powerful negative prognostic marker.

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