Original Article

Prevalence and Clinical Implications of Cyclin D1 Expression in Diffuse Large B-Cell Lymphoma (DLBCL) Treated With Immunochemotherapy

A Report From the International DLBCL Rituximab-CHOP Consortium Program

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BACKGROUND: Cyclin D1 expression has been reported in a subset of patients with diffuse large B-cell leukemia (DLBCL), but studies have been few and generally small, and they have demonstrated no obvious clinical implications attributable to cyclin D1 expression. **METHODS:** The authors reviewed 1435 patients who were diagnosed with DLBCL as part of the International DLBCL rituximab with cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (R-CHOP) Consortium Program and performed clinical, immunohistochemical, and genetic analyses with a focus on cyclin D1. All patients who were cyclin D1-positive according to immunohistochemistry were also assessed for rearrangements of the cyclin D1 gene (*CCND1*) using fluorescence in situ hybridization. Gene expression profiling was performed to compare patients who had DLBCL with and without cyclin D1 expression. **RESULTS:** In total, 30 patients (2.1%) who had DLBCL that expressed cyclin D1 and lacked *CCND1* gene rearrangements were identified. Patients with cyclin D1-positive DLBCL had a median age of 57 years (range, 16.0-82.6 years). There were 23 males and 7 females. Twelve patients (40%) had bulky disease. None of them expressed CD5. Two patients expressed cyclin D2. Gene expression profiling indicated that 17 tumors were of the germinal center type, and 13 were of the activated B-cell type. Genetic aberrations of B-cell leukemia/lymphoma 2 (*BCL2*), *BCL6*, v-myc avian myelocytomatosis viral oncogene homolog (*MYC*), mouse double minute 2 oncogene E3 ubiquitin protein ligase (*MDM2*), *MDM4*, and tumor protein 53 (*TP53*) were rare or absent. Gene expression profiling did not reveal any striking differences with respect to cyclin D1 in DLBCL. **CONCLUSIONS:** Compared with patients who had cyclin D1-negative DLBCL, men were more commonly affected with cyclin D1-positive DLBCL, and they were significantly younger. There were no other significant differences in clinical presentation, pathologic features, overall survival, or progression-free survival between these two subgroups of patients with DLBCL. ***Cancer*** **2014;120:1818–29.** *© 2014 American Cancer Society.*

KEYWORDS: cyclin D1, pleomorphic mantle cell lymphoma, diffuse large B-cell lymphoma.

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common type of B-cell lymphoma in the world.[1] DLBCL, as currently defined, is a heterogeneous group of diseases with many morphologic and immunophenotypic variants and molecular subtypes.[2] The standard therapy for patients with DLBCL is rituximab with cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (R-CHOP); and the 10-year overall survival (OS) and disease-free survival (DFS) rates are 43.5% and 36.5%, respectively.[3]

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