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Double hit lymphoma: from biology to therapeutic implications.

Burotto M, Berkovits A, Dunleavy K.

Abstract

INTRODUCTION: Diffuse large B-cell lymphoma (DLBCL) is a molecularly heterogeneous disease defined by different cellular origins and mechanisms of oncogenic activation. Approximately 10% of DLBCL cases harbor a MYC rearrangement and this has been associated with a more aggressive clinical course following standard therapy.

AREAS COVERED: So-called 'double-hit lymphomas' (DHL) or 'triple hit lymphomas' (THL) occur when MYC is concurrently rearranged with BCL2 and/or BCL6. These tumors are characterized by high proliferation rate and a very poor outcome following standard R-CHOP (rituximab, cyclophosphamide, doxorubicin vincristine and prednisone) therapy, in most (though not all) studies that have looked at this. Though there is a paucity of published experience with other chemotherapy regimens, there is emerging evidence that more intensive approaches may improve outcome. Recently, there has been a lot of focus in the literature on 'double-expresser lymphomas' (DEL) with high MYC, BCL2 and/or BCL6 expression but typically without rearrangements of these genes. These DEL cases, have a poor outcome with R-CHOP and there is little consensus on how they should be approached. Expert commentary: This review will focus on the biology and treatment of DHL and DEL, discuss the outcome of these diseases with current standard as well as promising new approaches and conclude with a section on novel agents that are in development for these diseases.

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