Chapter 13

MANAGEMENT OF MANTLE CELL LYMPHOMA

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INTRODUCTION

Mantle Cell Lymphoma (MCL) is a mature B cell lymphoma depicting %5-7 of adults with Non Hodgkin Lymphomas (NHL), with an annual incidence of 4-8 new cases per million. MCL occurs mainly in older adults, the average age of whom are 65-68. MCL is seen more often in males than in females with a 3:1 ratio (Bosch et al, 1998).

MCL, incurable by the standard therapy, often has an aggressive clinical course with a relapsing-refractory pattern. Historically, the median survival in past two decades was 4-5 years, but today younger fitter patients with a tolerance of modern intensive therapies and stem cell transplant, have 8-12 years of median survival (Hermann et al, 2009, Eskelund et al, 2016).

PATHOGENESIS

MCL is considered to have two distinct cellular origins, each of which leads to two different clinical forms of disease. The first one is the **Classical MCL,** typically involving lymph nodes and extra nodal sites, such as the gastrointestinal tract. Classical MCL is thought to result from naive B cells that express SOX-11, which is not expressed in normal B cells. Studies report that SOX-11 blocks B cell differentiation, which offers to play a direct role in MCL pathogenesis. The other origin is the **"leukemic" variant of MCL**, which primarily encompasses the peripheral blood, bone marrow, and/or spleen and rarely lymph nodes. This variant develops from SOX-11-negative B cells and is often clinically indolent, like CLL. However, this form may acquire secondary high risk mutations (eg:TP53) invoking disease with an aggressive course (Jares et al, 2012, Vigliante et al, 2013).

Both types of MCL are highly associated with a t(11,14) translocation which deregulates the cyclin D1 gene (CCND1). The major oncogenic driver of MCL is overexpression of CCND1 gene located at 11q13, which encodes the cyclin D1

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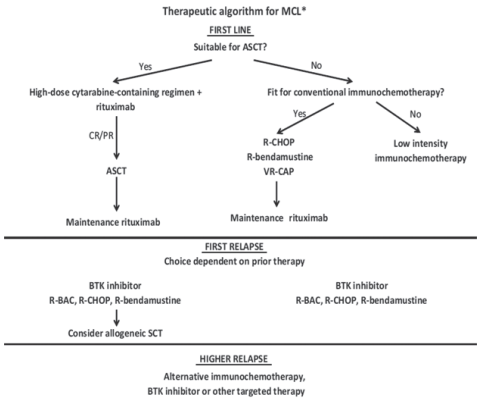

Figure 2. Treatment algorithm for MCL (Mckay et al, 2018).

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