Treatment strategies in Marginal Zone Lymphomas (MZL)

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In the World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues the group of marginal zone lymphomas (MZL) comprises three different entities, namely the extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (currently named "MALT lymphoma" and previously defined as "low grade B-cell lymphoma of MALT type"), the nodal marginal zone B-cell lymphoma (previously known as "monocytoid lymphoma"), and the splenic marginal zone B-cell lymphoma[1]. The term MZL means that extranodal MZL, nodal MZL, and splenic MZL are believed to derive from B cells normally present in the marginal zone, which is the outer part of the mantle zone of B-cell follicles. While splenic and nodal MZL are quite rare, each comprising approximately 2% of lymphomas, the extranodal MZL of MALT type is not uncommon, representing approximately 8% of the total number of non-Hodgkin lymphoma cases in western countries[2]. The most frequent localization of MALT lymphomas is represented by the stomach, however MALT lymphomas can arise virtually in any extranodal site[3]. The overall survival (OS) rates range between 80% to 95% at 5 years, but the progression-free-survival (PFS) is significantly shorter, especially for patients presenting with advanced stage or unfavorable international prognostic index (IPI)[1]. Splenic MZL, mainly occurring in the elderly, commonly pursue a truly indolent course with approximately 70% of patients alive at 10 years from the diagnosis and nearly 30% of patients eventually dying of causes unrelated with the lymphoma. However, a sizeable subgroup of patients may display a progressive disease with a less favourable outcome (56% of patients alive at 5 years)[4,5].

Despite abundant literature on histological, clinical and biologic features of MZL, results of controlled trials to define the optimal therapy have not yet been published. There are few published studies specifically reporting treatment outcome for MZL

and also the published studies often refer to retrospective series with no significant differences in outcome between patients who received different initial treatments[1,4-6].

As regard splenic MZL, decision-making about treatment should be based on symptoms, clinical features, together with the estimated risk[7].

Nevertheless, the presence of HCV infection candidates patients, already on presentation, to receive antiviral therapy with pegylated interferon-alfa and ribavirin due to the evidence of antitumor activity in patients achieving clearance of HCV RNA[8]. In case of symptomatic disease, effective recovery from signs and symptoms disease-related can be obtained with splenectomy, which, in most patients, may assure a long window period free of symptoms. For patients who progress after splenectomy, as well as for those who are unfit for splenectomy or unwilling to undergo surgery, systemic treatment, including chemotherapy and/or rituximab either alone or in combination, may be appropriate[4].

For localized gastric MALT lymphoma there is increasing evidence indicating that eradication of Helicobacter pylori infection can be effectively employed as the sole initial treatment: more than half of the treated patients attain a histological regression of the gastric lymphoma following eradication of H. pylori and long term local control is usually achieved[1]. No treatment guidelines exist for the management of patients with non-gastric MALT lymphoma, for those with gastric MALT lymphoma who fail antibiotic treatment or for the subset of gastric cases in which no evidence of H. pylori can be found. A choice can be made between conventional oncological modalities, including surgery, radiotherapy, chemotherapy and immunotherapy with rituximab, alone or in combination[1,9,10]. A randomized clinical trial suggests that the combination of rituximab plus chlorambucil produces superior event-free survival than the single alkylating agent alone[11].

Interesting information come from investigations on new drugs[12].

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