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Editorial
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EHA Endorsement of ESMO Clinical Practice Guidelines for Diagnosis, Treatment, and Follow-up for Waldenström's Macroglobulinemia

Philipp B. Staber[1], Marie José Kersten[2], on behalf of the EHA Guidelines Committee

Correspondence: Philipp B. Staber (philipp.staber@meduniwien.ac.at).

The European Hematology Association (EHA) and the European Society for Medical Oncology (ESMO) recently agreed to collaborate on the production of European Guidelines for different hematological malignancies. As a first step, a number of completed guidelines have been reviewed by the corresponding EHA Scientific Working Groups in a standardized review process. Representing an example of this collaboration, in the case of Waldenström's macroglobulinemia (WM), the EHA Lymphoma Working Group has recently endorsed the Waldenström's macroglobulinemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up manuscript published on July 5, 2018 (https://www.annalsofoncology.org/article/S0923-7534(19)31695-3/fulltext), in accordance with the ESMO standard operating procedures for Clinical Practice Guidelines development.[1,2]

With an incidence of only 3-7 per 1 million per year in the United States and Europe, WM is a rare indolent B-cell neoplasm that affects mostly elderly patients, since in most cases it is diagnosed at an age between 63 and 75 years. Diagnosis is based on the histopathological confirmation of bone marrow infiltration by lymphoplasmacytic/lymphoplasmacytic lymphoma cells and the detection of any amount of monoclonal IgM protein. More than 90% of WM cases harbor the myeloid differentiation primary response MYD88L265P gene mutation detected in bone marrow sampling. Activating C-X-C Motif Chemokine Receptor 4 mutations are found in approximately 30% of cases with WM that also carry an MYD88 mutation.

As for other indolent lymphoproliferative diseases, the goal of treatment is not cure, and start of therapy is only recommended in advanced stages with clinical symptoms. The most common indications for treatment initiation include anemia, B symptoms, and hyperviscosity; other indications such as neuropathy, bulky lymphadenopathy or organomegaly, and immune-related cytopenias are less common. Treatment choice is guided by the disease presentation (ie, mainly cytopenias versus hyperviscosity) or complications requiring immediate treatment response or presentation with bulky disease. For an immediate relief of symptomatic hyperviscosity, plasmapheresis should be used concomitantly with an appropriate systemic therapy.

Treatment options for WM increased significantly in the last decade with the addition of novel targeted approaches such as B-cell receptor inhibition; however, anti–CD20-based (rituximab-based) combinations still represent the core of first-line regimens. For patients with comorbidities and low tumor burden, a combination of rituximab with oral or intravenous cyclophosphamide and dexamethasone (DRC regimen for 6 cycles) remains one of the primary options with favorable short- and long-term safety profiles and a progression-free survival (PFS) of about 3 years. For patients with high tumor burden, the combination of bendamustin with rituximab (BR) has been shown to lead to longer PFS and overall survival (OS) than rituximab with cyclophosphamide/doxorubicin/vincristine/prednisolone. Bortezomib alone or in combination with rituximab and dexamethasone is also active in WM, and bortezomib should preferably be given subcutaneously and at weekly intervals (1.6 mg/m^2). Current evidence does not support routine use of rituximab maintenance. For elderly patients with comorbidities not tolerating conventional chemotherapy or with other contraindications, targeting the B-cell receptor pathway with ibrutinib, a Bruton's tyrosine kinase inhibitor, is an approved treatment option with substantial activity alone or in combination with rituximab.[3,4]

In relapsed disease, ibrutinib is particularly recommended in patients relapsing <1 year after their last rituximab-containing treatment, including rituximab-refractory patients. Ibrutinib is also recommended for relapse within 3 years after their last rituximab-containing treatment. For patients relapsing >3 years, an alternative rituximab-based combination could also be considered.

In conclusion, the ESMO guidelines for WM from 2018 provide practical, evidence-based, and approved guidance for clinicians.

Disclosures

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[1]Division of Hematology & Hemostaseology, Department of Medicine, Medical University of Vienna, Austria
[2]Department of Hematology, Amsterdam University Medical Centers, University of Amsterdam, LYMMCARE (Lymphoma and Myeloma Center Amsterdam), the Netherlands

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