HemaSphere
Powered by EHA

EUROPEAN HEMATOLOGY ASSOCIATION

Editorial
OPEN ACCESS

EHA Endorsement of ESMO Clinical Practice Guidelines for Newly Diagnosed and Relapsed Mantle Cell Lymphoma

Kim Linton[1], Martin Dreyling[2], on behalf of the EHA Guidelines Committee

Correspondence: Martin Dreyling (e-mail: Martin.Dreyling@med.uni-muenchen.de).

EHA and 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.

The ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up for Mantle Cell Lymphoma released in mid-2017 in accordance with the ESMO standard operating procedures for Clinical Practice Guidelines development,[1,2] was recently endorsed by the EHA Lymphoma Working Group (LyG) and represents an example of this collaboration.[3]

Like many B cell malignancies, mantle cell lymphoma encompasses a wide spectrum of biological and clinical variants. Treating and investigating this disease is compounded by its relative rarity and predilection for elderly patients.

The majority of patients present with advanced stage disease requiring systemic therapy; the current ESMO guidelines provide a helpful framework for treatment selection based on patient age and fitness, reserving intensive therapies for younger and fitter patients, and non-intensive approaches for fit older or frail patients, albeit with boundaries that are not clear-cut. Accumulating evidence has confirmed that rituximab and cytarabine are key components of successful induction and salvage regimens, and that bendamustine has substantial clinical activity as well as being a versatile backbone for new combination strategies. Furthermore, it is now clear that maintenance rituximab confers additional benefit after CHOP-like induction as well as high dose chemotherapy in the first line setting. Ongoing trials are investigating the possibility of replacing chemotherapy with novel agents, and these results are eagerly awaited. Autologous stem cell transplant is still advocated to consolidate treatment response in selected fit patients, although its independent value over rituximab and cytarabine has not been tested in randomized trials and its role in the context of newer biological agents is the subject of ongoing investigation.

Pathogenic reliance on dysregulated B cell receptor signaling is a hallmark feature of mantle cell lymphoma and the advent of therapeutic pathway inhibitors such as ibrutinib has revolutionized management of relapsed disease. Despite these advances, mantle cell lymphoma remains incurable and novel agents are needed to further improve outcomes. The guidelines reference an exciting clinical development program investigating licensed agents ibrutinib, lenalidomide and bortezomib as well as emerging BTK-, BCL2-, proteasome-, HDAC- and Pi3-kinase inhibitors, not to mention recent breakthroughs in the field of cellular immunotherapy.

One of the biggest challenges still to overcome is risk adapted and personalized management. Blastoid morphology indicates a more aggressive clinical case. Pre-treatment Ki-67 proliferation rate and post-treatment eradication of minimal residual disease are the single most important determinants of risk, and advances have been made around risk prediction using a combined biological MIPI index and simplified online tool. Recently, p53 mutations have been proven to predict a dismal prognosis after chemotherapy-based regimens. Whether, as in chronic lymphocytic leukemia (CLL), targeted approaches improve the inferior survival rates of this patient subset is currently unknown. Thus, so far therapy adaptation based on these factors is not yet a reality and cannot be implemented in routine practice until minimal residual disease (MRD) analysis is standardized and trials confirm the advantage of risk adapted therapies. Likewise, important advances have been made in elucidating the biology of indolent disease including a SOX-11 negative, indolent variant recognized in the updated WHO classification; however, the full spectrum of 'indolent' mantle cell lymphoma has not been mapped and clinical guidance still advocates cautious watchful waiting and deferred treatment if indolent disease is suspected. Results of ongoing observational studies suggest a higher proportion of indolent disease than previously reported, and development of biomarkers to reliably select low risk patients will be the next crucial step-change in refining the management approach.

The current ESMO guidelines provide practical evidence-based guidance for clinicians and showcase considerable progress, with an exciting glimpse into a brighter future for patients with this rare and complex disease.

[1]Division of Cancer Sciences, School of Medicine Sciences, University of Manchester, Manchester Cancer Research Centre, Manchester, UK
[2]Department of Medicine III, LMU Hospital, Munich, Germany

HemaSphere (2020) 4:5(e464). http://dx.doi.org/10.1097/HS9.0000000000000464.
Received: 20 May 2020 / Accepted: 5 July 2020

Disclosures

KL: Consultation for Celgene, Roche. Grants/pending grants from Roche. Royalties of payments for lectures/manuscript preparations/ etc from Roche, Hartley-Taylor. MD: Research support (institution) from Celgene, Janssen, Roche. Speaker honoraria from Bayer, Celgene, Gilead, Janssen, Roche. Scientific advisory board for Acerta, Bayer, Celgene, Gilead, Janssen, Novartis, Roche, Sandoz.

References

1. Dreyling M, Campo E, Hermine O, et al. ESMO Guidelines Committee. Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2017;28(suppl_4):iv62–iv71.
2. ESMO Guidelines Methodology. Available from: https://www.esmo.org/guidelines/esmo-guidelines-methodology. Accessed June 29, 2020.
3. EHA Lymphoma Group (EHA LyG) 2020. Available from: https://www.ehalyg.org/. Accessed June 29, 2020.