HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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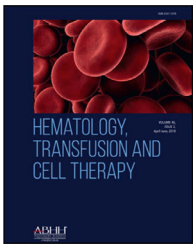

SPEAKER PRESENTATIONS

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CURRENT THERAPY FOR INDOLENT LYMPHOMAS

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Introduction

Indolent lymphomas are mature B-cell neoplasms with a tendency of slow progression and a possible period of observation without treatment. It's a group of heterogeneous diseases, with a less aggressive presentation when compare with other lymphomas, but with frequent relapses and consider incurable. This group contains follicular lymphoma, lymphoplasmacytic lymphoma and marginal zone lymphoma.

Follicular lymphoma (FL)

FL is the most common indolent lymphoma and the second in prevalence between non-Hodgkin`s lymphomas (NHL)[1]. About 20% of patients will progress within 2 years of first line treatment and have worse prognosis (POD24). This group has a markedly reduced overall survival (OS) (around 50% in 5 years), enriched by transformations to aggressive lymphomas. On the other hand, close to 30% of patients in need of therapy can be treated only with anti-CD20 monotherapy, highlighting the great heterogeneous of this disease. Albeit several prognosis factors and risk classification, how to best separate those different FL patients at diagnosis remains unclear. Generally, options for first-line treatment are based in chemotherapy (Bendamustine or CHOP/CVP) with anti-CD20 immunotherapy (Rituximab or Obinutuzumab). There are data supporting Bendamustine plus rituximab (BR) for grade I/II FL, but with no gain in OS in long term studies when compared to other chemotherapy regimens[2]. The same with anti-CD20, where although better progression-free survival (PFS) versus rituximab, obinutuzumab had no gain in OS[3]. After completing 6 cycles, it's common to offer the anti-CD20 used previously as maintenance therapy for 2 years (every other month). This is also a stablished practice, based in long term study with sustained PFS advantage, including reducing risk of transformation into aggressive lymphoma. However, since there is no OS benefit, it's still considered optional. Lenalidomide plus Rituximab ("R^2"), in untreated FL, had an equal PFS rate at 3 years compared with Rituximab plus Chemotherapy, with less hematological toxicity and neutropenic fever, but with no long follow-up data yet. The combination was also effective in the relapse setting, with a median of 40 months in PFS, and it is considered for patients unfit for intensive regimens with autologous transplant as consolidation. Chimeric antigen receptor-modified T cells (CAR-T) against CD19 is becoming widely use in lymphoma and has showed efficacy in relapse/refractory FL patients, with report of high complete remission rate and sustained remissions.

Lymphoplasmacytic lymphoma (LPL)

LPL is a lymphoma where lymphoplasmacytic cells infiltrates the bone marrow and lymph nodes and produces monoclonal protein. Almost always it is of IgM subtype, and it's called Waldenström macroglobulinemia (WM). The *MYD88* L265P mutation occurs in over 90% of cases and has a diagnostic and prognostic role, but it's not specific of WM. *CXCR4* mutation is present in about 30% of patients and is associated with symptomatic disease, higher IgM levels and bone marrow involvement. WM is a disease of elderly patients. Treatment should be delayed until symptoms occur or cytopenias related to the disease[4]. Patients with low tumor burden, frail and where treatment isn't urgent, the combination of dexamethasone, cyclophosphamide and rituximab (DRC) is a well-tolerate and unexpensive option. The change of cyclophosphamide for bortezomib (BDR) is also a good first-line

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option, especially for patients with cytopenias and no neuropathy. BR is an effective chemotherapy regimen for WM, but myelotoxicity can be an issue in already cytopenic patients. Ibrutinib with or without rituximab can be used in first line or relapsed patients, but it seems to have a worse response in patients with wild type *MYD88*. Acalabrutinib and Venetoclax are other new options with response in relapsed setting, including in patient's refractory to ibrutinib. Zanubritinib, a new BTK inhibitor for WM treatment, is at least as effective as ibrutinib with perhaps a better toxicity profile.

Marginal Zone B-cell lymphomas (MZL)

The marginal zone B-cell lymphomas (MZLs) comprise extra nodal MZL (EMZL) of mucosa-associated lymphoid tissue (MALT), splenic MZL (SMZL) with or without villous lymphocytes and nodal MZL (NMZL) with or without monocytoid B cells. These are three distinct clinical entities with specific diagnostic criteria, clinical and therapeutic implications.

Regarding to localize H. pylori-positive gastric MZL, the initial treatment should be H. pylori eradication. This treatment can induce lymphoma regression and long-term clinical disease control in the most of 50% of the patients. In patients who do not achieve lymphoma regression following antibiotic therapy, and the rare ones not associated with H. pylori infections, radiotherapy seems to be the best choice (considering localized disease). Patients who require systemic treatment are not very common, but long-term data from the randomized study IELGS-19 showed better response rates and event-free survival when adding rituximab to chlorambucil, but no OS gain compared to chlorambucil alone[5]. SMZL in asymptomatic patients should be observed. There are no randomize trials, but when treatment is required, splenectomy and rituximab monotherapy are considered first-line. For asymptomatic patient diagnosed with NMZL is also recommended only observation. If systemic treatment is indicated, chemo-immunotherapy can be performed.

REFERENCES

1. Freedman A, Jacobsen E. Follicular lymphoma: 2020 update on diagnosis and management. Am J Hematol. 2020;95:316–27.
2. Flinn IW, van der Jagt R, Kahl B, et al. First-line treatment of patients with indolent non-Hodgkin lymphoma or mantle-cell lymphoma with bendamustine plus rituximab versus R-CHOP or R-CVP: results of the BRIGHT 5-year follow-up study. J Clin Oncol. 2019;37:984–91.
3. Marcus R, Davies A, Ando K, et al. Obinutuzumab for the first-line treatment of follicular lymphoma. N Engl J Med. 2017;377:1331–44.
4. Dimopoulos MA, Kastritis E. How I treat Waldenström macroglobulinemia. Blood. 2019;134(23):2022–35.
5. Zucca E, Conconi A, Laszlo D, et al. Addition of rituximab to chlorambucil produces superior event-free survival in the treatment of patients with extranodal marginal-zone B-cell lymphoma: 5-year analysis of the IELSG-19 Randomized Study. J Clin Oncol. 2013 Feb 10;31(5):565–72.https://doi.org/10.1016/j.htct.2021.11.003

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ELN recommendations for treating MDS

David Bowen

Whilst peer-reviewed published guidelines have appropriate scrutiny and endorsement to support their validity, the reality is that these often become at least partially outdated soon after publication. In developing the latest iteration of guidelines for the diagnosis and management of MDS, the European LeukemiaNet MDS guideline group, has sought to create a web-based interface that is interactive, portable, and capable of dynamic updating at least annually. The guideline development process involved systematic literature review, expert opinion, and scenario analysis. The faculty was diverse; from 18 European countries. The group included Junior Faculty who fed back on content and the practicality for access from mobile devices. The final product is interactive and iterative, with upfront 'headline' recommendations supported by expanded information pages for readers requiring further detail [https://mds-europe.org/]. Examples of updates from our previous ELN guidance are:

Diagnosis: we suggest mutation analysis in all patients where available, to inform prognosis and management. We explain the strengths and the limitations of current knowledge, including discussion of the clonal cytopenias. We also include consideration of germline predisposition syndromes.

Prognosis: we provide calculation tools for IPSS-R and will update this with the forthcoming IPSS-Mol during late 2021/2022.

Low-risk MDS: we describe new data for iron chelation, for early use of Erythropoietic Stimulating Agents and for novel agents such as Luspatercept. Pathways for use of these agents are presented.

High-risk MDS: recommendations are given for the use of hypomethylating agents, chemotherapy, and allogeneic stem cell transplant. An interactive stem cell transplant algorithm including comorbidity is available to guide transplant decisions.

This project was supported by Horizon 2020 funding under the auspices of the MDS-RIGHT programme. The guidelines have recently been endorsed by the European Haematology Association. Discussions are ongoing with international colleagues such that the website may accommodate international variation of recommendations.

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How I treat Polycythemia vera

Barbara Mora, Frencesco Passamonti

Polycythemia vera (PV) is a Philadelphia-negative myeloproliferative neoplasms (MPNs),[1] characterized by high myeloid cells production secondary to mutations in Janus kinase 2 (JAK2) gene. [2,3] Incidence rate is higher in advanced age. [4]