LymphomaHub

PTCL, CLL/SLL, FL, HL, MCL, MZL

Educational theme: Prognostic factors in lymphoma

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This month's educational theme on the Lymphoma Hub is focusing on prognostic factors. These measurements, collected at the time of diagnosis, help to predict the outcome for individual patients. The most widely used prognostic factors in lymphoma are disease histology, anatomic and clinical stage, presence of systemic symptoms, and tumor burden. Their use allows risk stratification of patients and selection of the most appropriate therapy, which is important in the management of indolent lymphomas, as well as more aggressive types.

One of the most important prognostic factors in cancer is the stage of disease at diagnosis. However, looking at tumor spread alone is not adequate to confidently assign patients to a specific risk group. Therefore, different prognostic factors are often combined into models to improve the accuracy of the prediction. International Prognostic Index (IPI) is used in most lymphoma types excluding follicular, where the Follicular Lymphoma International Prognostic Index (FLIPI) is used instead. Some factors affecting the outcome in patients with non-Hodgkin lymphoma (NHL) such as age, disease stage, or serum LDH, are common between different subtypes. While others, like blood hemoglobin levels, are more subtype specific.[1,2]

However, when intermediate-risk is assigned by these models, it can be difficult to interpret with variable outcomes similar to those in the low-risk or high-risk groups. Therefore, researchers are looking to further improve the accuracy of the existing models and reduce their ambiguity by incorporating other clinically relevant factors.

Let us start by recapping some of the relevant articles and video interviews on the topic that were covered on the Lymphoma Hub earlier this year.

Prognostic value of NK cell count on DLBCL outcomes following immunochemotherapy

This article summarizes an exploratory analysis in patients with non-Hodgkin lymphoma (NHL) from phase III GOYA (NCT01287741) and GALLIUM (NCT01332968) trials, which sought to investigate the potential prognostic value of natural killer cell count (NKCC) in predicting patient outcomes following anti-CD20 immunochemotherapy. The results indicate that the number of peripheral blood circulating natural killer cells could act as a prognostic biomarker for follicular lymphoma (FL) or diffuse large B-cell lymphoma (DLBCL) patient outcomes and allow the development of novel combination treatment approaches tailored to the number of functional effector cells in NHL.

The potential role of liquid biopsy in NHL and its current limitations

During the cell-free DNA (cfDNA) workshop at 15-ICML, the Lymphoma Hub conducted an interview with Prof. Talaulikar on potential applications of liquid biopsy and how they can be translated into clinical practice. She believes in the prognostic value of liquid biopsies in lymphoma. DNA (or RNA) extracted from easily-obtainable blood and plasma samples allows for genetic diagnosis of lymphoma, as well as post-treatment monitoring of responses by assessing measurable residual disease (MRD). Additionally, liquid biopsies prevent the need for repeated standard biopsies and the results can be

combined with a positron emission tomography (PET) scan. Prof. Talaulikar also thinks that liquid biopsies provide a more accurate representation of the spatial heterogeneity of lymphoma, allowing clinicians to determine eligibility for targeted therapy.

IHC algorithm reliably predicts GATA3 and TBX21 subtypes of PTCL-NOS

Peripheral T cell lymphomas (PTCL), are a heterogeneous group of non-Hodgkin diseases with broad morphological and immunophenotypic characteristics. Many of the subsets remain undefined and are grouped into a PTCL-not otherwise specified (PTCL-NOS) subtype. Researchers aim to identify the clinical and pathologic features that could offer prognostic value to the different entities within PTCL-NOS. Recently, gene expression profiling (GEP) has identified two novel subtypes with different clinical outcomes. Moreover, these subtypes were found to be associated with enrichment of distinct oncogenic pathways and are therefore vulnerable to distinct targeted therapies. Routine use of GEP in clinical practice is not considered feasible due to high costs and a lack of accessibility. The authors of this study investigated whether using standard immunohistochemistry (IHC) could replicate the gene expression diagnostic signatures for routine use in clinical practice.

SOHO 2019 | What are the novel prognostic factors for the treatment of patients with CLL?

During SOHO 2019, Houston, US, Dr. Alessandra Ferrajoli from the University of Texas, MD Anderson Cancer Center, Houston, US, spoke to the Lymphoma Hub about new prognostic factors, and how they are used for the treatment of patients with chronic lymphocytic leukemia (CLL). She highlights mutational status as the most important prognostic factor, which should be supplemented with a cytogenetic assessment. She also describes other prognostic factors that should be considered, such as the age of the patient and TP53 status. Since only the mutational status of the IgG chain stays constant during disease progression, she highlights the need for reassessment before each line of therapy.

UK real-world gene expression profiling for DLBCL

DLBCL is the most common B-cell malignancy, which presents with a wide range of clinical characteristics and prognostic factors, depending on the subtype of the disease. GEP of DLBCL is crucial for outcome analysis and the planning of treatment for different molecular subgroups. This large real-world GEP of DLBCL included follow-up of all newly diagnosed DLBCL patients from 2004 until death up to March 2018, across 14 Haematological Malignancy Research Network (HMRN) hospitals in the UK. The results indicate that genetic profiling in DLBCL plays an important prognostic role and should be incorporated into routine diagnostic procedures. Furthermore, authors indicate that molecular high-grade (MHG) stratification might encourage the development of targeted trials for outcome improvement in this specific population.

Intratumor heterogeneity as a predictor of disease progression in DLBCL

Cellular heterogeneity plays a crucial role in tumor development, recurrence, and metastasis. It also impacts on the clinical diagnosis, as patients with high tumor heterogeneity have a poor prognosis due to limited therapeutic responses. In this study, the authors used a novel quantitative technique, mutant-allele tumor heterogeneity (MATH) to evaluate the effects of intratumor heterogeneity (ITH) on the risk of progression in patients with early-stage DLBCL. They found that higher ITH was associated with a higher risk of DLBCL progression. Moreover, MATH score based on whole-exome sequencing was an independent risk factor in patients with early-stage DLBCL and could potentially be used for deciding clinical treatment in these patients.

Combination of COO and CNS-IPI improves CNS relapse prognosis in DLBCL

This article summarizes the retrospective analysis of the phase III trial GOYA, where patients with DLBCL were treated with either obinutuzumab (G) or rituximab (R), plus cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP; G-CHOP versus R-CHOP). This analysis aimed to investigate the impact of cell-of-origin (COO), central nervous system (CNS)-International Prognostic Index (IPI), and BCL2/MYC double-expression on CNS relapse in these patients. High CNS-IPI score, activated B-cell (ABC) subtype, or unclassified COO subtypes were found to be independent risk factors for CNS relapse in patients with DLBCL. Additionally, combining CNS-IPI score and COO improved the identification of patients at risk of CNS relapse. Interestingly, no significant difference in the incidence of CNS relapse was observed between the intermediate and low-risk CNS-IPI subgroups.

References

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