

results of a phase-II study. Combinations of this drug with other agents are also expected. Immune check point inhibitors (Nivolumab, Pembrolizumab, Atezolizumab) are promising as third line treatment and beyond. Other agents under investigation include the inhibitor of nuclear export selinexor, the SYK inhibitor entospletinib, the dual SYK/JAK inhibitor certulatinib and the CDK inhibitors flavopiridol and dinaciclib.

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#### SP 28

##### Which aggressive B cell lymphoma should not be treated with RCHOP?

Christian Gisselbrecht

The standard treatment of high-grade B cell lymphoma with RCHOP did not change yet despite the description of the biological heterogeneity. With an overall survival rate superior to 80%, patients with an IPI score 0–2 define a good prognosis group and there is no need to modify this approach if chemotherapy still remain the main tool. How can you characterize high risk aggressive B cell Lymphoma? Important progress has been made in our understanding of the biology and immunology of the group of diseases now included within DLBCL, and now there is an expanding list of active, targeted options. The integration of molecular, genetic, and metabolic imaging studies is essential for clinical trials involving the rational assembly of drugs with various mechanisms of action and immunologic properties. Several adverse factors have been described, closely related to the technology used. In a first historical approach DLBCL can be biologically isolated in GCB and non-GCB subtype with a different outcome, Double hit Myc, Bcl2 translocations, or double expressors Myc, Bcl2 are associated with a poor prognosis. Attempts have been made to elaborate a new classification that integrate next-generation sequencing. In this heterogenous high risk lymphoma, RCHOP needs to be improved. Several targeted agents have been added to RCHOP however none of these new regimens were able until now to improve the outcome in randomized study. Another approach is to detect earlier patients still not achieving a satisfactory response. The percentage of is close to 30% and reflects the heterogeneity of the disease. Detecting early failure of response can be done by incorporating an evaluation with PET scan at diagnosis with the metabolic tumour volume and after two or four cycles for the quality of response. What can we propose for this population? Salvage chemotherapy and stem cell transplantation is the most common practice. Several studies have showed an improvement of survival for the patients with pet positive after two cycles. However, half of the patients will not be eligible for transplantation due to ineffective salvage treatment, and the other half will relapse after ASCT. There is clearly a need for new drugs that improve salvage efficacy. Impressive results have been reported with CAR-T cell engineering with a high response rate in refractory patients lasting over two years at the last report. This new approach will revolutionize the treatment of lymphoma.

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#### SP 29

##### How can we estimate early relapsed follicular lymphoma and how can we treat?

Ozan Salim

FL is the most common indolent non-Hodgkin lymphoma, generally with favorable outcomes (median overall survival [OS] >20 years). The median age at diagnosis is 65 years. Treatment options, both in the front line and in the relapse setting, are observation, immunotherapy and chemo-immunotherapy. The addition of rituximab to standard chemotherapy has significantly improved the OS. However, current treatment options for FL is not curative and a subgroup of the patients has a more aggressive clinical course (early progression, histologic transformation). Histological transformation of FL occurs at a risk of 2% per year. At the time of diagnosis, the FL international prognostic index (FLIPI) and tumor grade are used to distinguish low-risk from high-risk patients. Median progression free survival (PFS) by the FLIPI risk group was 84, 70, and 42 months for low, intermediate, and poor risk disease, respectively. POD24-PI and m7-FLIPI scores are also investigated to predict progression free survival (PFS) in a large cohort of patients receiving first-line chemo-immunotherapy. At the time of relapse, the best available predictor of poor survival is the duration of remission following initial treatment. Relapse of FL within 24 months of chemo-immunotherapy (POD24) occurs in approximately 20% of patients. POD24 was significantly associated with inferior OS at 5 years (50% vs. 90%). The FLIPI, m7-FLIPI, and POD24-PI have been evaluated to identify POD24 patients. Sensitivity and specificity of these prognostic indices in POD24 are 70–78% and 56–58% for high risk FLIPI, 43–61% and 79–86% for high risk m7-FLIPI, 61–78% and 67–73% for high risk POD24-PI, respectively. Furthermore, gene expression profiling and circulating tumor/cell-free DNA are other emerging methods for predicting POD24. However, there is no standardized method to prospectively predict POD24. Patients with relapse FL should undergo an excisional biopsy before initiating next therapy to confirm relapse and exclude histologic transformation. Because no treatment modality has been shown to be superior to another in this situation, POD24 patients should be encouraged to participate in clinical trials whenever possible. If a patient is not a candidate for a clinical trial, treatment options include chemo-immunotherapy (such as bendamustine plus obinutuzumab(O) or O-CHOP) and targeted therapies (such as immunomodulators and PI3K inhibitors). For fit patients age <65 years without an appropriate clinical trial option consolidative autologous stem cell transplant should be considered to induce prolonged remissions and improve prognosis. Nevertheless, there is an unmet need for better identification and treatment of POD 24 patients.

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