biomarkers and IPI, and indices which allow subtle refinements for identification of only low-risk patients. These data underline the need for critical biomarker validation in DLBCL.

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Open questions in the treatment of follicular lymphoma

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The introduction of monoclonal antibodies (in particular rituximab) in the treatment algorithm of follicular lymphoma has significantly improved the median survival of this disease. Nevertheless, with the exception of a few special cases, it remains an incurable disease. A number of questions remain open and we are going to discuss three of them: Is watch and wait still an option? Is R-CHOP the standard first-line treatment? What is the role of autologous and allogeneic transplantation?

The attitude of watching and waiting is regularly challenged because of concerns that delaying treatment could cause irreversible organ damage, permit the general condition of the patient to reduce, allow the appearance of chemotherapy resistant clones or transformation to high-grade lymphoma. Studies and experience confirm that, due to the usually slow progression of the disease, if a strict policy of regular follow-up visits is in place, organ damage and performance status reductions are readily recognized and dealt with. Studies also show that resistance to chemotherapy is not dependent on stage and finally transformation to high-grade is independent from the timing of first-line treatment. The 4 randomised studies performed in the last 2 decades confirmed that watch and wait does not confer a worse survival compared to immediate initial treatment.

The very good partial and complete response rates and response duration seen with aggressive first-line treatment, as CHOP combined with rituximab, has prompted some cooperative groups and centers to elect this regimen as a standard first-line. Nevertheless, many studies have shown in the past that increased response rate and duration do not translate into prolonged survival. This is still true today and the comparison of many studies with different kinds of protocols, ranging from single agent chemo- or immunotherapy to very complex and aggressive combination treatments all show in the long term (as 7 years follow-up) similar progression free survival rates. In addition, the recent demonstration that the combination of rituximab and single agent bendamustine is better tolerated and as active as R-CHOP will further question the primate of R-CHOP as first-line treatment. Several randomised trials are still ongoing to clarify which first-line treatment, if any, is optimal for follicular lymphoma.

High-dose chemotherapy with autologous stem cell transplantation proved to be a good salvage treatment for patients in first or second relapse. According to one small randomised and a few historical studies, this strategy could prolong survival compared to standard salvage chemo-immunotherapy. Nevertheless, in first-line, four randomised studies show no advantage for this strategy. It is probable that the secondary MDS/AML and the acute toxicities could jeopardise the minimal survival advantage. On the other hand allogeneic transplantation is probably the sole modality with curative potential in this disease. Nevertheless, it is bound to very important acute toxicity, translating in almost 50% early deaths in the fist year after transplantation. Because of this, despite of the curative potential, this modality is kept for patients with early aggressive relapse, who are young and fit enough to tolerate the treatment.

In conclusion the treatment algorithm for first-line follicular lymphoma should consider prognostic factors, symptoms and patient subjective priority to choose among watch and wait, intensive treatment or a milder treatment with single agents.

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Diffuse large B-cell lymphoma

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Treatment of diffuse large B-cell lymphomas (DLBCL) in the years 80–90's was characterized by various attempts to improve the results obtained with the classical CHOP regimen, including introduction of alternate drugs with CHOP, development of dose dense or intense regimens, or consolidation with high dose therapy (HDT). Those strategies yielded to some progress, usually restricted to some patients' subgroups, but were not adapted worldwide. The introduction of the anti-CD20 monoclonal antibody rituximab 10 years ago represented a new step forward, which significantly improved the survival of DLBCL patients. Although the benefit of rituximab use may differ in certain patients' subgroups, this lead to commonly administer immunochemotherapy in all DLBCL patients. This new R-CHOP standard may however challenge some of the previous findings form earlier trials and therefore their underlying concepts. Recent data regarding dose dense or dense intense chemotherapy combined with rituximab will be discussed. The recent introduction of