



A. Hagenbeek

Department of Hematology,  
Academic Medical Center,  
Amsterdam, The Netherlands

## Monoclonal antibodies (update): CD20, rituximab

Without any doubt, in the past 10 years Rituximab has caused a breakthrough in the prognosis of patients with both indolent and aggressive NHL. After it was shown that Rituximab as a single agent had significant activity in concert with a most favourable toxicity profile, the combination with appropriate chemotherapy showed not only an improved response rate and progression free survival, but – most strikingly – a significantly better overall survival. This has been particularly impressive in patients with advanced follicular NHL, in which group OS could not be improved during the past 30 years despite many attempts employing different treatment modalities (Marcus and Hagenbeek, 2007).

In addition, several prospective randomized phase III clinical trials clearly showed the value of Rituximab maintenance treatment in first remission follicular NHL. Again here, an improvement in OS was observed. Questions that remain are: what is the optimal Rituximab maintenance regimen, including the duration of maintenance? In diffuse large B-cell lymphoma, the role of Rituximab maintenance is less clear and currently ongoing studies should resolve this question.

It goes without saying that Rituximab shows activity as well in many subtypes of NHL, includ-

ing mantle cell lymphoma, m. Waldenström, CLL, etc., but this will not be addressed in this communication.

Despite these major achievements, it is well recognized – as with any other cancer treatment – that Rituximab resistance is an issue. Not all patients respond to Rituximab (primary refractoriness) and patients may progress during Rituximab treatment or relapse within 6 months after the last Rituximab treatment has been given (secondary refractoriness). In case of follicular NHL about 50% of all patients treated with Rituximab become refractory somewhere along the line.

If a patient is clearly refractory to Rituximab monotherapy, novel antibodies are being explored, of which some are thought to be effective against Rituximab-refractory lymphoma cells. In case of refractoriness to a Rituximab-chemotherapy regimen, there are currently 2 philosophies as far as second line treatment is concerned, i.e. (1) continue with Rituximab in combination with a non-cross resistant chemotherapy regimen, counting on synergism between the two or (2) start second line non-cross resistant chemotherapy without Rituximab. A properly designed prospective randomized trial is warranted to prove what the best approach is.

Finally, based on biological

prognostic factors (e.g. derived from tissue micro arrays on lymph node biopsies), it is currently being attempted by the Lunenburg Lymphoma Biomarker Consortium (LLBC) to predict which patient is going to respond to Rituximab (in combination with chemotherapy) and which patient not.

## **References**

Marcus R, Hagenbeek A. The therapeutic use of Rituximab in non-Hodgkin's lymphoma. *Eur J Haematol* 2007;78:5-14.