Absolute lymphocyte count as a predictive factor for response to monoclonal anti-CD20 antibody therapy

Over recent years, anti-CD20 monoclonal antibodies (Mab) have become available for the treatment of B-cell non-Hodgkin’s lymphoma (NHL). Despite a relatively high response rate, a few patients appear to remain resistant to treatment. In order to identify patients in whom rituximab could be beneficial, we evaluated the influence of various clinical and laboratory parameters on response to immunotherapy.

All patients with CD20+ NHL and treated with rituximab were included. Staging work-up was performed before and after treatment. The patients diagnosed as having follicular lymphoma were classified according to tumor burden status [1]. The dose of Mab was 375 mg/m², administered once weekly for a total of four infusions (days 1, 8, 15 and 22). Response to rituximab was assessed 4 weeks after completion of therapy. The influence of the initial parameters on response to rituximab was defined by univariate analysis (χ² test).

Twenty-nine patients were included in the study. Seventeen patients were diagnosed as having follicular lymphoma, 65% of whom had a low tumor burden status, four patients had other low-grade NHL, four patients had mantle cell lymphoma, and six patients had diffuse large B-cell lymphoma. All but four patients presented with a good performance status (0–1). Twenty-five cases were classified as stage III or IV, 65% with bone marrow involvement. Seven patients had more than one extranodal site. Lactate dehydrogenase was elevated in 19% of patients. Hemoglobin level was <100 g/l in 32% of patients and absolute lymphocyte count (ALC) was >1000/µl in 48% of cases. According to the International Prognostic Index (IPI), 48% of cases were classified in the low-risk group, 20% in the low- to intermediate-risk group, 17% in the intermediate- to high-risk group, and 14% in the high-risk group.

The overall response rate was 55%, with 32% having complete responses. Univariate analysis identified ALC as the only factor that influences the response rate. The overall response rate was 75% when ALC was >1000/µl and 33% when ALC was <1000/µl (P = 0.02). The mean ALC according to the response to rituximab was: 1215/µl in cases of complete response; 1001/µl in partial responses; 873/µl in minor responses and stable disease; and 720/µl in cases of lymphomatous progression after rituximab (Figure 1). No other clinical or laboratory parameters, including IPI score and tumor burden status, significantly influenced the response to rituximab.

Our study is the first to show that an ALC <1000/µl before starting Mab adversely influences the response to rituximab. No details concerning peripheral lymphoid subpopulations (B-, T- or NK-cells) are available. A variety of effector mechanisms for rituximab have been reported, particularly complement-dependent cytolysis, antibody-dependent cell-mediated cytotoxicity, and Mab-triggered B-cell apoptosis induction [2, 3, 4]. Although a cellular and tumor-specific immune response has not yet been reported after rituximab, some papers suggest T-cell activation and/or expansion based on the observation of T-cell lymphoid aggregates in bone marrow after rituximab therapy [5]. Because ALC is simple to perform as a routine test, and despite the small number of patients, our findings emphasize the strong prognostic value of the ALC, making it a particularly useful criterion.

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Figure 1. ALC (per µl) before rituximab, according to the response to Mab (CR, complete response; PR, partial response; MR, minor response).
References


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