

### **Enhancing Rituximab Efficacy with IFN- $\alpha$**

**Eva Kimby, Dept. of Hematology**

**Karolinska Institute at Huddinge University Hospital, Stockholm.**

Monotherapy with the human-mouse chimeric anti-CD20 monoclonal antibody rituximab is effective and well-tolerated in the treatment of CD20+ indolent lymphoma, but the majority of patients relapse. Combination of chemotherapeutic agents with rituximab results in greater efficacy, but at the cost of increased toxicity. Interferon- $\alpha$ 2a (IFN) is another treatment option for patients with indolent lymphoma. Immunomodulatory effects of IFN, such as enhancement of antibody-dependent cell-mediated cytotoxicity (ADCC), which is one of the mechanisms by which rituximab kills lymphoma cells, might increase the efficacy of rituximab. In a Phase II study with a combination of IFN and rituximab, 38 patients with relapsed or refractory low grade or follicular lymphoma showed an overall response rate of 45% with a prolonged median time to progression (25 months) (Davis et al 2000). Sachi et al (2001) treated 64 patients with relapsed low grade lymphoma with rituximab and IFN resulting in a 70% overall response rate with a median duration of 19 months. In a study by the Nordic Lymphoma Group, 69 patients with symptomatic indolent lymphoma, who had shown a suboptimal response to initial conventional rituximab monotherapy, were randomized to a second cycle of rituximab +/- IFN. The addition of IFN seemed to increase the responsiveness to rituximab with a response rate (CR+PR) of 94% vs 78% with rituximab only ( $p=0.087$ ). Moreover, the CR rate was higher with the combination; 16 pts (48%) vs 8 pts (22%) ( $p=0.05$ ). Some late responses were seen. Median time to treatment failure (from time of randomization) was 31 months for the rituximab group, but has not been reached in patients with the combination (70% still failure-free at this time point). Rituximab is effective also in patients with Waldenström's macroglobulinemia and currently available data suggest an advantage with the combination with IFN.

In patients with indolent lymphoma with few symptoms from their disease, it is essential to minimize treatment morbidity, especially as there is no known curative chemotherapy. IFN might augment the effectiveness of rituximab without compromising tolerability. Further studies are required to identify which patients are most likely to benefit from such combination.