Efficacy of chronic pre-emptive Rituximab treatment in ANCA-associated vasculitis

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Background

Rituximab (RTX) is an anti-CD20 antibody used successfully in ANCA-associated vasculitis (AAV) for induction and maintenance of remission.

Objective

To evaluate the long term efficacy and safety of chronic pre-emptive RTX therapy in AAV.

Methods

Retrospective study of 38 AAV patients treated with RTX between April 2004 and September 2011 for active disease. Cumulative CYC dose prior to RTX was 14 (0-250) grams. RTX was initiated as two 1-gram infusions 2 weeks apart and thereafter 2gr RTX was re-administered annually to achieve long-term B cell depletion. Patients were closely monitored during 46.5 (2-88) months follow up with clinical and serological surveillance (Ig levels, lymphocyte subsets). Values given indicate median and range.

Results

A total of 38 AAV patients were treated with RTX after 58.5 months (1-270) disease duration; 58% had renal and 63% had lung involvement. Median RTX dose was 8 (2-13) grams during 5 (1-10) infusion rounds. All patients had a clinical response, but eleven relapses were recorded (flare rate of 7.4 /100 patient years). At last follow up all patients were off immunosuppressive (IS) drugs aside from 4 transplanted patients and 1 psoriatic patient. Daily prednisolone dose at last follow-up was 5 mg (0-30).
Fourteen patients (37%) discontinued RTX: 6 patients for hypogammaglobulinemia, 3 for severe infections, 2 for transplantation, 2 for malignancy, 2 for late-onset neutropenia, 1 for colitis, 1 for inefficacy and 1 for pregnancy.

Severe infections necessitating hospitalization and intravenous treatment occurred in 9 patients (26%). Risk factors for severe infections were renal involvement (p=0.003), higher cumulative CYC dose (OR=1.04, p=0.027) and higher prednisolone dose at last visit (OR=1.18, p=0.05). On the other hand, patients with orbital and subglottic involvements had decreased risk for severe infections (p=0.025). Neither the cumulative dose nor the number of rounds of RTX was associated with severe infections.

Lower ratio CD4/CD8 prior RTX (OR=0.22, p=0.066) and at last visit (OR=0.28, p=0.052) increased the risk for severe infections. The decrease in total immunoglobulin during RTX therapy (OR=1.34, p=0.056) increased the risk for severe infections.

Conclusions

Chronic preemptive RTX treatment aimed to deplete peripheral B cells is effective and leads to relapse rates lower than with standard therapy in AAV patients. Chronic preemptive RTX therapy also allows discontinuation of IS drugs in most patients and significantly reduces steroid use. However, 37% of AAV patients discontinued RTX due to side effects. The risk for severe infections was increased with renal involvement, cumulative CYC dose, prednisolone dose, T cells defect and decrease in total immunoglobulin during RTX therapy.