INTERNATIONAL SYMPOSIUM on IgG4-RD & Fibrosis

Rituximab retreatment for relapse and maintenance therapy in IgG4-related disease

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Background:

Encouraging results have been obtained with B-cell depletion by rituximab (RTX) but data reporting long-term follow-up and multiple retreatments are lacking.

Methods, *materials, and analytical procedure used*:

This was a retrospective, multicenter study of patients treated with at least one course of RTX from a nationwide database for IgG4-RD. Response to treatment, relapse rate and tolerance were analyzed. Kaplan-Meier curves were plotted and risk factors for relapse studied with a Cox regression model. Patients retreated for relapse or systematically for maintenance therapy were specifically analyzed.

Results:

Thirty-three patients with IgG4-RD were treated with RTX and clinical response was noted in 93.5% of 31 symptomatic patients. After a mean follow-up of 24.8 months, 13 patients (41.9% of responders) experienced relapse, with a mean delay of 19 months after RTX. B-cell reconstitution was observed in 57.1%, with a median delay of 12.5 months. Seventy-five percent of these experienced a relapse. A most active disease, defined by IgG4-RD Responder Index >9 before RTX, was significantly associated with relapse (HR=3.68, 95% CI: 1.1, 12.6) (*P*=0.04), whereas systematic RTX maintenance retreatment was associated with longer relapse-free survival (41 versus 21 months; *P*=0.02). Seventeen patients (51.5%) received more than 1 course of RTX, with a total number of 58 retreatment courses. Median number of retreatment per patient was 2 (range: 1–12). Retreatment was used for relapses in 9 cases, and as systematic in 12. Clinical response was obtained in all 8 evaluable patients retreated for relapse but one (non-responder to a first RTX course). For maintenance therapy, doses were variable ranging from 300 mg to 1 g, and frequency from every month to 17 months. Relapse after systematic RTX retreatment occurred in 4/12 (33%), with a median delay of 17 months after RTX (range: 14–18). Follow-up after the last maintenance RTX infusion was < 12 months in 7/8 other patients. Eight severe infections occurred in 4 patients (severe infections rate: 12.1/100 patient-years) and hypogammaglobulinemia ≤5 g/L occurred in 3.

Conclusions:

RTX is effective for the treatment of IgG4-RD at diagnosis and in case of relapse. However, relapses are frequent after B-cell reconstitution. Maintenance therapy with RTX could represent a good strategy, especially in patients with initial most active disease (IgG4-RD RI>9) and with B-cell reconstitution during follow-up, but is limited by the high incidence of infectious adverse events.