1. From molecular pathways to clinical trials

LONG-TERM EFFECTS OF RITUXIMAB ON B CELL COUNTS AND AUTOANTIBODY PRODUCTION IN RHEUMATOID ARTHRITIS: USE OF HIGH-SENSITIVITY FLOW-CYTOMETRY FOR MORE SENSITIVE ASSESSMENT OF B CELL DEPLETION

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Objective Rituximab (RTX) treatment results in B cell depletion in rheumatoid arthritis (RA), however, clinical responses to RTX may differ. In this study, the authors wished to assess the efficacy and safety of long-term RTX therapy and study correlations between B cell depletion, clinical response and autoantibody production.

Patients and methods Seventy-seven patients with active RA (male:female ratio 12:65) received 1000 mg of rituximab in two infusions, 2 weeks apart. Patients were re-treated with these two infusions every 6 months following a fixed protocol regardless of the extent of clinical response. All patients received at least 5 cycles of RTX. The authors included RA patients exerting active disease (DAS28>5.1) despite treatment with conventional DMARDs and at least one antitumour necrosis factor α agent. The authors assessed DAS28, as well as IgM rheumatoid factor (RF) and anticyclic citrullinated peptide (CCP) antibody levels at baseline, after 15 days and then every 6 months for 24 months. Clinical response was recorded according to EULAR response criteria. Absolute CD19+ B lymphocyte counts were also determined in 50 patients using high-sensitivity flow-cytometry (hsFACS). The authors considered complete depletion if absolute B cell counts were <0.0001 G/l. The authors also recorded side-effects during and after treatment for up to 48 months.

Results Patients received an initial and at least 4 re-treatment cycles. After 6, 12, 18 and 24 months, 51.6%, 51.9%, 73.3% and 83.8% of patients showed good EULAR responses, respectively. Significant and sustained reduction in IgM RF and anti-CCP levels were observed as early as after 6 months and then every 6 months for 24 months. Clinical response was recorded according to EULAR response criteria. Absolute CD19+ B lymphocyte counts were also determined in 50 patients using high-sensitivity flow-cytometry (hsFACS). The authors considered complete depletion if absolute B cell counts were <0.0001 G/l. The authors also recorded side-effects during and after treatment for up to 48 months.

Conclusions In RA, clinical response to RTX is associated with the extent of B cell depletion, as well as with autoantibody production. hsFACS may be a useful method to more accurately assess incomplete B cell depletion and maybe, as in oncohematology, minimal residual disease.