

PRESS RELEASE

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Prophylaxis after relapse of ANCA-associated vasculitis

Rituximab clearly superior to azathioprine

ABSTRACT: Relapses are not uncommon in ANCA-associated vasculitis (AAV). The disease can cause severe injury to kidneys and other organs, even death. After a relapse, there is an increased risk of further relapses, so there is an urgent need for the most effective relapse prevention strategy. The RITAZAREM study impressively demonstrated that the monoclonal antibody rituximab is superior to conventional therapy with azathioprine following relapse.

ANCA-associated vasculitis (AAV) is an autoimmune disease involving vascular inflammation and the formation of autoantibodies (anti-neutrophil cytoplasmic antibodies – ANCA). AAV diseases include a variety of conditions accompanied by the involvement of different organs. The kidneys, lungs and upper respiratory tract are most frequently affected, as are the heart, skin and nervous system. Severe, potentially life-threatening courses of disease are feared. Therapy is with immunosuppressants; conjunctive therapy with glucocorticoids and rituximab (RTX, a monoclonal anti-CD20 antibody) is frequently used for initial remission induction. Recurrent episodes of AAV are not uncommon, especially if relapses have occurred in the past. As the effect of RTX is not persistent, maintenance therapy is required.

The international, multi-center RITAZAREM study was a randomized, controlled (open label) trial of two strategies for preventing relapse in AAV patients after remission induction with RTX and glucocorticoids. The efficacy of fixed interval repeated RTX doses was compared with daily oral azathioprine. If remission was achieved after four months, participants were randomized equally and received either 1000 mg of RTX (every four months, five times in total) or daily doses of azathioprine (2 mg/kg). The follow-up was at least 36 months. At four months, 170 patients were randomized (85 RTX; 85 azathioprine). All patients were followed up for at least 24 months. Median age was 59 (19–89) years, and the duration of the disease was 5.3 years (0.4–38.5). The results showed that rituximab was superior to azathioprine (preliminary HR 0.36; $p < 0.001$): After 24 months (20 months after randomization), 11/85 patients (13%) of the RTX group had relapsed compared to 32/85 patients (38%) of the azathioprine group.

Among the RTX group, only 2/11 relapses (18%) were severe “major relapses”, compared to 12/32 (38%) among the azathioprine group. Severe adverse events occurred in 19/85 patients (22%) on RTX, and in 31/85 patients (36%) on azathioprine. As a recognised side effect of RTX, 25/85 patients (29%) developed hypogammaglobulinemia (low immunoglobulin levels as a sign of immunosuppression) and 42/85 patients (49%) had infections (but not severe). Hypogammaglobulinaemia was seen in 25% of the azathioprine group and non-severe infections in 48%.

“AAV is a disease that can be life-threatening and/or lead to kidney failure requiring dialysis, so for that reason it is so important to prevent relapses”, explains the study’s first author, Dr. Rona Smith, Cambridge, UK. “The study results clearly showed the superiority of RTX over azathioprine during the treatment period, without our finding any evidence that the substance has a worse risk profile – on the contrary.”

“The RITAZAREM study is of groundbreaking importance because RTX, as a remission-sustaining therapy, is not recommended for all AAV patients, so it is essential, therefore, to refine the guidelines in future so as to indicate which patient groups benefit most from the therapy,” adds ERA-EDTA Press Officer Professor Ron Gansevoort. “This seems to apply especially to maintenance therapy after an early relapse, but possibly also for elderly, frail subjects after a first presentation. Further large-scale studies also need to clarify the optimal RTX dose, the necessary duration of RTX maintenance therapy and other unanswered questions, so that more precise statements can be made in this regard when the guidelines are next revised.”

[1] Smith R, Jayne D, Merkel P. A randomized, controlled trial of rituximab versus azathioprine after induction of remission with rituximab for patients with anca-associated vasculitis and relapsing disease. ERA-EDTA 2020, Abstract 4553

About ERA-EDTA

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