Treatment of anca associated vasculitis: is there still an indication for cyclophosphamide?

Ulrich Specks, MD.

For the last forty years the standard remission induction regimen for severe granulomatosis with polyangiitis (Wegener's, GPA) and microscopic polyangiitis (MPA) consisted of the combination of glucocorticoids and cyclophosphamide. About 10% of patients could not achieve remission with this regimen. For such refractory patients or for patients who did not tolerate cyclophosphamide, remission induction with rituximab was introduced a decade ago, and several small pilot trials and case series have confirmed that rituximab represents an alternative for such patients with which sustained remissions and discontinuation of glucocorticoid use can be achieved.[1] Based on these promising results and evidence that B cells play a significant role in the pathogenesis of WG and MPA, the RAVE trial was designed which compared rituximab head-to-head to cyclophosphamide for remission induction in patients with severe WG and MPA.[2] The RAVE trial was a double-blind, randomized, double-dummy controlled trial conducted in 197 patients. The primary endpoint results of this trial confirmed that rituximab was not inferior to cyclophosphamide for remission induction and superior to cyclophosphamide for patients presenting with a severe disease flare. Another smaller open-label randomized controlled trial conducted in 44 patients (RITUXVAS) compared rituximab to intravenous bolus cyclophosphamide for remission induction in newly diagnosed patients with active renal disease.[3] The results of the RITUXVAS trial complement the RAVE trial results in an older patient population with more severe renal disease. The long-term follow-up in the RAVE trial has further shown that one course of rituximab is as effective as 18 months of standard therapy. In addition to the RAVE and RITUXVAS trial results, the 10 year experience at the Mayo Clinic with rituximab for remission maintenance in refractory relapsing WG will also be reviewed.

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