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RANDOMIZED TRIAL OF CYCLOPHOSPHAMIDE VERSUS METHOTREXATE FOR INDUCTION OF REMISSION IN "NON-RENAL" ANCA-ASSOCIATED VASCULITIS

de Groot K[1], Rasmussen N[2], Cohen Tervaert JW[3], Jayne DRW[4] for EUVAS (European Vasculitis Study Group). [1]Dept. of Nephrology, Medical School Hannover, Germany; [2]Dept. of Otolaryngology, Rigshospitalet, Copenhagen, Denmark; [3]Dept. of Immunology, University Hospital Maastricht, the Netherlands; [4]Dept. of Medicine, Addenbrooke's Hospital, Cambridge, UK.

Background: This trial (NORAM) aimed to determine whether methotrexate (MTX) was as effective as cyclophosphamide (CYC) for the induction of remission in systemic ANCA-associated vasculitis (AASV: Wegener's granulomatosis and microscopic polyangiitis) without significant impairment of renal function.

Patients and Methods: Patients with newly diagnosed systemic AASV in the absence of life- or organ-threatening disease manifestations and near normal renal function (serum creatinine < 1.5 mg/dl) were included. They were randomized to either oral CYC, 2 mg/kg/day, or oral MTX, 15-25 mg/week. Both limbs received the same concomitant tapering steroid regimen starting at 1 mg/kg/day prednisolone equivalent. All drugs were tapered and withdrawn by 12 months and follow-up continued to 18 months from entry.

Results: Preliminary results are now available: 100 patients from 26 centers in 10 European countries were recruited over 63 months. Fifty-one were randomized to MTX, 49 to CYC. At randomization there was no significant difference in mean age, sex distribution, serum creatinine and BVAS between the limbs. Remission rates at 3 months were 59% and 65%, at 6 months 83% and 84% for MTX and CYC, respectively. Relapse rates and median time to relapse from trial entry were 69% and 13.5 months for MTX and 42% and 15 months for CYC.

Conclusion: MTX and prednisolone achieved a similar remission rate to the standard oral CYC/prednisolone regimen. However, this preliminary data indicates a higher relapse rate in the MTX limb. A final conclusion will require analysis of adverse effect rates and scores for damage and quality of life between the two limbs. This data will shortly become available. Prolonged immunosuppression, beyond the first year of treatment, is probably necessary to reduce relapse.