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Comparison of the efficacy and safety of combined tacrolimus and low-dose corticosteroid with high-dose corticosteroid in adults with minimal change nephrotic syndrome

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Objectives: Tacrolimus is a steroid-sparing immunosuppressant used to reduce the negative effects of long-term or repeated steroid treatment in minimal change nephrotic syndrome (MCNS). The objective of this study was to compare combined tacrolimus and low-dose steroid treatment with high-dose steroid for induction of clinical remission in adults with MCNS.

Methods: In this multicenter, randomized, 24-week non-inferiority study, adult patients with MCNS (n=144) were randomized to either combined 0.05mg/kg/day tacrolimus and 0.5mg/kg/day steroid (n=69), or 1mg/kg/day steroid alone (n=75). Two weeks after complete remission (urine protein creatinine ratio <0.2) the steroid dose was tapered to a maintenance dose of 7.5mg/day. The primary endpoint was complete remission within 8 weeks. Secondary endpoints included time until remission and relapse (proteinuria, UPCr >3.0) after complete remission up to 24 weeks.

Results: Complete remission within 8 weeks occurred in 79.1% of patients treated with tacrolimus and low-dose steroid and 76.8% on high-dose steroid. The difference between the groups demonstrated non-inferiority, with an upper confidence limit below the pre-defined threshold (20%) in both the intent-to-treat (11.63%) and per-protocol (17.0%) analyses. Median time until remission was not significantly different between groups. Relapse occurred in significantly fewer patients in the tacrolimus and low-dose steroid group (5.7%) compared with the high-dose steroid group (22.6%; p=0.012). The relapse-free survival rate for patients receiving combined tacrolimus and low-dose steroid was significantly greater than that for high-dose steroid (p=0.016). There were no clinically-relevant differences in safety findings between the groups.

Conclusions: Combined tacrolimus and low-dose steroid was non-inferior to high-dose steroid treatment for complete remission induction in adults with MCNS. Relapse rates were significantly improved with no clinically-relevant differences in safety findings between the groups. Combined tacrolimus and low-dose steroid represents an important therapeutic option to limit exposure to steroids, especially for MCNS patients with contraindications or intolerance to standard treatment.