Background: Objectives: To report the 10-year outcome of a cohort of patients with lupus nephritis (LN) treated with combined glucocorticoids with either mycophenolate mofetil (MMF) or tacrolimus (TAC) as induction in a randomized controlled trial (RCT).

Methods: 150 patients with active lupus nephritis were randomized to receive either MMF (2-3g/day) or TAC (0.1-0.6mg/kg/day) (N=74) in combination with high-dose prednisolone (0.6mg/kg/day for 6-8 weeks and tapered) as induction therapy between 2005 and 2012. Complete renal (CR) or good partial renal responders were switched to azathioprine (AZA) (2mg/kg/day) for maintenance. We hereby report the 10-year outcomes of the patients in terms of renal flares (proteinuric/nephritic), renal function decline (drop in eGFR by ≥30% from baseline), development of chronic kidney disease (CKD) stage 4/5 or death at 5 and 10 years.

Results: 150 patients (92% women) with active LN were studied (ISN/RPS class III/IV 36%; IV/IVa 46%; pure V 19%). The mean age was 35.5±12.8 years and SLE duration was 50.2±62 months. The mean histological activity and chronicity score was 8.2±3.4 and 2.6±1.6, respectively. At baseline, 59 (39%) patients were hypertensive, 62 (41%) had active urinary casts, 112 (75%) had microscopic hematuria and 67% patients had eGFR<90ml/min. As reported previously, the rate of complete renal response (CR) was 59% in the MMF and 62% in the TAC group (p=0.71). Maintenance therapy with AZA was given to 79% patients. A follow-up of 118.2±42 months, proteinuric and nephritic renal flares occurred in 34% and 37% of patients studied initially with MMF and 53% and 30% in those treated with TAC, respectively. There was a total of 77 renal flares in 43 (57%) patients treated with MMF (0.11/patient-year) and 92 renal flares in 46 (62%) of patients treated with TAC (0.12/patient-year; p=0.44). The cumulative risk of having a renal flare of patients treated with MMF/AZA was 28% at 3 years, 42% at 5 years and 58% at 10 years, whereas the corresponding figures for patients treated with TAC/AZA was 32% at 3 years, 53% in 5 years and 66% in 10 years (p=0.43). For those who achieved CR after induction therapy, the mean time to first renal flare was 70.4±47.1 months in the MMF group and 65.2±50 months in the TAC group (p=0.61). The cumulative incidence of a composite outcome of decline of eGFR by ≥30%, development of CKD stage 4/5 or death at 5 years and 24% and 33%, respectively, in patients treated with MMF, and 17% and 33%, respectively, in those treated with TAC (p=0.90). Factors significantly associated with this outcome were first time lupus nephritis (HR 0.28[0.11-0.59]; p=0.001), uPCR at 6 months (HR 1.33[1.02-1.76]; p=0.04) and eGFR at 6 months (HR 0.98[0.97-0.997]; p=0.02). Exploratory ROC analysis demonstrated that an eGFR cut-off > 60ml/min best predicted a better outcome at 5 years, and should be considered as a target for induction/consolidation therapy.

Conclusion: Long-term data of our RCT showed that TAC remained non-inferior to MMF as induction therapy of LN in terms of renal flares, renal function decline and mortality. Relapsed renal disease, lower eGFR and more proteinuria post-induction therapy were associated with a poorer outcome. An uPCR ≤0.75 and eGFR of >80ml/min at 18 months best predicted a better outcome at 10 years, and should be considered as a target for induction/consolidation therapy.

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