

ISN Trial-List

August 2017



Once a month, the ISN-ACT (Advancing Clinical Trials) initiative team collects and publishes a list of important nephrology trials from the latest medical literature.

Transplant

ISN Academy: [Transplant](#)

Replacing cyclosporine with everolimus improves eGFR without increasing rejection in a low-risk cohort of renal transplant recipients

Everolimus with cyclosporine withdrawal or low-exposure cyclosporine in kidney transplantation from Month 3: a multicentre, randomized trial.

Budde, et al. Nephrol Dial Transplant. 2017;32(6):1060-1070

Avoidance or minimization of calcineurin inhibitors (CnI) with mTOR inhibitor-based regimens may improve long-term renal graft function in appropriate patients but the optimal approach remains unknown. Budde, et al. randomized 499 renal transplant recipients at month 3 post-transplant to continue cyclosporine plus mycophenolate (standard CnI), switch to everolimus plus mycophenolate (CnI free) or to everolimus plus low-dose cyclosporine (low-dose CnI). At month 12 mean eGFR had increased significantly in the CnI free arm but not in either the standard CnI or low-dose CnI (5.6ml/min/1.73m² vs 0.4ml/min/1.73m² and 0.6ml/min/1.73m², respectively). There was also no significant difference in the rate of biopsy-proven acute rejection (11.7%, 7.9% and 8.1% respectively), although the study was not powered for this endpoint. The number of participants discontinuing allocated therapy was significantly greater in the CnI free arm (25.7%) than the standard CnI or low-dose CnI arms (15.2% and 16.8%). Adverse events related to study drug were also more common in the CnI free arm (principally due to increased rates of leukopenia, aphthous stomatitis and diarrhoea). Overall, this study demonstrates improvement in eGFR with a CnI free regimen from 3 months, without a significant increase in acute rejection (in a relatively low immunological risk cohort). Tolerability of everolimus remains a challenge in a minority of patients. The long-term follow up results are eagerly awaited.

<https://academic.oup.com/ndt/article-abstract/32/6/1060/3866771/Everolimus-with-cyclosporine-withdrawal-or-low?redirectedFrom=fulltext>

Pediatric Nephrology, Glomerular Diseases

ISN Academy: [Pediatric Nephrology, Glomerular Diseases](#)

Tacrolimus is superior to mycophenolate as maintenance therapy for steroid-resistant nephrotic syndrome in children.

Mycophenolate mofetil is inferior to tacrolimus in sustaining remission in children with idiopathic steroid-resistant nephrotic syndrome.

Sinha, et al. Kidney Int. 2017;92(1):248-257

Calcineurin inhibitors (CnI) are generally considered first-line treatment for steroid-resistant nephrotic syndrome in childhood but are accompanied by a range of adverse metabolic side effects. Sinha, et al. aimed to determine if mycophenolate could replace CnI as maintenance therapy in children who have responded to a 6 month CnI induction. Sixty children (median age 5.5 years) with steroid-resistant nephrotic syndrome who had had a complete or partial response to 6 months of tacrolimus were randomized in an open-label fashion to either continue tacrolimus or to switch to mycophenolate mofetil. They were followed for a further 12 months. The study was concluded early

on the basis of an interim analysis as the primary outcome of a 'favourable response' (defined as being in complete or partial remission and having had no more than two relapses during the past 12 months) had occurred in 90% of those randomized to continue tacrolimus versus 45% of those swapped to mycophenolate. Serious adverse events (predominantly infections) were also more common in the mycophenolate group. While small, this study is likely to assist clinicians in managing children with this difficult condition and suggests that Cnl have a role in maintaining as well as inducing remission.

<http://www.sciencedirect.com/science/article/pii/S0085253817300704>

Chronic Kidney Disease

ISN Academy: [Chronic Kidney Disease](#)

A simple home-based exercise program can improve strength and physical activity over 12 months in patients with CKD.

Effects of home-based exercise on pre-dialysis chronic kidney disease patients: a randomized pilot and feasibility trial.

Hiraki, et al. BMC Nephrology. 2017;18(1):198

Decline in physical function accompanies decline in renal function and is a poor prognostic indicator. Increasing physical activity over a sustained period of time can be difficult and centre-based programs may be limited by cost and lower recruitment. In a pilot study, Hiraki, et al. recruited 36 male participants with CKD stage 3-4 (mean age 68.7 years, mean eGFR 39ml/min/1.73m²) and randomly assigned them to an intervention group which received pedometers plus training on a variety of home-based aerobic and resistance exercises and a record sheet to document their activity or a control group which received pedometers only. Both groups were followed up every 2-3 months for 12 months. At the end of the follow up period the intervention group had increased their daily step count as well as handgrip and knee extensor strength. No significant changes were observed in the control group. There were no differences between groups in proteinuria or rate of decline in renal function. This study, although just a pilot, suggests that a single training episode, backed by low intensity follow up can lead to objective improvements in physical function over a 12 month period. Further research is warranted to determine if these effects can be replicated in larger cohorts.

<https://bmcnephrol.biomedcentral.com/articles/10.1186/s12882-017-0613-7>
