ISN Trial-List

August 2018

Once a month, the ISN-ACT (Advancing Clinical Trials) team collects and publishes a list of important nephrology trials from the latest medical literature. Each trial is reviewed in context and their risk of bias in seven key areas assessed.

Key to risk of bias assessment

- (R) Random sequence generation
- (A) Allocation concealment
- (BP) Blinding of participants/personnel
- (BO) Blinding of outcome assessment
- (CD) Complete outcome data
- (CR) Complete outcome reporting
- (B) No other sources of bias

- High risk
- Uncertain risk / not stated
- Low risk

ISN Academy: Transplant

Low dose CnI and everolimus non-inferior to standard dose CnI and mycophenolate

Everolimus with Reduced Calcineurin Inhibitor Exposure in Renal Transplantation

Pascual, et al. J Am Soc Nephrol. 2018;29(7):1979-1991

Calcineurin inhibitor (CnI) minimisation strategies aim to reduce the impact of the nephrotoxic and metabolic side effects of CnIs, and improve long-term kidney transplant function. The TRANSFORM trial randomized 2037 kidney transplant recipients (at low-moderate immunological risk) to a regimen of standard dose CnI plus mycophenolate or a low dose CnI plus everolimus. Both arms received standard induction (predominantly basiliximab) and corticosteroids. The primary endpoint of biopsy-proven acute rejection or eGFR<50ml/min/1.73m^2 at 12 months was reached in 45.1% of the standard arm and 48.2% of the low-dose CnI plus everolimus arm (between group difference 3.2% [95%CI -1.3-7.6]; achieving the 10% non-inferiority margin). The results did not differ between those on tacrolimus or cyclosporine and there were no differences in the appearance of de novo donor specific antibodies. CMV and BK virus infections were lower in the low-dose CnI plus everolimus arm but drug discontinuation due to side-effects was higher. While not transformative, this important study does provide clear evidence of the risks and benefits of each regimen and so will help clinicians more confidently tailor their treatment to individual patients. Long-term follow up data will be keenly anticipated.

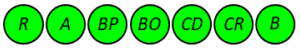
ISN Academy: Transplant

Ignorance (of alloantigens) is BLyS: a small step towards transplant happiness?

Belimumab in kidney transplantation: an experimental medicine, randomised, placebo-controlled phase 2 trial

Banham, et al. Lancet. 2018;391(10140):2619-2630

B-cells play an important role in transplant rejection, especially via the production of donor specific antibodies (DSA). Control of the B-cell response remains a major challenge in modern transplantation. Banham, et al. randomized 28 transplant recipients to receive belimumab (a monoclonal antibody directed against the B-cell survival cytokine B-lymphocyte stimulator (BLyS)) or placebo. Participants were standard risk kidney transplant recipients and all were treated with basiliximab, mycophenolate, tacrolimus and prednisolone plus 7 doses of belimumab or placebo over 20 weeks from the day of transplantation. The primary outcome of number of circulating naïve B-cells was not significantly reduced by belimumab (-34.4 cells per microliter [95%CI -109.5, 40.7]), although there was a significant decrease in de novo DSA. There were no significant differences in safety outcomes. Based on the lack of observed adverse effects and the suggestion of a reduction in DSA, this study paves the way for a larger study to determine if antibody-mediated rejection and, ultimately, graft function and survival, can be improved by the addition of belimumab to standard anti-rejection therapy.



Intensive dietitian review equivalent to standard dietitian care in the post-transplant period

A Randomized Controlled Trial of an Intensive Nutrition Intervention Versus Standard Nutrition Care to Avoid Excess Weight Gain After Kidney Transplantation: The INTENT Trial

Henggeler, et al. J Ren Nutr. 2018: doi.org/10.1053/j.jrn.2018.03.001

Weight gain after renal transplant is common and associated with an increased risk of new-onset diabetes, cardiovascular disease and graft loss. Personalized dietary and physical activity advice may aid patients in minimising weight gain, with potentially important long-term benefits. Henggeler, et al. randomized 37 transplant recipients at a single centre to intensive or less intensive dietitian and physiotherapy review (four versus twelve consultations) over the first 12 post-transplant months. The primary endpoint of weight at 6 months did not differ between the two groups (mean difference 0.4 kg [95%CI -2.2, 3.0]; P=0.7). Nor were significant differences observed in any of the secondary outcomes, including weight at 12 months. Overall weight gain in the two groups was modest at 4.6%. As the 95% confidence interval for the primary outcome included the possibility of what are likely to be clinically important benefits or harms, one suspects that the study may have been underpowered. In addition, the intensive anthropometry obtained in both study arms required extraordinary visits to the trial centre, which may have had the effect of encouraging dietary and physical activity compliance in the standard treatment arm. This study does not definitively imply that intensive dietician involvement is futile as the outcome of a larger trial with follow up integrated with routine care might yet be different.