ISN Trial-List

July 2019

Once a month, the ISN-ACT (Advancing Clinical Trials) team collects and publishes a list of latest randomized research from nephrologists all around the world. 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

*Join the debate on Twitter by following **@ISNeducation**: Will these trials affect your practice? Are the results valid? How could the trials have been improved? What further studies are needed?*

If you would like to suggest any trials for inclusion in future editions, please send suggestions to research@theisn.org.

Contents

ISN Academy: Peritoneal Dialysis

Polyhexanide: an alternative to iodine for PD catheter exit site care?

Effect of Local Polyhexanide Application in Preventing Exit-Site Infection and Peritonitis: A Randomized Controlled Trial

Ceri, et al. Ther Apher Dial. 2019 May 8. doi: 10.1111/1744-9987.12836.1283

Population	93 peritoneal dialysis patients
Intervention *vs* Comparator	Regular exit site application of polyhexanide vs. povidone-iodine — **Time** 12 months
Outcomes	Rates of exit site infections (ESIs) were similar, with 3 ESIs in the polyhexanide group and 5 ESIs in the povidone-iodine group (0.06 episodes/patient-year vs. 0.12 episodes/patient-year; P=NS). Peritonitis rates were also similar, with 12 episodes with polyhexanide and 13 with povidone-iodine (0.26 episodes/patient-year vs. 0.32 episodes/patient-year, P=NS).

Polyhexanide appeared similarly effective to povidone-iodine for infection prophylaxis in patients on PD. However the small size and methodological limitations of this study mean these findings should be interpreted with caution.

ISN Academy: Anaemia, Iron and Trace elements, Chronic Kidney Disease

Roxadustat may be effectively dosed three times per week or weekly

Roxadustat Treatment of Chronic Kidney Disease-Associated Anemia in Japanese Patients Not on Dialysis: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial

Akizawa, et al. Adv Ther. 2019;36(6):1438-1454

Population	107 patients with non-dialysis dependent CKD and anemia

Intervention *vs* Comparator	Roxadustat (thrice-weekly, variable dosing) vs. placebo	Time 24 weeks
Outcomes	Response rate (Hb > 100g/L or >10g/L above baseline) was 94% in the roxadustat group vs. 15% in the placebo group (P<0.001) A subgroup of 56 participants who achieved Hb>110g/L on roxadustat were re-randomized to continue thrice-weekly dosing or to reduce to once-weekly dosing. Both approaches resulted in a mean Hb > 10g/L at week 24.	

This study suggests that less frequent dosing of roxadustat is feasible, although the long-term safety of this approach is not yet known.

*ISN Academy: **Chronic Kidney Disease***

CKD practice nurse and regular medical record audit does not affect progression of CKD in primary care

The Primary-Secondary Care Partnership to Improve Outcomes in Chronic Kidney Disease (PSP-CKD) Study: A Cluster Randomized Trial in Primary Care

Major, et al. J Am Soc Nephrol. 2019 May 16. doi: 10.1681/ASN.2018101042

Population	46 primary care practices	
Intervention *vs* Comparator	CKD nurse-specialist support to review and improve CKD care plus biannual medial record audit of renal function, blood pressure and related parameters vs. unsupported provision of biannual audit data	Time 42 months
Outcomes	No difference in change in eGFR. Coding accuracy improved. At most timepoints, patients in the intervention practices were more likely to achieve BP targets	

Nurse supported CKD management in primary care did not protect renal function, but improvements in some aspects of care were noted.

*ISN Academy: **Anaemia, Iron and Trace elements**, **Transplant***

EPO post-transplant does not affect eGFR in pilot study

Treating Posttransplant Anemia With Erythropoietin Improves Quality of Life but Does Not Affect Progression of Chronic Kidney Disease

Pile, et al. Exp Clin Transplant. 2019 Jun 10. doi: 10.6002/ect.2018.0283.

Population	55 patients 3-months post-renal transplant with hemoglobin 90-115g/L	
Intervention *vs* Comparator	Epoetin-beta titrated to target 115-135g/L vs. no treatment	Time 2 years
Outcomes	No differences in eGFR, proteinuria or blood pressure The authors report improvement in one of eight domains of SF-36 quality of life (vitality)	

In this pilot study, two years of epoetin therapy following renal transplant did not affect decline in eGFR. The effect on quality of life is difficult to judge given the limitations of this study.

*ISN Academy: **Transplant***

Lower tacrolimus dosing feasible in low-risk Asian transplant recipients

Safety and Efficacy of Reduced Prolonged-release Tacrolimus Exposure in De Novo Kidney Transplantation: A Randomized, Open-label, Pilot Study in Asia-OPTIMIZE Study

Kim, et al. Transplant Direct. 2019 Mar 25;5(4):e340

Population	66 low immunological risk kidney transplant recipients; all received basiliximab induction, mycophenolate and corticosteroids, and tacrolimus targeted to 6-10ng/L weeks 1-4.	
Intervention *vs* Comparator	Reduced dose prolonged-release (PR) tacrolimus [trough 4-6ng/L wk 4-12, then 3-5ng/L wk 12-52] vs. standard dose PR tacrolimus [trough 6-10 wk 4-52].	Time 52 weeks

Outcomes	No difference in primary outcome of eGFR at 52 weeks No differences in acute rejection (4 vs. 3), de-novo DSA at 52 weeks (3 vs. 2 participants) or adverse events

In this small study, at 1 year post-transplant, reduced-dose prolonged-release tacrolimus was as effective as standard-dose in Asian kidney transplant recipients with low immunologic risk.

R A BP BO CD CR B

ISN Academy: Pediatric Nephrology, Glomerular Diseases

Longer courses of prednisolone might lower healthcare costs but do not affect relapse rate in childhood nephrotic syndrome.

Long term tapering versus standard prednisolone treatment for first episode of childhood nephrotic syndrome: phase III randomised controlled trial and economic evaluation. The PREDNOS trial

Webb et al. BMJ 2019;365:l1800

Population	237 children aged 1-14 with a first episode of steroid sensitive nephrotic syndrome	
Intervention *vs* Comparator	16 weeks of prednisolone vs. 8 weeks of prednisolone	Time 24 months
Outcomes	No significant difference in time to first relapse (HR 0.87, 95% CI 0.65 to 1.17, P=0.28) No difference in incidence of frequently relapsing nephrotic syndrome, steroid dependence or use of alternative immunosuppressive treatment. No difference in adverse event rates (17% extended course vs. 25% standard, P=0.13) There was a cost saving in the longer tapering arm (difference -£1673, 95% CI -£3455 to £109)	

Clinical outcomes appear similar between 8 and 16 week courses of corticosteroids for pediatric steroid responsive nephrotic syndrome. A cost benefit to the healthcare system was estimated for the longer treatment course, mainly due to reduced health care encounters over the follow up period.

R A BP BO CD CR B

ISN Academy: Hypertension

Perindopril-amlodipine equal to perindopril-indapamide in pilot BP lowering study in Sub-Saharan diabetics

Short-term effects of perindopril-amlodipine vs perindopril-indapamide on blood pressure control in sub-Saharan type 2 diabetic individuals newly diagnosed for hypertension: A double-blinded randomised controlled trial

Sobngwi, et al. J Clin Hypertens (Greenwich). 2019 Jun 8. doi: 10.1111/jch.13557

Population	30 type 2 diabetic participants with Grade I-II hypertension (treatment naïve)	
Intervention *vs* Comparator	Perindopril 5mg-amlodipine 5mg vs. perindopril 5mg-indapamide 1.25mg	Time 6 weeks
Outcomes	No difference in BP lowering between two arms (24-hour SBP 144mmHg to 128mmHg [P=0.003] with perindopril/amlodipine vs. 145mmHg to 126mmHg with perindopril/indapamide [P=0.003]) No significant adverse events	

This pilot study suggests perindopril-amlodipine and perindopril-indapamide are equally efficacious in a Sub-Saharan population. Although of insufficient size and duration to adequately assess adverse effects, this study may aid in the design of future trials in this population.

R A BP BO CD CR B