

# ISN Trial-List

June 2019



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

- Random sequence generation
- Allocation concealment
- Blinding of participants/personnel
- Blinding of outcome assessment
- Complete outcome data
- Complete outcome reporting
- No other sources of bias
- High risk
- Uncertain risk / not stated
- Low risk

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ISN Academy: [Chronic Kidney Disease](#), [Diabetes](#)

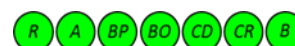
### Taking DELIGHT in lowering BSL and albuminuria in type 2 diabetics with CKD

Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): a randomised, double-blind, placebo-controlled trial

[Pollock, et al. Lancet Diabetes Endocrinol. 2019;7\(6\):429-441](#)

Population	461 adults with CKD (eGFR 25-75mL/min per 1.73 <sup>2</sup> , uACR 30-3500mg/g) and type 2 diabetes	
Intervention vs Comparator	Dapagliflozin vs. dapagliflozin and saxagliptin vs. placebo (1:1:1)	Time ■ 24 weeks
Outcomes	Dapagliflozin reduced albuminuria vs. placebo (-21.0% [-34.1, -5.2]; P=0.011) Saxagliptin-dapagliflozin reduced both albuminuria and lowered HbA1c vs. placebo (-38.0% [-48.2, -25.8; P<0.0001], and -0.58% [-0.80, -0.37; P<0.0001], respectively)	

A combination of SGLT2 inhibitor and DPP4 inhibitor reduced albuminuria and HbA1c in participants with diabetic kidney disease. It remains unclear if this approach provides additional benefit beyond that provided by SGLT2 inhibitors alone.



**PCKD puzzle: Octreotide fails to slow GFR decline, but does slow kidney growth and may reduce ESKD**  
**Octreotide-LAR in later-stage autosomal dominant polycystic kidney disease (ALADIN 2): A randomized, double-blind, placebo-controlled, multicenter trial**  
[Perico, et al. PLoS Med. 2019;16\(4\):e1002777](#)

Population	100 adults with ADPKD and eGFR 15-40ml/min/1.73m <sup>2</sup>	
Intervention vs Comparator	Long-acting octreotide (octreotide-LAR) 40mg IM injection every 4 weeks vs. placebo	Time = 3 years
Outcomes	No difference in rate of measured GFR decline (0.56 [-0.63, 1.75] ml/min/1.73m <sup>2</sup> per year; P=0.295), but kidney volume growth reduced (difference in median: 423ml [150, 695]; P=0.002). 9/51 participants on octreotide-LAR progressed to the composite endpoint of doubling of serum creatinine or ESRD vs. 21/49 on placebo (hazard ratio 0.412 [0.188; 0.899]; P=0.026)	

Like the recent DIPAK-1 trial (Triallist, January 2019), ALADIN 2 found that, despite their effect on kidney volume, somatostatin analogues do not affect GFR decline. However, the tantalizing reduction in progression of CKD suggests that interest in these agents may continue.



**Interactive decision aid reduces uncertainty and conflict, and improves knowledge in patients choosing dialysis modality**

**Use of a Decision Aid for Patients Considering Peritoneal Dialysis and In-Center Hemodialysis: A Randomized Controlled Trial**  
[Subramanian, et al. Am J Kidney Dis. 2019 Apr 3. pii: S0272-6386\(19\)30160-X](#)

Population	234 adults with CKD and eGFR <25ml/min/1.73m <sup>2</sup>	
Intervention vs Comparator	Interactive online decision aid vs. standard of care	
Outcomes	Reduced uncertainty in dialysis modality choice (10% vs. 28%; P<0.001), lower decisional conflict score (29.1±13.7 vs. 42.5±17.1; P<0.001) and higher knowledge scores (90.3±11.9 vs. 76.5±15.3; p<0.001)	

Online provision of information and interactive decision aids may be useful adjuncts to pre-dialysis care.



**Magnesium may slow coronary artery calcification in stage 3-4 CKD**

**A Randomized Trial of Magnesium Oxide and Oral Carbon Adsorbent for Coronary Artery Calcification in Predialysis CKD**  
[Sakaguchi, et al. J Am Soc Nephrol. 2019;30\(6\):1073-1085](#)

Population	123 adults with stage 3-4 CKD plus at least one risk factor for coronary artery calcification (CAC)	
Intervention vs Comparator	Factorial randomization to magnesium oxide 330mg daily vs. placebo AND carbon adsorbent (AST-120) 6g daily vs. placebo	Time = 2 years
Outcomes	Lower CAC score with magnesium oxide vs. control (11.3% vs 39.5%; p<0.001) but no difference in CAC score between AST-120 vs. control (23.1% vs 31.9%; p=0.57). No additive effects	

In contrast to a carbon-based adsorbent (to bind uremic toxins), magnesium may slow the development of coronary vascular calcification. Although the small number of participants and high loss to follow up leave a question mark over these findings, further study appears warranted.



**Bee resin creating a buzz: Brazilian green propolis reduces proteinuria in small study**

**Effects of Brazilian green propolis on proteinuria and renal function in patients with chronic kidney disease: a randomized, double-blind, placebo-controlled trial**  
[Silveira, et al. BMC Nephrol. 2019;20\(1\):140](#)

Population	32 CKD patients with eGR 25-70ml/min/1.73m <sup>2</sup> and proteinuria (>300mg/day or UACR >30mg/mmol)	
Intervention vs Comparator	Brazilian green propolis extract 500mg/day vs. placebo	Time ■ 12 months
Outcomes	Lower proteinuria in propolis group (695mg/24h [95% CI 483, 999] vs. 1403mg/24h [95% CI 1031, 1909]; P=0.004) No difference in eGFR or BP	

Brazilian propolis extract, a natural resin produced by bees from plant materials, may be effective in reducing proteinuria in both diabetic and non-diabetic CKD. Larger studies are needed to confirm this finding.



ISN Academy: [Transplant](#)

## Everolimus-CnI regime may not stack up to mycophenolate-tacrolimus in transplantation

An open-label, randomized trial indicates that everolimus with tacrolimus or cyclosporine is comparable to standard immunosuppression in de novo kidney transplant patients

[Sommerer et. al. Kidney Int. 2019 Feb 27. pii: S0085-2538\(19\)30193-0](#)

Population	655 de novo kidney transplant patients	
Intervention vs Comparator	Everolimus (EVR) with tacrolimus (TAC) vs. EVR with cyclosporine (CsA) vs. mycophenolic acid (MPA) with TAC (control arm). Similar TAC exposure across all groups.	Time ■ 12 months
Outcomes	Compared to MPA-TAC, both EVR-TAC and EVR-CsA were inferior in terms of eGFR at 12 months (mean difference -4.98ml/min/1.73m <sup>2</sup> [95% CI -8.2, -1.8] and -5.0ml/min/1.73m <sup>2</sup> [95% CI -8.3, -1.7], respectively)	

Non-inferiority of everolimus-cyclosporin or everolimus-tacrolimus regimes was not shown compared to standard immunosuppression with tacrolimus-mycophenolate. Interpretation of these results is complicated by high rates of study drug discontinuation and withdrawal from study.



ISN Academy: [Hemodialysis](#)

## No improvement in quality of life or strength with cholecalciferol supplementation in dialysis patients

Placebo-controlled, randomized clinical trial of high-dose cholecalciferol in renal dialysis patients: effect on muscle strength and quality of life

[Singer, et. al. Clin Kidney J. 2018;12\(2\):281-287](#)

Population	68 dialysis patients with 25(OH)D levels <50nmol/L	
Intervention vs Comparator	50 000 U / week cholecalciferol vs. placebo	Time ■ 12 months
Outcomes	No difference in hand grip strength, symptom scores. No difference in calcium, phosphate, PTH, blood pressure or adverse events at 12 months	

High dose cholecalciferol, albeit safe, did not make a difference in symptoms, quality of life or hand grip strength in 25(OH)D deficient dialysis patients.



ISN Academy: [Transplant](#)

## Intraoperative use of saline-bicarbonate solution associated with better early graft function

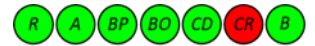
Half Saline-Bicarbonate Solution as Intraoperative Fluid Replacement Therapy Leads to Less Acidosis and Better Early Renal Function During Deceased-Donor Transplant

[Pourfakhr, et al. Exp Clin Transplant. 2019 Apr 17. doi: 10.6002/ect.2018.0328](#)

Population	100 transplant recipients	
Intervention vs Comparator	Normal saline vs. 50:50 mix of saline and bicarbonate as intraoperative fluid during deceased donor kidney transplant	
Outcomes	Creatinine was lower on Day 1, 2 and 3 in saline-bicarbonate group (P=0.019 overall; eg: Day 3: 212±93mmol/l vs. 324±117mmol/l) and urine output was higher in the first 24 hours (3052±815ml vs 1351±569ml; P=001)	

Day 7 creatinines were similar

Early markers of graft function (urine output and creatinine fall) were better with a low chloride, high bicarbonate solution compared to normal saline. Although these findings are line with previous work, this study is limited by the failure to report donor characteristics or need for dialysis in the post-operative period.



ISN Academy: [Transplant](#)

## Corticosteroid reduction when switching from cyclosporine to PR tacrolimus may be possible in selected transplant recipients

Randomized, Open-Label, Phase IV, Korean Study of Kidney Transplant Patients Converting from Cyclosporine to Prolonged-Release Tacrolimus Plus Standard- or Reduced-Dose Corticosteroids

[Baek, et al. Transplant Proc. 2019;51\(3\):749-760](#)

Population	150 stable kidney transplant recipients $\geq$ 12 months post-transplant
Intervention vs Comparator	All participants first switched from cyclosporine to prolonged release tacrolimus, then randomised to continue standard-dose corticosteroids vs. reduced-dose corticosteroids (50% lower) Time $\square$ 24 weeks
Outcomes	There was no difference in change in eGFR (mean change: standard-dose $3.4 \pm 10.6$ ml/min/1.73m <sup>2</sup> vs. reduced-dose $1.5 \pm 9.1$ ml/min/1.73m <sup>2</sup> ; P=0.25) No acute rejection was recorded and metabolic parameters were similar in both groups

This exploratory study suggests steroid dose reduction in the context of switching cyclosporine to PR tacrolimus may be safe. However, it remains unclear if this would result in benefit.



ISN Academy: [Hemodialysis](#)

## Busting B-lines: a way to better blood pressure

The effect of dry-weight reduction guided by lung ultrasound on ambulatory blood pressure in hemodialysis patients: a randomized controlled trial

[Loutradis, et al. Kidney Int. 2019;95\(6\):1505-1513](#)

Population	71 hypertensive euvolemic hemodialysis patients
Intervention vs Comparator	Lung-ultrasound (LUS) guided vs. standard of care dry weight reduction Time $\square$ 8 weeks
Outcomes	Dry weight reduction was more common in the LUS group (54% vs 14%; P<0.001) and systolic blood pressure was lower ( $-6.6 \pm 9.6$ vs. $-0.7 \pm 13.1$ ; P=0.033) Intradialytic hypotension did not differ

LUS is a simple technique that may aid in the attainment of ideal body weight and lower blood pressures.



ISN Academy: [Hemodialysis](#)

## Lavender oil may ease the pain of cannulation

The effect of diluted lavender oil inhalation on pain development during vascular access among patients undergoing haemodialysis

[Taşan, et al. Complement Ther Clin Pract. 2019;35:177-182](#)

Population	60 hemodialysis patients
Intervention vs Comparator	Lavender oil inhalation vs. no treatment prior to fistula cannulation
Outcomes	Pain decreased with lavender oil (visual analogue scale [VAS] $-0.7 \pm 0.2$ ; P=0.001) but did not change in the control group (VAS $0.2 \pm 0.7$ ; P=0.77)

A whiff of lavender oil may well make fistula cannulation more tolerable, but the lack of blinding or placebo is a serious limitation to this study.

