STUDY B

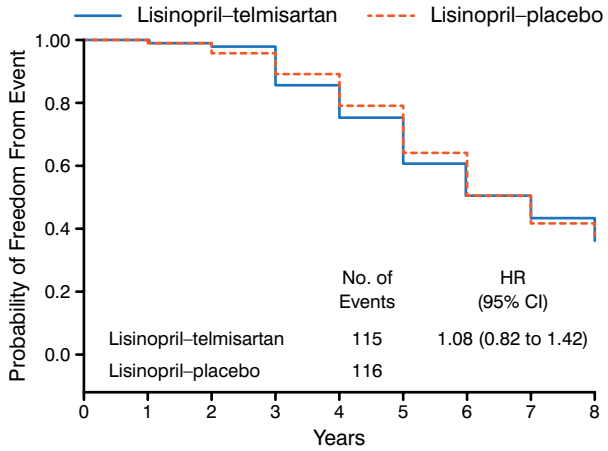
Study B comprised ADPKD patients (n = 485) 18 to 64 years of age (mean, 49 years) with an eGFR of 25 to 60 mL/min/1.73 m^2 (mean, 48-49). Participants were randomized to receive telmisartan plus lisinopril (n = 244) or lisinopril plus placebo (n = 242). Doses were adjusted to achieve a BP of 110/70 to 130/80 mm Hg. The primary end point in Study B was a composite of time to death, ESRD, or 50% reduction in eGFR. Secondary end points were the slope of change in eGFR, urine albumin, and aldosterone excretion; the frequency of all-cause and cardiovascular hospitalizations; quality of life; pain; and PKD-related symptoms. Patients were followed for 5 to 8 years (mean, 5.2 to 6.7 years).

Equal proportions of men and women participated in Study B. Participants had a mean age of 49 years and were mostly white (≥ 93%), with a mean eGFR of 48 to 49. There was no significant difference between the study groups in the incidence of the primary outcome either as a composite or individually (Figure 1). There were also no treatment differences in the change in slope for eGFR and urine albumin excretion rates, frequency of polycystic kidney disease–related symptoms, quality of life, or pain.

Both dual blockade and monotherapy with an ACE-I produced similar BP control, while both treatments lowered urinary aldosterone excretion similarly.

The investigators concluded that dual therapy was as effective and safe as monotherapy in ADPKD and chronic kidney disease patients in stages 1 to 3. Adding an ARB to ACE-I does not confer additional benefits.

Figure 1. Primary Outcome



Adapted from *New England Journal of Medicine*, Torres VE et al, Angiotensin blockade in late autosomal dominant polycystic kidney disease. 371:2267-2276. Copyright © 2014 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Ergocalciferol Supplementation in Patients Undergoing Hemodialysis Is Safe But Without Benefit

Written by Lynne Lederman

Vitamin D deficiency has been linked to cardiovascular events and mortality, infection, and autoimmune disorders [Nigwekar SU et al. *Am J Kidney Dis.* 2012]. Deficiency of 25-hydroxyvitamin D [25(OH)D] <30 ng/mL occurs in about 80% of patients undergoing dialysis. Retrospective observational studies in dialysis have shown mixed results of 25(OH)D supplementation on parathyroid hormone (PTH) and erythropoiesis-stimulating agent use. Clinical trials of 25(OH)D supplementation showed mixed results, were limited by small numbers of patients, and showed no effect on outcomes.

Dana C. Miskulin, MD, Tufts Medical Center, Boston, Massachusetts, USA, reported on Safety and Effects of Supplementation With Ergocalciferol on Erythropoietin Dosing in Hemodialysis Patients [NCT01395823], a double-blind, placebo-controlled trial to confirm safety and determine the effects of dosing on dialysis patients.

Patients who were receiving dialysis, on a stable erythropoietin (EPO) dose, with no impairment to oral 25(OH)D absorption, and deficient in 25(OH)D (< 30 ng/mL) were eligible. Ergocalciferol doses were determined using baseline 25(OH)D levels.

Study outcomes included changes in doses of EPO, 1,25(OH)2D, and phosphate binders; changes in levels of calcium, phosphorous, PTH, and C-reactive protein (CRP); use of cinacalcet; and incidence of hypercalcemia or hyperphosphatemia, all-cause hospitalization, infectious hospitalization, total infections, falls, and fractures.

Eligible patients with baseline 25(OH)D < 30 ng/mL (n = 276) were randomly assigned to placebo (n = 139) or ergocalciferol (n = 137). In both the treatment and placebo groups, there were 4 deaths and 15 patients dropped out. The 2 groups were well balanced for demographic characteristics, including age (median 61 years), sex, race, 25(OH)D levels and dose, and EPO dose; about 80% were taking active vitamin D.

Mean 25(OH)D levels increased to 40 ng/mL at 3 months and to 38 ng/mL at 6 months in the ergocalciferol group compared with the placebo group (P<.0001). For patients with a baseline 25(OH)D of 16 to 30 ng/mL, there was an increase at 3 months but a decline at 6 months; however, 25(OH)D levels remained significantly increased (P<.0001).

There was no significant difference ($P = .76$) between placebo and ergocalciferol in the change in EPO dose or change in PTH ($P = .60$). In addition, there were no significant changes in calcium, phosphorous, calcitriol dose, phosphate binder use, cinacalcet use, or CRP levels or significant differences between groups in all-cause hospitalization, cardiovascular hospitalization, infectious hospitalization, total infections, falls, and fracture events.

The only significant difference between groups was in doxercalciferol; the change in micrograms/treatment/month for the ergocalciferol group was 0.21 (95% CI, 0.10 to 0.31) and for the placebo group was 0.04 (–0.06 to 0.15; $P = .02$). However, Dr Miskulin did not consider this to be clinically significant.

Although it was the largest randomized controlled trial of vitamin D supplementation in patients on dialysis, this study was subject to limitations, including a high percentage of black patients (n = 160), who have lower total 25(OH)D levels than whites [Powe CE et al. *N Engl J Med*. 2013], although in a subgroup analysis, no differences by race were found for any outcome.

Supplementation with 25(OH)D to achieve levels ≥ 30 ng/mL in patients on dialysis is safe, but in this short, underpowered study, it does not appear to offer any benefits.

Fluency Plus ePTFE Stent Superior to PTA for In-stent Restenosis

Written by Emma Hitt Nichols, PhD

Placement of a Fluency Plus stent graft after percutaneous transluminal angioplasty (PTA) was superior to PTA alone in treating in-stent restenosis for restoring access circuit tertiary patency (ACPP) at 6 months. Alexander Yevzlin, MD, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA, presented data from the FLUENCY PLUS Endovascular Stent Graft for In-stent Restenosis trial [RESCUE; NCT01257438].

In-stent restenosis occurs in about 54% to 59% of cases and is the primary location of restenosis in the access circuit [Chan MR et al. *Hemodial Int.* 2009; Vogel PM, Parise C. *J Vasc Interv Radiol.* 2004]. Yet there is no evidence-based recommendation for the treatment of in-stent restenosis. However, expanded polytetrafluoroethylene (ePTFE) stent grafts may offer a potential treatment option for in-stent restenosis. The purpose of the RESCUE study was to determine the safety and efficacy of the Fluency Plus ePTFE stent.

In the multicenter RESCUE trial, 265 patients with in-stent restenosis were randomly assigned to receive PTA or PTA plus the Fluency Plus stent graft. Patients were included in the study if they had atriovenous (AV) fistulae or AV graft, they had peripheral or central vein stenoses, the target lesion was located in the restenosed bare metal stent, the target lesion was ≤ 10 cm in length, and the reference vessel diameter was 5 to 12 mm. Patients were excluded if the target lesion had a corresponding thrombosis within 7 days of the procedure, the graft or fistula was infected, a pseudoaneurysm was present in the target lesion, the device was placed across a > 90° angle, and the lesion was located across an elbow joint, cephalic arch, superior vena cava, or the cannulation zone. Patients were followed for 24 months and received a mandatory angiogram at day 90.

The primary efficacy end point of the RESCUE trial was ACPP at 6 months. The primary safety end point was freedom from any localized or systemic adverse events related to the AV access circuit that required additional intervention, hospitalization or prolonged hospitalization, or death.

PTA plus the Fluency Plus stent graft was statistically superior to PTA alone, with 16.7% of patients in the Fluency Plus arm achieving ACPP at 6 months compared with 3% in the PTA-only arm ($P < .001$). There was no difference in outcomes based on access type, and there was no difference in outcomes between AV graft or fistula. However, there was a significantly greater benefit for patients with central lesions compared with peripheral lesions at 6 months ($P = .023$). The rate of freedom from binary restenosis at the mandatory angiogram at 90 days was 81% and 25% in the Fluency Plus and PTA-only arms, respectively ($P < .001$). In the intention-to-treat analysis, there was no significant difference in the primary safety end point of freedom from safety events up to 30 days, with a rate of 97% in both arms.

In conclusion, Dr Yevzlin stated that, in his opinion, the data from the RESCUE trial indicate that PTA with placement of the Fluency Plus stent graft was superior to PTA alone for the primary end point of ACPP, as well as binary restenosis > 50%, with similar safety outcomes.

MSCs Do Not Reduce Time to Recovery in Postcardiopulmonary Bypass AKI

Written by Lynne Lederman

Acute kidney injury (AKI) is a major complication of cardiac surgery and can progress to chronic kidney disease and death. AKI rates in cardiac surgery have been increasing, and treatment strategies are needed since post-AKI recovery of kidney function is associated with