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

improved survival. Allogeneic mesenchymal stem cells (MSCs) have been shown to reduce the severity of and improve the recovery from AKI in preclinical studies.

Madhav Swaminathan, MD, Duke University Health System, Durham, North Carolina, USA, discussed A Study to Evaluate the Safety and Efficacy of AC607 for the Treatment of Kidney Injury in Cardiac Surgery Subjects [NCT01602328]. The objective of this phase 2 randomized double-blind study was to compare the time to kidney recovery (TKR) with AC607 (human MSCs that have been isolated and expanded, then administered via catheter in the groin) vs placebo in the setting of postcardiac surgery.

The study included patients who were undergoing cardiac surgery, including cardiopulmonary bypass (CPB) surgery, with a baseline creatinine within 30 days of surgery. Postoperative AKI was defined as a ≥0.5-mg/dL rise in serum creatinine from baseline within 48 hours after CPB. The primary end point was TKR (creatinine return to preoperative baseline). The secondary end point was all-cause mortality or dialysis at 30 or 90 days. Exploratory end points included length of stay, intensive care unit stay, and in-hospital mortality.

Of 26 548 patients tracked, 1990 were eligible, and 156 patients were randomly assigned to AC607 (2×10^6 human MSCs per kg; n = 77) or placebo (n = 79). Equal numbers in each group completed 30 (n = 60) and 90 days (n = 57) of follow-up. Patients were well matched for baseline characteristics, including age, sex, and baseline renal function.

There was no difference between treatment groups for any of the following parameters: median TKR (15 days–treatment vs 12 days–placebo), TKR for patients whose CPB time was >120 minutes, TKR recovery by CPB time quartiles, or TKR by timing of dosing (<24, >24 to 36, or >36 hours).

All-cause mortality or dialysis at day 30 for AC607 vs placebo was 11 vs 8, respectively; at day 90, it was 12 vs 9. All-cause mortality for AC607 vs placebo at day 30 was 6 vs 5, respectively; at day 90 it was 8 vs 6. In-hospital mortality for AC607 vs placebo was 7 vs 4 days, respectively; dialysis at day 30 for AC607 vs placebo was 7 vs 5; and median hospital length of stay for AC607 vs placebo was 14 vs 12 days. There was no statistical difference between treatment groups for any of these events.

Although AC607 appears safe and well tolerated in postcardiac surgery patients with AKI, it did not reduce the TKR compared with placebo. The low event rates make it difficult to observe a treatment effect without a large study population—but a large study would require investigators to screen a prohibitive number of patients for randomization.

Patiromer Controls RAASi-Associated HK in Patients With Diabetes and CKD

Written by Lynne Lederman

Renin-angiotensin-aldosterone system inhibitors (RAASis) are beneficial and recommended for patients with chronic kidney disease (CKD) and type 2 diabetes mellitus (T2DM) [ADA. *Diabetes Care*. 2014]. However, hyperkalemia (HK) often limits RAASi therapy [Einhorn LM et al. *Arch Intern Med*. 2009]. Current treatment options for chronic management of HK are limited [Fordjour KN et al. *Am J Med Sci*. 2014; Harel Z et al. *Am J Med*. 2013], and an unmet need remains for safe and effective HK treatment.

Patiromer has previously been shown to normalize serum potassium (s-K^+) and prevent HK recurrence compared with placebo in A Two-Part, Single-Blind, Phase 3 Study Evaluating the Efficacy and Safety of Patiromer for the Treatment of Hyperkalemia [OPAL-HK; NCT01810939]. Matthew R. Weir, MD, University of Maryland, Baltimore, Maryland, USA, presented poster FR-PO792, which described the prespecified analysis of the subgroup with T2DM in OPAL-HK.

In part A (4-week treatment phase), patients with CKD with and without T2DM on stable doses of ≥1 RAASi with mild HK (s-K^+ 5.1 to <5.5 mEq/L; n = 92) received patiromer 4.2 g BID; those with moderate-to-severe HK (s-K^+ 5.5 to <6.5 mEq/L; n = 151) received patiromer 8.4 g BID. After 4 weeks, patients with moderate-to-severe HK continued on to the 8-week withdrawal phase (part B) and were randomly assigned to patiromer plus RAASi (n = 55) or placebo plus RAASi (n = 52).

End points included change in s-K^+ from baseline to week 4, percentage of patients with s-K^+ within target at week 4, between-group difference in s-K^+ change over the first 4 weeks, and percentage of patients with recurrent HK.

T2DM was present in 138 (57%) of patients assessed for the primary end point. The mean change from baseline to week 4 for patients with T2DM was –1.00 ± 0.04 (95% CI, –1.08 to –0.92; $P < .001$); for those without T2DM it was –1.02 ± 0.05 (95% CI, –1.12 to –0.92; $P < .001$); ($P = .77$ for interaction). In a secondary end point, 78% and 73% of patients with and without T2DM, respectively, had s-K^+ within range at week 4.

The median increase in s-K^+ from baseline at week 4 of the withdrawal phase was larger for the placebo group (n = 33; 0.69 mEq/L; 95% CI, 0.19 to 1.29) than for the patiromer group (n = 34; 0.03 mEq/L; 95% CI, –0.20 to 0.30; $P < .001$) in patients with T2DM ($P < .001$).