Sevelamer
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affected two-thirds of the patients on calcium-containing PBAs but slightly less than 40 percent of those taking sevelamer (p < 0.001). It appeared that cardiac arrhythmias were a significant contributor to the CV deaths because sevelamer was associated with a 93 percent reduction in the risk of arrhythmias. Adjusting for other parameters yielded essentially the same result. The corrected QT interval remained fairly constant in the sevelamer group but somewhat prolonged over time for the patients assigned to a calcium-containing BPA (p < 0.001). Prolongation of the corrected QT interval can lead to arrhythmia. Sevelamer did not appear to reduce the risk of death from non-CV causes, and its beneficial effect on all-cause mortality risk was most likely a result of its lowering the risk of CV mortality, which contributed to the all-cause mortality. Non-CV deaths—a secondary end point of the trial—were essentially no different at 36 months between the two groups. There were 19 deaths in the sevelamer group and 21 in the calcium-containing BPA group. Bellasi concluded that the study lends support to the view that incident hemodialysis patients "may benefit greatly from treatment of hyperphosphatemia with use of the non-calcium containing phosphate binder sevelamer when compared to treatment with calcium-based binders." The study was fairly large and was conducted long enough to see the effects of the treatments on CV events and mortality. However, before the results can be accepted as conclusive and applied generally, some points need to be clarified. The chairman of the session in which the results were presented, David Goldsmith, MB, BChir, consultant nephrologist at Guy's and St. Thomas' Hospital in London, told *Kidney News* that he has questions about the level of compliance with therapy in the two treatment groups, and he would like to see data on hypercalcemic episodes as well as on mortality according to the levels of serum calcium and phosphate that were actually achieved.

Dr. Bellasi has received honoraria from Genzyme, Amgen, and Sanofi, now the parent company of Genzyme. There was no commercial funding for the study. Dr. Goldsmith was not involved in the study. He has received research support from Genzyme, the maker of sevelamer, and is a consultant to Sanofi.

Dual RAS Blockade No Better Than Monotherapy to Prevent Renal Disease Progression

For type 2 diabetes patients with established nephropathy, blocking the renin-angiotensin system (RAS) with two blood pressure drugs does not add any benefit over using just one of the drugs. A combination of the ACE inhibitor lisinopril with the angiotensin receptor blocker irbesartan had similar effects to monotherapy with either drug at doses that achieved the same level of blood pressure reduction.

José Luño, MD, head of the department of nephrology at the Hospital General Universitario Gregoria Marañón, presented results of this late breaking trial at the 49th European Renal Association–European Dialysis and Transplant Association Congress in Paris in May. He said that more severe proteinuria and lower estimated glomerular filtration rate (eGFR) at baseline, as well as vitamin D deficiency, were independent predictors of progression of type 2 diabetic nephropathy.

This multicenter, open-label, four-year follow-up clinical trial ran from 2005 to 2011. After a four-week drug wash out period, 133 participants were randomly assigned in a 1:1:2 fashion to lisinopril titrated from 150 to 600 mg/day (n = 35), to irbesartan titrated from 150 to 600 mg/day (n = 28), or to lisinopril 20 mg plus irbesartan 300 mg (n = 70) to achieve equivalent blood pressure lowering in each group. Medication doses were titrated up at the first and second monthly visits. Median follow-up was 32 months, over which time blood pressure, renal function, and proteinuria were measured.

Participants were at least 35 years old, had type 2 diabetes, hypertension, and clinical proteinuria with a urinary protein-to-creatinine ratio (UPCR) of at least 300 mg/g.

Luño reported that blood pressure control was similar among the three arms of the study. Although eGFR declined in each group, there were no differences in the amount of decline among the lisinopril, irbesartan, and combination therapy groups at 6, 12, or 24 months, or at the end of the study. For each group the annual rate of decline in eGFR was about 3.4 ml/min/1.73 m².

The composite primary endpoint is the incidence of more than 50 percent in serum creatinine, progression to end stage renal disease (ESRD), or death was the same among the groups, with 29–30 in each group reaching it (hazard ratio 0.95). There was also no statistical difference among the groups in the proportion who achieved the individual components of the primary endpoint — 21–23 percent with a creatinine increase of at least 50 percent, 14–18 percent developing ESRD, and 4–7 percent dying.

"Those patients that achieved the renal endpoint — that progressed to renal disease — had at baseline higher proteinuria and lower renal function, [and] lower glomerular filtration rate," Luño said. They also had lower blood hemoglobin values at baseline (p < .05) for all values, comparing patients who had progression of renal disease to those who did not.

Also, vitamin D levels were lower at baseline in the patients whose renal disease progressed (12.6 ng/mL) than in the ones who did not progress (16.9 ng/mL, p < 0.01). In a multivariate regression analysis adjusting for age, sex, body mass index, treatment group, and vitamin D levels, the only significant independent predictors of the primary composite outcome were the baseline proteinuria (UPCR, hazard ratio = 1.32, p < 0.001) and the baseline eGFR (hazard ratio = 0.96, p < 0.05).

Four patients dropped out of the study because of hyperpotassemia, an important adverse effect when the RAS was blocked. Nine patients died in the study. Luño noted that the study was limited by the relatively small sample size, and the study was not done in a double-blind fashion. There may also have been confounding effects by the use of other drugs to control blood pressure and diabetes, which was permitted according to good clinical practice, and the investigators could not evaluate these possible effects.

The trial was funded in part by Bristol-Myers Squibb of Spain.


Glucose-sparing Peritoneal Dialysis Regimen Shows Positive HbA1c and Lipids Results

In a study of patients with diabetes and end stage renal disease (ESRD) on peritoneal dialysis (PD), use of a low-glucose PD fluid showed beneficial effects on metabolic measures such as blood glucose control, serum cholesterol, and triglycerides compared with conventional PD solutions with higher glucose content.

Joanne Bargman, MD, professor of medicine at the University of Toronto and a staff nephrologist at the Toronto General Hospital in Toronto, Ontario, Canada, presented the combined results of the IMPENDIA (Improved Metabolic Control of Physiological, Extraneal, Nutrinetal versus Dulanal only in Diabetic CAPD and APD Patients) and EDEN (Evaluation of Dianeal, Extraneal, and Nutrinetal versus Dianeal Only in Diabetic CAPD Patients) trials at the 49th European Renal Association–European Dialysis and Transplant Association Congress in Paris in May.

Diabetic nephropathy accounts for 25 percent to 50 percent of new cases of ESRD in developed countries. Patients on PD or hemodialysis have similar survival rates, but overall, survival is poor. Each form of dialysis has certain adverse effects associated with it. In the case of PD, continuous glucose loading from the conventional dialysis solution may contribute to the increased cardiovascular risk that is a major cause of death in ESRD patients. Glucose absorption makes it difficult for patients with diabetes to achieve...
Glucose-sparing

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their target blood glucose levels. “The sugar that’s absorbed from the PD fluid is going to make their blood sugar go even higher,” Bargman explained, “and that’s going to affect their sugar control, how much insulin they have to use, and more downstream, will raise some types of cholesterol and fats in the blood. So every study that has looked at it has shown that patients on PD have worse levels of blood cholesterol and fats compared to hemodialysis,” she said.

Patients on PD typically use four fluid bags exchanges a day containing glucose. In the IMPENDIA and EDEN trials, two of the bags were substituted with osmotic solutions not containing glucose.

Glucose-sparing regimen

Bargman said that all the deaths and serious adverse events happened at two participating clinical sites in Chile, and the investigators are trying to determine the reasons. Nonetheless, even if the reasons can be discerned, the results from these sites must be included in the overall analysis and cannot be ignored.

Glucose-sparing was more expensive than NGS ones, but Bargman noted that in either case, PD is less expensive than in-center hemodialysis.

IMPENDIA: Improved Metabolic Control of Physiological, Extraneal, Nutrineal versus Dialaneal only in Diabetic CAPD and APD Patients

EDEN: Evaluation of Dialaneal, Extraneal, and Nutrineal versus Dialaneal only in Diabetic CAPD Patients

Dr. Bargman is a consultant for Baxter, Amgen, and Onitsuka. She is on the speaker’s bureau of DaVita, Amgen, Baxter, and Onitsuka. The trial was sponsored by Baxter Healthcare Corporation.

49th European Renal Association—European Dialysis and Transplant Association Congress: No abstract (Late Breaker).