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PHOSPHORUS-LOWERING DRUGS LINKED TO LOWER MORTALITY IN DIALYSIS PATIENTS

Washington, DC (Tuesday, December 16, 2008) — For patients on dialysis, taking medications to reduce levels of the mineral phosphorus in the blood may reduce the risk of death by 25 to 30 percent, reports a study in the *Journal of the American Society of Nephrology* (JASN).

The drugs, called phosphorus binders, were associated with improved survival in new dialysis patients, including those patients with only modest or even no increase in their blood phosphorus levels. "This important finding suggests that perhaps treatment with phosphorus binders should be extended back to patients with less-severe chronic kidney disease (CKD)," comments Myles Wolf, MD, MMSc, of the University of Miami in Miami, Florida, one of the study authors. "This is a much larger population of patients, virtually all of whom have near-normal blood levels of phosphorus but a markedly increased risk of premature death."

The researchers compared mortality rates in two groups of dialysis patients: 3,555 patients who started treatment with phosphorus binders during the first 90 days after starting dialysis and 5,055 who did not receive phosphorus-lowering treatment during the same period. During the first year on dialysis, patients treated with phosphorus binders had a significantly lower risk of death—30 percent lower, after adjustment for other risk factors.

A further analysis compared mortality rates in a large subgroup of treated and untreated patients, who were closely matched in terms of their initial blood phosphorus levels and their likelihood of receiving phosphorus-lowering treatment. In this "propensity score-matched" analysis, risk of death was 25 percent lower in patients treated with phosphorus binders. The protective effect of phosphorus binders was smaller, but still significant, in an analysis that excluded patients who died in the first 90 days on dialysis.

High phosphorus levels (hyperphosphatemia) are common in patients with kidney disease. "Because hyperphosphatemia is a risk factor for death, phosphorus binders are widely prescribed to dialysis patients," Dr. Wolf explains. "Nephrologists have assumed that this treatment strategy will improve the

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clinical outcomes of our patients, such that the target range for serum phosphate levels in dialysis patients has been lowered in recent years."

However, these recommendations are based largely on opinion. "Whether treatment with any dietary phosphorus binders versus no treatment would improve survival had never been studied until now," says Dr. Wolf. The new results provide an important missing piece of information by showing a lower risk of death in dialysis patients receiving phosphorus binders.

If phosphorus binders improve survival even in new dialysis patients with relatively normal phosphorus levels, then it is possible that they might also be beneficial for the much larger group of patients with less-advanced kidney disease. "Whereas there are roughly 400,000 dialysis patients in the US, there are estimated to be more than 15 million patients with less severe CKD," adds Dr. Wolf. "These patients are typically not considered for treatment with phosphorus binders, which are approved by the FDA only for use on dialysis. If further studies could demonstrate a similar survival benefit of binders in patients with pre-dialysis CKD, the results could have a significant impact on the public health."

The study has some important limitations. Since it was not a randomized trial, it is prone to certain forms of bias and confounding. Other limitations include the limited (one year) follow-up and the lack of data on patients' dietary phosphorus intake and whether they actually took their prescribed phosphorus binders.

Dr. Wolf has received research support from Shire and honoraria from Genzyme, Abbott and Ineos.

The study will appear online at <http://jasn.asnjournals.org/> on December 17, 2008, and in the February 2009 print issue of JASN.

ASN is a not-for-profit organization of 11,000 physicians and scientists dedicated to the study of nephrology and committed to providing a forum for the promulgation of information regarding the latest research and clinical findings on kidney diseases. ASN publishes JASN, the *Clinical Journal of the American Society of Nephrology* (CJASN), and the *Nephrology Self-Assessment Program* (NephSAP). In January 2009, the Society will launch *ASN Kidney News*, a newsmagazine for nephrologists, scientists, allied health professionals, and staff.

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