# Study finds promising treatment to slow kidney disease doesn't prove out in clinical trial

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Historically, half or more of people with type 1 diabetes develop kidney disease, which frequently progresses to kidney failure, requiring dialysis treatment or kidney transplantation for survival, according to a study in *Diabetes Care*. Development and progression of kidney disease in type 1 diabetes is associated with higher levels of a chemical in the blood called uric acid. A new study from the University of Minnesota Medical School found that allopurinol, an inexpensive generic drug that reduces uric acid levels, did not show benefits in protecting from loss of filtering function in the kidney. The findings were recently published in the *New England Journal of Medicine*.

Previous studies suggested that allopurinol may be a promising treatment to slow kidney function, but the smaller size of the studies indicated the need for a more definitive, large-scale trial to answer this important question.

Michael Mauer, MD, professor in the Departments of Pediatrics and Medicine and kidney specialist at the University of Minnesota Medical School, and his colleagues conducted an international, multi-institution, randomized clinical trial that enrolled 530 participants to study whether allopurinol would slow the disease. The study participants had type 1 diabetes and early to moderate loss of the kidney's filtering function.

Mauer is the co-principal investigator of the study called, Preventing

Early Renal Loss in Diabetes (PERL), along with his colleague, Alessandro Doria, MD, Ph.D., MPH, senior investigator in Joslin Diabetes Center's Section on Genetics and Epidemiology and professor of Medicine at Harvard Medical School. Mauer has conducted studies of diabetic kidney disease for more than 40 years and has published extensively in this field.

The PERL consortium consisted of 16 sites each led by excellent clinical scientists. Participants in the three-year, placebo-controlled and double-blinded trial received the current standard of care, including a renin-angiotensin system inhibitor—an existing type of drug shown in the 1990s to slow kidney damage, albeit incompletely.

The key outcome measurement of kidney function for PERL was glomerular filtration rate (GFR), a measure of how much blood is filtered every minute by the kidneys. GFR drops as kidney disease progresses, and when very low, requires dialysis or kidney transplantation for survival. Over the three years of the study, levels of uric acid was decreased, on average, by about 35% among people given allopurinol compared to those who were not. Despite the reduction in uric acid levels, the study showed there was no effect on GFR.

"PERL was a textbook example of using basic science, epidemiology findings and preliminary pilot studies to identify a treatment target, and then to design a study to answer an important question," Mauer said. "In this case, we didn't get the result we were hoping for, but we got a clear answer to an important scientific question."

**More information:** Alessandro Doria et al, Serum Urate Lowering with Allopurinol and Kidney Function in Type 1 Diabetes, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1916624

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