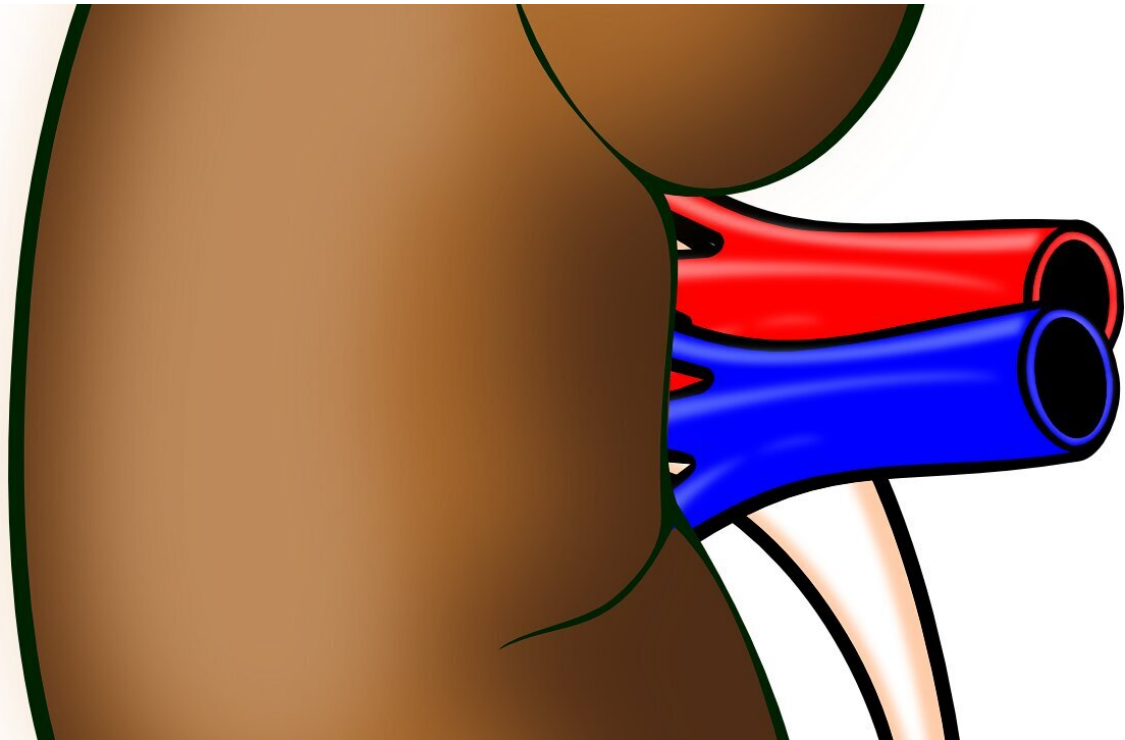


Research finds promising treatment to protect kidney function in diabetes

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A clinical trial involving researchers at University of Limerick, Ireland has demonstrated the potential benefits of new drugs in protecting kidney function in diabetes.

The new study has found that combining two treatments that lower uric

acid concentrations in the blood reduces the leakage of albumin in the urine, one of the earliest signs of kidney damage in [diabetes](#).

The discovery could help to prevent kidney failure in [diabetes patients](#), the UL researchers believe.

Researchers from the University of Limerick School of Medicine and University Hospital Limerick, working with investigators from the University of California San Diego, USA and AstraZeneca, found that the combination of Verinurad and Febuxostat reduced albuminuria in the urine by 39.4% in patients with Type 2 diabetes after 12 weeks of treatment compared to placebo.

The results of this AstraZeneca sponsored Phase 2a clinical trial were recently published in the *American Journal of Kidney Disease*.

Verinurad is a novel inhibitor of the uric acid transporter (URAT1) and is currently under investigation for the treatment of hyperuricaemia and kidney disease. Febuxostat is a potent, selective xanthine oxidase inhibitor used to lower urate levels in patients with gout and hyperuricaemia.

The CITRINE clinical trial results show that the combination of drugs reduces the leaking of protein through the kidney.

"This is exciting news as leaking of protein is the earliest clinical sign of kidney damage," said Professor Austin Stack, Foundation Chair of Medicine at UL's School of Medicine and Consultant Nephrologist at University Hospital Limerick, who was lead author of the study.

"The results are very promising as they demonstrate an important reduction in albuminuria and hyperuricaemia in patients with type 2 diabetes when treated with a combination of Verinurad and Febuxostat.

"If we can intervene early on then we are more likely to prevent patients from going into kidney failure. The findings raise hope for the 350 million people with type 2 diabetes globally who are at increased risk of kidney failure," added Professor Stack, director of the National Kidney Disease Surveillance System (NKDSS).

In the multicentre randomized clinical trial, 60 patients with type 2 diabetes with albuminuria and elevated uric acid levels were randomized to receive either Verinurad 9mg, and Febuxostat 80mg or placebo. The patients were followed up for 24 weeks.

The primary endpoint of the study was met and showed a 39% reduction in albuminuria, after 12 weeks with combined treatment of Verinurad and Febuxostat versus placebo. This effect persisted at 24 weeks with an overall 49% reduction in albuminuria. Treated patients also experienced a 57% reduction in uric acid levels at 12 weeks. Both Verinurad and Febuxostat were well tolerated by patients, according to the study.

"One of the earliest signals of kidney disease is development of albuminuria (leaking of albumin into the urine) and recent studies have shown that this can be associated with high levels of uric acid," said Professor Stack, a HRB-funded principal investigator whose work in this area has raised the profile of uric acid as a potential risk factor for kidney and heart disease.

"A key goal in protecting [kidney function](#) is the lowering of albuminuria in the urine, as patients with high levels are at risk of progressing to kidney failure. This clinical trial was designed to examine the effects of an intensive uric acid lowering strategy on albuminuria by combining Verinurad with Febuxostat in patients with type 2 diabetes mellitus with pre-existing albuminuria.

"Although these are early clinical findings, our results show that

combined treatment with Verinurad and Febuxostat in patients with diabetes results in a rapid reduction in [albuminuria](#) that was sustained through week 24," Professor Stack added.

A larger clinical trial, the SAPPHIRE study, is currently underway to determine whether an intensive uric acid lowering strategy combining Verinurad with a xanthine oxidase inhibitor will slow the progression of chronic kidney disease.

"Diabetes is the greatest contributor to the 850 million globally with chronic kidney disease," explained Professor Stack.

"More than 40% of patients with diabetes are at risk for developing kidney disease and significant number of these will progress to [kidney failure](#). Preventing [kidney failure](#) is a key goal in all healthcare systems to reduce morbidity of diabetes and improve patient outcomes," he added.

More information: Austin G. Stack et al, Effect of Intensive Urate Lowering With Combined Verinurad and Febuxostat on Albuminuria in Patients With Type 2 Diabetes: A Randomized Trial, *American Journal of Kidney Diseases* (2020). [DOI: 10.1053/j.ajkd.2020.09.009](https://doi.org/10.1053/j.ajkd.2020.09.009)

Provided by University of Limerick

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