No benefit from drug used to reduce heart disease in kidney patients

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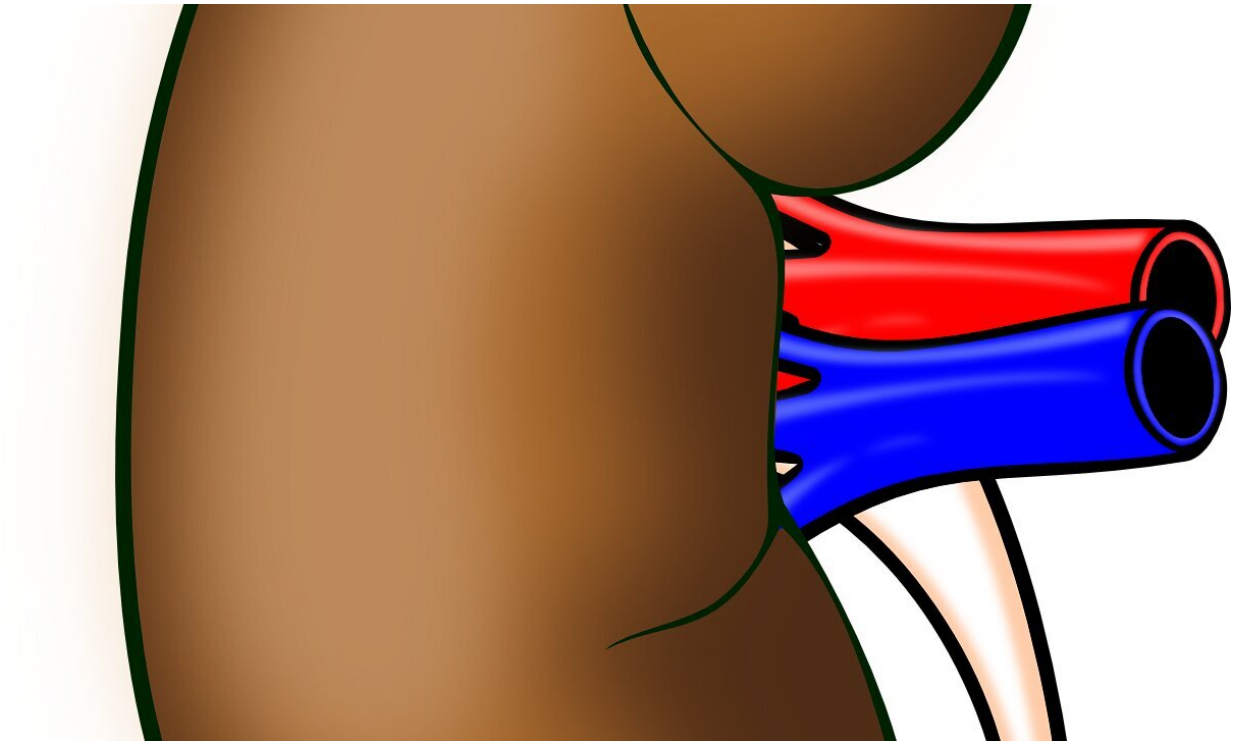

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Following a large-scale clinical trial, researchers have found that lanthanum carbonate does not reduce the risk of cardiovascular disease developing in patients with chronic kidney disease.

The drug is routinely prescribed to patients with chronic kidney disease

to help reduce the risk of both bone disease and cardiovascular disease, with cardiovascular disease the most common complication and cause of death for this group.

The new findings follow a seven-year clinical trial led by a collaboration of kidney disease specialists from Australia, New Zealand and Malaysia as well as The University of Queensland's Australasian Kidney Trials Network, which is based at the Translational Research Institute.

Co-Principal Investigator, Associate Professor Nigel Toussaint from The Royal Melbourne Hospital, says high phosphate levels are a common problem in kidney disease and are linked to the onset and degree of cardiovascular disease.

"Phosphate binder medication has long been a treatment for high phosphate levels in people with kidney disease, especially those on dialysis," said A/Prof Toussaint.

"There was some evidence that phosphate lowering may be effective in reducing risk factors for cardiovascular disease, but there were no adequate studies looking at the effect of lanthanum carbonate on cardiovascular risk factors in people with chronic kidney disease not on dialysis.

"In our clinical trial involving more than 270 patients from 18 hospitals, we found that lanthanum carbonate did not have a beneficial effect on cardiovascular disease indicators such as arterial stiffness or aortic calcification when compared to placebo."

The study was the largest trial of its kind to look at the effect of lanthanum carbonate, a phosphate binder medication, in people with chronic kidney disease.

The results will be critical for Nephrologists to determine the best treatment pathways for patients and provide high value care, according to lead New Zealand Investigator, Professor Rob Walker from Dunedin Hospital.

"The pill and symptom burden along with the economic impact for people with chronic diseases is very high, and if we can determine that certain treatments provide limited benefit then that is just as important as finding something that works," said Prof Walker.

Australasian Kidney Trials Network Chair of the Executive Operations Secretariat, Professor Carmel Hawley said that while further trials were needed to ensure consistency of the findings and generalizability of the results, in relation to phosphate binders, the use of these medications was associated with significant side-effects, particularly gastrointestinal, and they were inconvenient as they have to be taken with meals.

Clinicians enrolled 278 adult participants who had stage 3 or 4 chronic kidney disease from 18 hospitals across Australia, New Zealand and Malaysia. Half the participants received lanthanum carbonate and the other half of participants received a placebo for 96 weeks.

During the trial, clinicians performed pulse wave velocity—a measure of stiffness of arteries—and CT scans looking at calcium build up in arteries. Medical information was collected and blood samples taken. This was the longest trial to date in this study population.

The main results for the IMPROVE-CKD trial were published in the *Journal of the American Society of Nephrology*, with an editorial also published in the journal.

Lanthanum carbonate reduces the absorption of dietary phosphate from the gut, and its ability to potentially lower phosphate balance in the body

was thought to possibly prevent stiffening of blood vessels.

Approximately 1.7 million Australians and 400,000 New Zealanders aged 18 years and over have chronic kidney disease. Many people have a progressive decline in kidney function, also known as progression of chronic kidney disease, to the point of needing dialysis or kidney transplantation. In Australia and New Zealand, about 3600 individuals progress to end-stage kidney disease each year. There are more than 15,500 individuals receiving dialysis.

The IMPROVE-CKD study was sponsored by The University of Queensland, coordinated by the Australasian Kidney Trials Network and funded through research grants from the National Medical and Medical Research Council (NHMRC) and Shire International GmbH, a member of the Takeda group of companies, IST-AUS-000108.

More information: A Randomized Trial on the Effect of Phosphate Reduction on Vascular End Points in CKD (IMPROVE-CKD). Nigel D. Toussaint et al. *JASN* September 2020, ASN.202004041 DOI: 10.1681/ASN.2020040411

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