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DIABETES

# Dual RAAS blocker trial stopped prematurely

The renin–angiotensin–aldosterone system (RAAS) regulates blood pressure through both direct and indirect mechanisms. RAAS blockers that act at the level of angiotensin or lower in the cascade can cause compensatory increases in the plasma renin level. To overcome this effect, investigators in the ALTITUDE study used a strategy of blocking the RAAS at multiple levels, including renin itself. The results were presented at the 2012 meeting of the *American Society of Nephrology*.

ALTITUDE researchers randomly assigned 8,561 patients with type 2 diabetes mellitus as well as either chronic kidney disease, cardiovascular disease, or both, to be treated with either aliskiren (a renin blocker) or placebo, alongside an angiotensin-converting-enzyme inhibitor or angiotensin-receptor blocker. Dual RAAS blockade did not reduce the incidence of major cardiovascular or renal events associated with high blood pressure compared with placebo (18.3% versus 17.1%) during follow-up (median 32.9 months). Consequently, the researchers stopped the trial early. ALTITUDE data suggest that aliskiren might even be harmful to these individuals. Patients treated with aliskiren were more likely to be hyperkalaemic or hypotensive than were patients who received placebo (11.2% versus 7.2%, and 12.1% versus 8.3%, respectively). Given that previous studies of aliskiren have shown improvements in surrogate markers for cardiovascular and nephrologic risk, the ALTITUDE trial serves as a reminder that risk–benefit data remain the gold standard for study end points.

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