Aliskiren 'may have renoprotective effects'

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MedWire News: Treatment with the direct renin inhibitor aliskiren significantly reduces albuminuria in patients with hypertension, Type 2 diabetes, and nephropathy receiving maximal renoprotective treatment with losartan and optimal antihypertensive therapy, AVOID results indicate.

The study investigators suggest that aliskiren may have renoprotective effects that are independent of its blood-pressure lowering effects.

The AVOID (Aliskiren in the Evaluation of Proteinuria in Diabetes) study included 599 patients with hypertension, Type 2 diabetes, and nephropathy, defined as an early-morning urinary albumin-to-creatinine ratio of >300 mg/g, or >200 mg/g in patients receiving therapy targeting the renin-angiotensin-system (RAS).

The patients received losartan at the maximum recommended dose of 100 mg daily over a 3-month run-in period. After this time they were randomly assigned to receive 6 months of treatment with aliskiren, at 150 mg daily for the first 3 months followed by 300 mg daily, or placebo, in addition to losartan.

At 6 months' follow-up, the aliskiren group had a significant 20% relative reduction in mean urinary albumin-to-creatinine ratio compared with the placebo group (p<0.001). The reduction remained significant after adjustment for systolic blood pressure, at 18% (p=0.002).

Indeed, the proportion of patients achieving a reduction of 50% or more in urinary albumin-to-creatinine ratio was 24.7% in patients receiving aliskiren, almost double that of patients receiving placebo, at 12.5%.

The authors note that blood pressure was slightly lower in the aliskiren than placebo group at the end of the study, by 2 mmHg for systolic and 1 mmHg for diastolic blood pressure.

But Hans-Henrik Parving (Rigshospitalet, Copenhagen, Denmark) and team say the differences were marginal, and point out: "The benefits of aliskiren appear to be independent of the systemic blood pressure."

Commenting on the potential harm of dual RAS blockade in an accompanying editorial, Julie Ingelfinger (Massachusetts General Hospital, Boston, USA) noted: "Although adverse events were not marked, participating patients were chosen carefully - patients with glomerular filtration rates of less than 30 ml per minute or potassium levels greater than 5.1 mmol per liter were excluded."

Thus she concluded: "Whether dual therapy to block the RAS with aliskiren and another agent or agents would provide sustained renoprotection remains to be demonstrated." *N Engl J Med* 2008; **358**: 2433-2446