

## HYPERTENSION

## Aliskerin outshines diuretic

Short-term studies of the direct renin inhibitor aliskerin have provided encouraging results with regard to the efficacy of this new antihypertensive agent. A 12-month, multicenter, randomized, double-blind, controlled trial has now demonstrated that aliskerin is superior to the diuretic hydrochlorothiazide in achieving blood pressure (BP) reductions.

Current guidelines recommend the use of diuretics as first-line treatment of patients with hypertension. However, given that only a third of patients with hypertension achieve BP reductions to a level below the recommended target (<140/90 mmHg), Schmieder and colleagues argue that there is a clear need for antihypertensive agents with better efficacy, and set out to determine whether aliskerin is such a drug.

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The FDA and the European Medicines Agency have approved once-daily use of aliskerin at doses of 150 mg and 300 mg in patients with hypertension. In the study by Schmieder *et al.*, 1,124 patients were randomly assigned to receive once-daily treatment with aliskerin 150 mg for 3 weeks followed by forced-dose titration to 300 mg

for a subsequent 3 weeks ( $n = 459$ ), hydrochlorothiazide 12.5 mg for 3 weeks with forced-dose titration to 25 mg for the following 3 weeks ( $n = 444$ ), or placebo for 6 weeks ( $n = 221$ ). Patients in the placebo group were then reassigned to the aliskerin 300 mg or hydrochlorothiazide 25 mg treatment groups and once-daily treatment was continued for the rest of the 12-month study. From week 12 and week 18, patients were allowed to receive additional amlodipine treatment at doses of 5 mg per day and 10 mg per day, respectively, if they had not achieved the target BP of <140/90 mmHg.

Of the 1,124 patients, 918 completed the 52-week follow-up. More patients receiving the diuretic than those receiving aliskerin discontinued treatment at some point during the study (107 versus 70, respectively). There was no difference between the two treatment groups in the number of adverse events, most of which were mild or moderate in intensity, and no deaths occurred in either group during the trial. Similar proportions of patients in the aliskerin and hydrochlorothiazide groups required additional amlodipine treatment to help control their BP. Both aliskerin and hydrochlorothiazide were more efficacious at reducing BP than placebo after 6 weeks of treatment; however, aliskerin was found to be a better antihypertensive agent than the diuretic at the 6-week, 12-week, 26-week, and 52-week time points.



Schmieder *et al.* conclude that aliskerin “provides effective BP lowering that is maintained during long-term treatment in patients with mild to moderate hypertension” and that aliskerin can be used safely and efficaciously in combination with amlodipine—an important finding since many patients use more than one antihypertensive drug to control their BP.

*Bryony M. Mearns*

**Original article** Schmieder, R. E. *et al.* Long-term antihypertensive efficacy and safety of the oral direct renin inhibitor aliskerin. A 12-month randomized, double-blind comparator trial with hydrochlorothiazide. *Circulation* **119**, 417–425 (2009).