HYPERTENSION FIRST-IN-CLASS AGENT LOWERS BP

A novel inhibitor of aldosterone synthase, LCI699, safely reduces serum aldosterone levels, as well as clinic and ambulatory blood pressure in patients with primary hypertension. “Aldosterone, in combination with high dietary salt, [is] an important mediator of target-organ damage, including endothelial function, cardiac hypertrophy, and renal disease,” says Professor David Calhoun, lead author of a report on a phase II trial of LCI699.

Aldosterone is produced in the zona glomerulosa of the adrenal cortex by aldosterone synthase, and acts primarily at the renal distal convoluted tubules as a regulator of fluid and electrolyte homeostasis. Mineralocorticoid-receptor blockers (such as spironolactone and eplerenone) block the actions of aldosterone at the level of the receptor and effectively lower blood pressure, but can cause reactive increases in circulating aldosterone levels with potential nonreceptor-mediated, nongenomic effects. “Blocking production of aldosterone through inhibition of aldosterone synthase represents a novel and potentially more-effective means of preventing the deleterious effects of aldosterone,” hopes Professor Calhoun.

The investigators randomly allocated 524 patients with primary hypertension to receive 0.25, 0.5, or 1.0 mg of LCI699 once daily or 0.5 mg twice daily, eplerenone 50 mg twice daily, or placebo. After 8 weeks, LCI699 1.0 mg and eplerenone significantly reduced clinic diastolic blood pressure compared with placebo. Clinic systolic blood pressure was significantly reduced by 12.6 and 13.8 mmHg by LCI699 1.0 mg and eplerenone, respectively, and by the other regimens of LCI699, compared with placebo. 24 h mean ambulatory diastolic and systolic blood pressure was reduced in all the active-treatment groups after 8 weeks. No differences in the rate of adverse events were observed between the groups.

Professor Calhoun believes “the positive findings of this study support the testing of this class of agent in other disease processes linked to aldosterone, such as resistant hypertension and congestive heart failure”.

Gregory B. Lim

Original article Calhoun, D. A. *et al.* Effects of a novel aldosterone synthase inhibitor for treatment of primary hypertension. Results of a randomized, double-blind, placebo- and active-controlled phase 2 trial. *Circulation* doi:10.1161/CIRCULATIONAHA.111.029892