Letter by Keidar and Gamliel-Lazarovich
Regarding Article, “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”

To the Editor:

We read with great interest the recent report by Calhoun et al. in which the authors tested the effect of a novel aldosterone synthase inhibitor, LCI699, for treatment of primary hypertension. An 8-week course of treatment with LCI699 indeed resulted in a significant decrease in blood pressure for all doses tested, although this effect was not consistent with dose. The authors reported a moderate effect of this drug on aldosterone levels, and, according to their data, the only significant reduction of serum aldosterone level was observed for a dose of 0.5 mg twice a day. However, treatment with 0.5 mg once or twice a day resulted in a similar reduction in blood pressure, which was not a reflection of serum aldosterone levels. Thus, even if half-life considerations are taken into account, we are not convinced that these results support a correlation between the antihypertensive and the antialdosterone effects of LCI699 as was concluded. The discrepancy between serum aldosterone and blood pressure changes could reflect differences in response rate. The authors provided data only for blood pressure reduction. It could have been of value if the authors had provided similar data for aldosterone reduction. Moreover, an analysis of blood pressure changes in correlation with aldosterone changes, per patient, could shed light on the relationships between these 2 phenomena.

A similar discrepancy between aldosterone synthesis inhibition and beneficial effects of the inhibitor was previously reported in our study with another aldosterone synthase inhibitor, FAD286. We have reported dose-dependent beneficial antiatherosclerosis and antiinflammatory effects of this compound in apolipoprotein E knockout mice that were surprisingly dissociated from the aldosterone synthesis inhibition.

Thus, further studies are needed to understand the mechanism by which aldosterone synthase inhibitors exert their beneficial effects, which are probably dissociated from the serum aldosterone–lowering action.

Disclosures

None.

Shlomo Keidar, MD
Aviva Gamliel-Lazarovich, MSc
Lipid Research Laboratory
Technion Rappaport Faculty of Medicine
Rambam Medical Center
Haifa, Israel

References


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Shlomo Keidar and Aviva Gamliel-Lazarovich

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