It Is the Plasma Renin Activity Level That Counts, not Stoichiometry

To the Editor:

We disagree with Danser et al1 that, in patients taking the renin inhibitor aliskiren, “it is the stoichiometry that counts, not the rise in renin.” In fact, plasma renin activity (PRA) is a more explicit indicator than stoichiometry. A PRA fall during aliskiren means that renal renin secretion did not increase by much. A PRA rise means that the increase in renal renin secretion was large enough to overwhelm the aliskiren blockade of PRA. It is that simple.

PRA falls during aliskiren therapy in most patients with mild-to-moderate hypertension2 (Figure). However, the magnitude of the fall differs among patients, and PRA actually increases in ∼1 in 20 patients, indicating that aliskiren can be overwhelmed by a reactive rise in renin.3 Moreover, 2 patients reported by Stanton et al2 had >20 mm Hg sustained increases in daytime systolic pressure (measured by ambulatory blood pressure monitoring), thereby indicating that blood pressure can rise during aliskiren.

A rise in blood pressure during aliskiren can alert the clinician to excessive kidney renin secretion; such a patient is likely to respond to a β-blocker, because β-blockers reduce renin secretion. However, there are 2 quite different reasons for the absence of a blood pressure fall during aliskiren. The patient may have had low renin to begin with and no renin to block, or, alternatively, renin secretion may have increased so much that it overcame the blocking action of the drug. PRA will be low in the former type of patient but not in the latter. The low-renin patient is likely to respond to a natriuretic drug, whereas adding a natriuretic drug instead of an antirenin drug to the hyperreactive renin patient will increase renin secretion even more to reduce the likelihood of a fall in blood pressure. Thus, knowing the PRA level is what counts, not stoichiometry.

Sources of Funding
This work was supported by the May and Samuel Rudin Family Foundation, the Trust of Frederick Schwartz, and the Lawrence M. Gelb Foundation.

Disclosures
J.E.S. and J.H.L. are consultants to Diasorin Inc. J.H.L. has licensed patent 09/657,027, “Method for Evaluating and Treating Hypertension,” to Diasorin Inc.

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2. Stanton A, Jensen C, Nussberger J, O’Brien E. Blood pressure lowering in essential hypertension were treated for 4 weeks with 150 mg (triangles) or 300 mg (circles) of aliskiren. Vertical line =1 SD from the median value.Redrawn from Stanton et al.2
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Hypertension. 2008;52:e20; originally published online July 7, 2008;
doi: 10.1161/HYPERTENSIONAHA.108.116319

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/52/2/e20

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