## COMMENTS AND RESPONSES

## Effects of Combined Ezetimibe and Simvastatin Therapy as Compared With Simvastatin Alone in Patients With Type 2 Diabetes: A Prospective Randomized Double-Blind Clinical Trial

Response to Sarigianni, Katsiki, and Mikhailidis

arigianni et al. (1) properly pointed out that in the Ezetimibe and Simvastatin in dyslipidemia of Diabetes (ESD) randomized clinical trial "the serum HDL cholesterol was significantly lower after adding ezetimibe compared with simvastatin monotherapy." The concomitant reduction in LDL cholesterol observed during simvastatin and ezetimibe combination therapy, however, exceeded the decrease in HDL cholesterol (2). Consequently, the LDL-to-HDL cholesterol ratio decreased from (mean  $\pm$  SD)  $2.11 \pm 0.64$  at randomization to  $1.52 \pm$ 0.50 at the end of the 6-month ezetimibe add-on treatment period-a change that was highly significant (P < 0.0005). Conversely, no appreciable change was observed during simvastatin and placebo therapy  $(1.88 \pm 0.64 \text{ vs.} 1.96 \pm 0.71)$ P = 0.26). Thus, changes in LDL-to-HDL cholesterol ratio were significantly different between treatment arms (P < 0.0001, ANCOVA).

As suggested, we also assessed the effect of ezetimibe on renal function. Serum creatinine levels at randomization and at the end of the treatment period were similar in subjects randomized to simvastatin and ezetimibe combined therapy  $(\text{mean} \pm \text{SD}, 0.90 \pm 0.18 \text{ vs}, 0.91 \pm 0.17)$ mg/dl, P = 0.73) as well as in control subjects on simvastatin and placebo  $(0.87 \pm 0.20 \text{ vs.} 0.88 \pm 0.21 \text{ mg/dl}, P =$ 0.36). Serum creatinine changes were not significantly different between treatment groups (P = 0.48, ANCOVA). Throughout the study, no specific effect of ezetimibe on serum creatinine levels was observed in any considered patient subgroup.

The above findings provide additional evidence that adding ezetimibe to simvastatin therapy helps improve the proatherogenic lipoprotein profile in type 2 diabetic patients while avoiding the drawbacks of maximizing statin doses but challenge previous data that it might ameliorate kidney function in this population (3,4).

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Study Investigators is included in the online appendix available at http://care.diabetesjournals.org/ cgi/content/full/dc10-1412/DC1.

- DOI: 10.2337dc10-1412
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Acknowledgments— No potential conflicts of interest relevant to this article were reported.

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