Response by Takase and Matoba to Letter Regarding Article, “Ezetimibe in Combination With Statins Ameliorates Endothelial Dysfunction in Coronary Arteries After Stenting: The CuVIC Trial (Effect of Cholesterol Absorption Inhibitor Usage on Target Vessel Dysfunction After Coronary Stenting), a Multicenter Randomized Controlled Trial”

In Response:

We appreciate the letter regarding our recently published CuVIC trial (Effect of Cholesterol Absorption Inhibitor Usage on Target Vessel Dysfunction After Coronary Stenting).1 As pointed out in the letter, there were no differences at the baseline, in background characteristics (sex, age, systolic blood pressure, and ejection fraction) and coronary risk factors (hypertension, diabetes mellitus, dyslipidemia, family history, smoking habits, and metabolic syndrome). There were also no differences in laboratory data (total cholesterol, triglyceride, high-density lipoprotein cholesterol, LDL-C, apolipoprotein A1, apolipoprotein B, and high-sensitive C-reactive protein) at the baseline. Changes in lipids during study treatment were analyzed using ANCOVA to correct baseline LDL-C values, and a significant decrease of the total oxysterol level was observed in ezetimibe plus statin arm, as shown in Figure III in the online Data Supplement.1 Although there might be unmeasured confounders in the post hoc analysis, the decreases in oxysterols seem to be substantial by the treatment with ezetimibe and were associated with an improvement of coronary endothelial function.

It is also interesting to discuss the mechanisms of vasculo-protective effects of lipid-lowering therapy, namely the reduction in LDL-C, pleiotropic effects by statins,2 or now reductions in oxysterol-lowering agents with different mechanisms. In the previous study, the correlation of coronary responses to ACh (acetylcholine) and brachial dilator response to reactive hyperemia (R²=0.13)3 and the change of coronary blood flow and reactive hyperemia peripheral arterial tonometry index measured by EndoPAT (R²=0.16)4 were less than sufficient to estimate the effects of drug therapies on coronary endothelial function by these peripheral endothelial function studies. Third, the difference of treatment period, 7 months in the CuVIC trial and 6 weeks in the PANACEA study, might also affect the findings. Because of these notions, we had better not simply dismiss the pleiotropic effects of statins or ezetimibe beyond LDL-C-lowering effect on the results of the PANACEA study.3 Rather, it is time to reconsider the mechanisms of lipid-lowering therapy, including the oxysterol-lowering effect of ezetimibe, on coronary endothelial function, which apparently requires further investigations by the use of lipid-lowering agents with different mechanisms.

Disclosures

Dr Matoba has received honoraria as a speaker from MSD. The other authors report no conflicts.

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References


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