3. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med 2004;350:1495–504.
4. Tobis JM, Perlowski A. Atheroma volume by intravascular ultrasound as a surrogate for clinical end points. J Am Coll Cardiol 2009;53:1116–8.

Reply

First, we express our deep appreciation for the sincere criticism by Dr. Kaneda and colleagues of our paper (1). However, we have a few concerns regarding their arguments.

1. The REVERSAL (REVERSing Atherosclerosis with Aggressive Lipid Lowering) study (2) examined patients with stable coronary artery disease who could undergo an elective cardiac catheterization, whereas the PROVE-IT–TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22) (3) and our JAPAN-ACS (Japan Assessment of Pitavastatin and Atorvastatin in Acute Coronary Syndrome) study examined patients with acute coronary syndrome. Several reports have been published that nonculprit plaque differs in tissue characteristics between acute coronary syndrome and stable coronary artery disease. Therefore, extrapolations of the data between the REVERSAL and the PROVE-IT–TIMI 22 studies have major limitations.
2. Their criticism was not based on any kind of rational statistical meta-analysis. The value of the difference in the mean percentage of change in plaque volume of 1.3% in the REVERSAL study cannot necessarily be considered similar to the 1.1% in our study. The value of 1.3% of the REVERSAL study came from the difference between 5.4% and 4.1%, whereas the value of 1.1% in our study resulted from the difference between −16.9% and −18.1%. Therefore, 1.3% of the REVERSAL study might be considerably more remarkable than 1.1% in our study.
3. The intravenous ultrasound measurement of plaque volume differed between the REVERSAL study and our study. The REVERSAL study measured the longer segment with a total of 30 mm or more integrated with 1-mm interval cross-sectional area tracings, whereas our study measured a specific plaque segment of a total length of approximately 7 mm with 0.1-mm interval tracings. Therefore, even a similar difference in the mean percentage of change in plaque volume in the REVERSAL study might have a more significant clinical impact on future cardiac events than that in our study.

Takafumi Hiro, MD
Takeshi Kimura, MD
Takeshi Morimoto, MD
Katsumi Miyauchi, MD
Yoshihisa Nakagawa, MD
Masakazu Yamagishi, MD
Yukio Ozaki, MD
Kazuo Kimura, MD
Satoshi Saito, MD
Tetsu Yamaguchi, MD
Hiroyuki Daida, MD
***Masunori Matsuzaki, MD**

*Department of Medicine and Clinical Science
Division of Cardiology
Yamaguchi University Graduate School of Medicine
1-1-1 Minamikogushi
Ube, Yamaguchi 755-8505
Japan
E-mail: masunori@yamaguchi-u.ac.jp

doi:10.1016/j.jacc.2009.08.056

REFERENCES

1. Hiro T, Kimura T, Morimoto T, et al. Effect of intensive statin therapy on regression of coronary atherosclerosis in patients with acute coronary syndrome: a multicenter randomized trial evaluated by volumetric intravascular ultrasound using pitavastatin versus atorvastatin (JAPAN-ACS [Japan assessment of pitavastatin and atorvastatin in acute coronary syndrome] study). J Am Coll Cardiol 2009;54:293–302.
2. Nissen SE, Tuzcu EM, Schoenhagen P, et al. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. JAMA 2004;291:1071–80.
3. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med 2004;350:1495–504.

The BALANCE Study

Too Early to Speculate on Mortality Effects

We read with great interest the paper by Yousef et al. (1) and the accompanying editorial (2) demonstrating and discussing long-term data on cardiac function and mortality in patients treated with autologous bone marrow cell (BMC) transplantation after myocardial infarction.

We do not agree with the editorial's statement that, based on the new data, BMC infusion "can now be considered safe and modestly efficacious" (2), despite the finding that fatal events were more frequent in the control group. The patient cohort studied and the event rate observed were far too small to draw such conclusions. The total number of fatal events was only 8. Also, if the authors had included hospitalizations in the analyses, as is often done in outcome studies, such a combined end point would not have provided conclusive results. Of note, taking the results from Table 1 of their paper (1), there were 9 unplanned hospitalizations in the BMC group and 8 in the intervention group.

In addition, a recent 4-year follow-up study with 86 patients, despite slight improvements in cardiac function, could not identify significant differences in myocardial viability or mortality (3). The BALANCE (Clinical Benefit and Long-Term Outcome After Intracoronary Autologous Bone Marrow Cell Transplantation in Patients With Acute Myocardial Infarction) trial thus may be viewed as a successful proof-of-principle study, but there still is a need for large-scale, placebo-controlled, double-blind clinical end point studies to justify any conclusion with regard to safety or even mortality. Fortunately, such large trials are currently underway at several places worldwide and will clarify those important outstanding issues.

Furthermore, the authors addressed paracrine effects of transplanted autologous cells as the major mechanism explaining the beneficial effects of BMC transplantation. In our view, additional mechanisms should be taken into account. BMC transplantation