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Letters

TO THE EDITOR

Pleiotropic Effects of Ticagrelor Beyond its Potent Antiplatelet Effects Contributing to Additional Clinical Benefits

We read with interest the report in which Ariotti et al. (1) investigated whether ticagrelor improves endothelium-dependent dilation. This is an excellent randomized, crossover trial.

However, these results were inconsistent with previous studies. In comparison to our previous study (2), the enrolled patients were not at relatively high risk because the prevalence of diabetes was only 20%. Sample size calculation was based on the reactive hyperemia index which targeted disease-free participants. Consequently, absolute number needed for confirming vascular benefits of ticagrelor by the reactive hyperemia index should be higher. In this trial, because changes of flow-mediated dilation improved significantly in the ticagrelor group compared with the clopidogrel group, the pleiotropic effects of ticagrelor should be further investigated.

More importantly, the authors enrolled the stabilized patients after acute coronary syndrome. Sixty-nine percent of patients had been prescribed ticagrelor before randomization. In our study (2), improvement of vascular function accessed by flow-mediated dilation was observed during the periods of administrating ticagrelor with partial maintenance of beneficial effects even after crossover. Because there were no washout periods, retained effects of ticagrelor could not be excluded. How long-term uses of ticagrelor could impact the vascular functions or biomarkers was not investigated until now.

In addition, targeting vascular biomarkers should focus on the pathways of adenosine. In our study (2), we already confirmed that circulating adhesion molecules and C-reactive protein did not show significant differences between ticagrelor and prasugrel; however, interleukin-6 and tumor necrosis factor-α decreased significantly only after ticagrelor administration, presumably via stimulating adenosine 2A and 2B receptors.

In this trial, adenosine level was not increased even in the ticagrelor group. To measure the adenosine plasma level, it is known that the role of stop solution is critical to prevent adenosine degradation and uptake right after the blood collection. For instance, the treatment time of stop solution to blood, the ratio of blood and stop solution, and the volume of blood are critical parameters influencing the plasma adenosine concentration (μmol/l). Detailed description about materials and methods of adenosine measurement would help in understanding the results.

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REPLY: Pleiotropic Effects of Ticagrelor Beyond Its Potent Antiplatelet Effects Contributing to Additional Clinical Benefits

We appreciate the comments of Dr. Jeong and colleagues on the HI-TECH (Hunting for the Off-Target Properties of Ticagrelor on Endothelial Function and Other Circulating Biomarkers in Humans) trial (1).