Trade-Off Between Lipid-Lowering Therapy and Costs in Patients With Cardiovascular Disease

Hideki Ishii, MD, PhD; Toyoaki Murohara, MD, PhD

In most of the world, atherosclerotic cardiovascular (CV) disease is an important healthcare issue. In fact, atherosclerotic events are the cause of death in approximately one-quarter of Japanese individuals.

It is well known that lifestyle modifications and medical therapy for intensive lipid-lowering improve prognosis and prevent CV events. Studies and meta-analyses in Western countries have shown that aggressive low-density lipoprotein cholesterol (LDL-C) lowering therapies have beneficial effects on reducing atherosclerosis, resulting in a significant reduction in CV events. These findings suggest that the lower the LDL-C level, the better. However, there has not been any recently published evidence to support this concept of lowering of LDL-C.

Recently, the Randomized Evaluation of Aggressive or Moderate Lipid Lowering Therapy with Pitavastatin in Coronary Artery Disease (REAL-CAD) study clearly showed that 4-mg compared with 1-mg doses of pitavastatin significantly reduced CV events in Japanese patients with stable CAD. Therefore, the ‘lower is better’ theory has been extended to Japanese subjects. The Japanese Atherosclerosis Society has recommended consideration of lower targets for LDL-C (i.e., <70 mg/dL) in patients with familial hypercholesterolemia, those with acute coronary syndrome, and diabetic subjects at high risk in the guideline revised in 2017. To date, many agents, particularly statins, have been clearly proven to improve lipid profiles. In recent years, clinical trials have shown that proprotein convertase subtilisin-kexin type 9 (PCSK-9) inhibitors dramatically reduce LDL-C levels, resulting in regression of coronary plaques and improved clinical outcomes. Even in high-risk patients with goals that might be thought impossible to reach 5 years ago, target LDL-C levels can be achieved with combination therapies in the clinical setting.

However, cost-effectiveness is an important issue. In this...
issue of the Journal, Kodera et al conclude that combined use of a PCSK9 inhibitor plus a statin is not cost-effective in Japanese patients with triple-vessel coronary artery disease but shows good cost-effectiveness in those with poorly controlled familial hypercholesterolemia.\textsuperscript{7} The Japanese Ministry of Health, Labour and Welfare reported in 2017 that national medical expenditure in fiscal year 2015 exceeded 42.364 billion yen, a 3.8\%, or 1,557 billion yen increase over the previous year.\textsuperscript{8} Therefore, a trade-off between health care and cost is necessary.

The cost-effectiveness of various medications depends on characteristics that include race and target disease. For example, few reports have shown the effectiveness of treatment with omega-3 polyunsaturated fatty acids in Western countries. However, the Japan EPA Lipid Intervention Study (JELIS) suggested that eicosapentaenoic acid in combination with a statin is a cost-effective treatment compared with statin monotherapy for secondary prevention of CV disease in Japan.\textsuperscript{9} In a subgroup analysis of the JELIS, additional treatment with eicosapentaenoic acid significantly reduced the incidence of major coronary events during a 5-year follow-up, and the number needed to treat was only 10 among patients with prior myocardial infarction and coronary intervention.\textsuperscript{10}

Essentially, Japanese patients with ischemic heart disease have a low incidence of CV events. In the REAL-CAD study, LDL-C levels were 91.0 mg/dL and 76.6 mg/dL in patients treated with 1 mg or 4 mg pitavastatin/day, respectively. However, the 3-year cumulative incidence of a composite of CV death, nonfatal myocardial infarction, nonfatal ischemic stroke, unstable angina requiring emergency hospitalization, or coronary revascularization based on clinical indication was only 8.0\% and 6.7\% in each group, respectively.\textsuperscript{3} However, in the Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Patients With Elevated Risk (FOURIER) trial, the 3-year cumulative incidence of a composite of CV death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization was 12.6\% in patients with LDL-C levels of approximately 30 mg/dL under evolocumab treatment, although a significant reduction in endpoints was seen compared with the placebo group\textsuperscript{8} (Figure). Therefore, cost-effectiveness may be quite different between Japan and Western countries. In addition, there is a trend towards a higher incidence of stroke and lower incidence of CV events in East Asian countries, including Japan, than in Western countries.\textsuperscript{11} Accordingly, Japanese data should be evaluated.

Disclosures


References


