Table 1. Dual Antiplatelet Therapy Study Results: Drug-Eluting Stent Patients 12 to 30 Months After Index Event

End Points	Continued Thienopyridine, % n = 5020	Placebo, % n = 4941	HR (95% CI)	*P* Value
Primary				
Definite or probable ST	0.4	1.4	0.29 (0.17 to 0.48)	< .001
MACCE	4.3	5.9	0.71 (0.59 to 0.85)	< .001
Other				
ST				
Definite	0.3	1.2	0.26 (0.14 to 0.45)	< .001
Probable	0.1	0.1	0.71 (0.22 to 2.23)	.55
All-cause mortality	2.0	1.5	1.36 (1.00 to 1.85)	.052
MI	2.1	4.1	0.47 (0.37 to 0.61)	< .001
Non-ST MI	1.8	2.9	0.59 (0.45 to 0.78)	< .001
Stroke				
Ischemic	0.5	0.7	0.68 (0.40 to 1.17)	.16
Hemorrhagic	0.3	0.2	1.20 (0.50 to 2.91)	.68
	n = 4710	**n = 4649**	**Difference (95% CI)**	
Bleeding				
Moderate/severe bleeding[a]	2.5	1.6	1.0 (0.4 to 1.5)	.001
Moderate	1.7	1.0	0.7 (0.2 to 1.2)	.004
Severe	0.8	0.6	0.2 (–0.1 to 0.6)	.15
BARC				
Type 2	3.1	1.5	1.5 (0.9 to 2.1)	< .001
Type 3	2.6	1.5	1.1 (0.6 to 1.7)	< .001
Type 5	0.1	0.1	0.1 (–0.1 to 0.2)	.38

BARC, Bleeding Academic Research Consortium; DAPT, Dual Antiplatelet Therapy; DES, drug-eluting stent; MACCE, major adverse cardiac or cerebrovascular event; MI, myocardial infarction; ST, stent thrombosis.

[a]GUSTO classification.

Source: Mauri L et al. New Engl J Med. 2014.

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known to be present before enrollment in the study, all-cause mortality was no longer statistically significant ($P = .14$).

The benefit of prolonged thienopyridine therapy reduced both stent-related MI and MI occurring at other coronary locations. Subgroup analyses found that this treatment benefit was consistent across most subgroups. In addition, a small increase in total MI and ST was detected in the 30 days following discontinuation of thienopyridine therapy: both at 12 months and at 30 months. In her concluding remarks, Dr Mauri noted that whether the treatment benefits seen in the DAPT study will be generalizable to other types of stents or nonthienopyridine P2Y12 inhibitors has not been established.

Aspirin Fails to Reduce CVD in Elderly Japanese

Written by Emma Hitt Nichols, PhD

Kazuyuki Shimada, University of Shin-Oyama City Hospital, Tochigi, Japan, presented data from the Japanese Primary Prevention Project study [JPPP; Ikeda Y et al. *JAMA*. 2014], which found that daily, low-dose aspirin did not reduce the risk of cardiovascular disease (CVD) in elderly Japanese patients with risk factors for atherosclerosis.

The use of aspirin as a preventative for CVD is controversial. Although meta-analyses have reported benefits

of aspirin for CVD prevention, risks have also been documented [Raju NC, Eikelboom JW. *Curr Opin Cardiol.* 2012]. In addition, the US Food and Drug Administration (FDA) recently stated that current evidence does not support the general use of aspirin for the prevention of CVD [FDA. Use of Aspirin for Primary Prevention of Heart Attack and Stroke. 2014]. The purpose of the JPPP trial was to evaluate if the daily use of low-dose aspirin was effective in reducing the risk of cardiovascular (CV) events in an elderly Japanese population with risk factors for atherosclerosis.

In the prospective, randomized, open-blinded trial, 14 658 Japanese patients aged 60 to 85 years with hypertension, dyslipidemia, or diabetes mellitus were randomly assigned in a 1:1 fashion to receive enteric-coated aspirin 100 mg/d or no aspirin, in addition to their current medication to control underlying disease(s). The median follow-up was 5.02 years. At baseline, the mean age was about 71 years, about 42% were men, the mean body mass index was 24 kg/m^2, and approximately 13% of the patients were current smokers.

The primary end point was a composite of death from CV causes, nonfatal stroke, and nonfatal myocardial infarction (MI). Secondary end points included a composite of the primary end point plus transient ischemic attack, angina pectoris, and arteriosclerotic disease that required intervention. Secondary end points also included individual end points that made up the composite end points and death from causes other than CV events, all-cause mortality, and serious extracranial hemorrhage.

There was no significant difference in the proportion of patients who experienced the primary end point among the aspirin and no-aspirin arms at year 6 (2.77% with aspirin vs 2.96 with placebo; HR, 0.94; 95% CI, 0.77 to 1.15; P=.54). The results were consistent among major subgroups. Several secondary efficacy end points reached appeared to be lower with aspirin, including nonfatal MI (HR, 0.53; 95% CI, 0.31 to 0.91; P=.02) and transient ischemic attacks (HR, 0.57; 95% CI, 0.32 to 0.99; P=.04).

Aspirin treatment resulted in a significantly greater rate of serious extracranial hemorrhage (HR, 1.85; 95% CI, 1.22 to 2.81; P=.004). In addition, patients who received aspirin were more likely to experience abdominal discomfort, gastroduodenal ulcer, abdominal pain, heartburn, reflux esophagitis, erosive gastritis, gastrointestinal hemorrhage, and nausea.

Prof Shimada concluded that the data from the JPPP trial suggest that daily low-dose aspirin is not effective in decreasing the risk of CVD in elderly Japanese patients. However, he pointed out that the study was terminated early before statistical power was reached, which may have attributed to the observed lack of benefit for the primary end point.

Alirocumab Has Greater Reduction of LDL-C Than Ezetimibe in Patients With Statin Intolerance

Written by Emma Hitt Nichols, PhD

Treatment of patients who are statin intolerant with alirocumab resulted in a significantly greater reduction in low-density lipoprotein cholesterol (LDL-C) when compared with ezetimibe. Patrick M. Moriarty, MD, University of Kansas Medical Center, Kansas City, Kansas, USA, presented these results from the Study of Alirocumab (REGN727/SAR236553) in Patients With Primary Hypercholesterolemia and Moderate, High, or Very High Cardiovascular Risk, Who Are Intolerant to Statins [Odyssey Alternative; NCT01709513].

In clinical practice, up to 25% of patients are statin intolerant as a result of symptoms and abnormalities in biomarkers [Mancini GB et al. *Can J Cardiol.* 2013; Cohen JD et al. *J Clin Lipidol.* 2012; Bruckert E et al. *Cardiovasc Drugs Ther.* 2005]. However, evidence from well-designed randomized trials is lacking for alternative cholesterol-lowering agents [Guyton JR et al. *J Clin Lipidol.* 2014]. The purpose of the Odyssey Alternative trial was to evaluate the efficacy and safety of the monoclonal antibody alirocumab in patients intolerant of statins.

In the double-blind phase 3 trial, 314 patients with statin intolerance were randomly assigned to receive alirocumab, ezetimibe, or atorvastatin for 24 weeks, followed by 2 years of open-label alirocumab treatment. Statin intolerance was defined as intolerance caused by muscle-related symptoms to a minimum of 2 statin drugs, including 1 at the lowest recommended dosage. All patients received placebo for 4 weeks before randomization. This was 1 of 3 periods of validation for these patients to determine their true intolerance to statins. During this period, 13% of patients dropped out, a majority because of muscle complaints. The patients who finished that section then were randomized into the blinded 24-week therapy section. These patients were blinded to alirocumab, ezetimibe, or atorvastatin for further validation of their intolerance to stains. At week 12, the dose of the study drug was increased if the LDL-C was ≥ 70 or ≥ 100 mg/dL, according to cardiovascular risk. The primary end point was percentage change in LDL-C from baseline in the alirocumab and ezetimibe arms.

At baseline, the mean age among all 3 cohorts was 63 years; slightly more than half were men; mean body mass index ranged from 28 to 30 kg/m^2; and 7% of patients were current smokers. Hypertension was present in 62% of the patients, type 2 DM in 24%, and chronic heart disease in 46%. The mean LDL-C, high-density