Society for Immunotherapy of Cancer
And
American Heart Association

Walter Alexander

Urelumab Is Safe and Active as Monotherapy
And in Combination With Nivolumab in
Hematologic and Solid Malignancies

• Erminia Massarelli, MD, Associate Clinical Professor, University of Texas MD Anderson Cancer Center, Houston, Texas

Preclinical models of combined urelumab and nivolumab have demonstrated robust antitumor activity with increased interferon gamma (IFNγ) production versus monotherapy. Because each enhances immune cell activity through distinctly different mechanisms, their activity in patients with advanced cancers may be synergistic, Dr. Massarelli said. Urelumab is a fully human IgG4 monoclonal antibody that binds to and activates CD137-expressing cytotoxic T cells.

A monotherapy study evaluated urelumab in patients with advanced malignancies (0.1 or 0.3 mg/kg every three weeks) or advanced non-Hodgkin’s lymphoma (8 mg every three or six weeks). The combination study evaluated urelumab (3 mg or 8 mg every four weeks) plus nivolumab (3 mg/kg or 240 mg every two weeks) in patients with advanced solid tumors or B-cell lymphoma or patients with diffuse large B-cell lymphoma (DLBCL), melanoma, non–small-cell lung cancer (NSCLC), or squamous cell carcinoma of the head and neck (SCCHN; cohort expansion). Mean age was approximately 65 years. In the combination study, 28% of patients had no prior treatment, and 70% had one or more prior lines of therapy. In the monotherapy study, all patients had been treated previously.

With the urelumab plus nivolumab combination, increases in IFNγ-induced peripheral cytokine expression (CXCL9/ CXCL10) following treatment were larger than those that occurred with urelumab monotherapy. In a small sample of melanoma tumors, greater numbers of CD8-positive T cells and increased CXCL9 gene expression (and a trend toward increased IFNγ gene expression) were observed.

In the monotherapy trial, drug-induced liver injury in one patient led to discontinuation of the 0.3-mg/kg dose of urelumab. No treatment-related deaths were reported, and only three of 70 patients withdrew due to treatment-related adverse events.

The monotherapy overall response rate (ORR) was 10% (5% complete and 5% partial remission), with all responses occurring in those with B-cell non-Hodgkin’s lymphoma (B-NHL). The confirmed disease control rates (DCR) for B-NHL, colorectal cancer (CRC), SCCHN, and other solid tumors were 28%, 18%, 20%, and 39%, respectively.

Among the 128 combination-therapy patients receiving flat-dose urelumab (8 mg every four weeks) and nivolumab (240 mg every two weeks), adverse events led to discontinuation in 10% of patients (seven of 128 patients any grade; six of 128 patients grades 3–4). Fatigue was the most commonly reported adverse event (31% any grade; 0% grades 3–4). “This indicates that these two agents can be safely administered together,” Dr. Massarelli said.

The ORR (confirmed and unconfirmed) was 50% among 46 melanoma anti-programmed cell death-1 (PD-1)/ programmed death ligand-1 (PD-L1) naïve patients and the DCR rate (confirmed and unconfirmed) was 70%. DCRs were 21% for DLBCL, 21% for NSCLC (anti-PD-1/PD-L1) progressors, 35% for NSCLC (anti-PD-1/PD-L1 naïve), 23% for SCCHN, and 33% for other solid tumors.

PD-L1 status (1% or greater or less than 1%) had no effect on ORR in melanoma patients receiving the urelumab plus nivolumab combination who were anti-PD-1/PD-L1 naïve, with rates of 50% (1% or greater) and 47% (less than 1%).

Among patients receiving combination therapy with urelumab and nivolumab, safety was manageable at all evaluated doses. Dr. Massarelli concluded that in the urelumab monotherapy trial, the 0.1-mg/kg and 8-mg doses demonstrated manageable safety profiles and peripheral pharmacodynamic activity. Promising antitumor activity was observed in melanoma patients.

Greater Benefit for Nivolumab 1 mg/
Ipilimumab 3 mg in Previously Treated
Metastatic Urothelial Cancer

• Padmanee Sharma, MD, University of Texas MD Anderson Cancer Center, Houston, Texas

In previously treated patients with metastatic urothelial carcinoma (mUC), chemotherapy efficacy is poor and associated with significant toxicity, Dr. Sharma said. Monotherapy trials (phase 1/2 and 2) of nivolumab have shown notable antitumor activity in patients previously treated for mUC,
with overall response rates (ORR) of 19.6% and median overall survival (OS) of 8.7 months. Both preclinical and clinical data with the combination of nivolumab, a programmed cell death-1 blockade, and ipilimumab (Yervoy, Bristol-Myers Squibb), a cytotoxic T-lymphocyte–associated antigen-4 blockade, have shown improved antitumor activity in advanced melanoma, non–small-cell lung cancer, and metastatic renal cell carcinoma.

Dr. Sharma presented first results from Checkmate 032, the first trial of combination immunotherapy in mUC. The phase 1/2 study compared two dosing strategies of nivolumab combined with ipilimumab in patients with previously treated metastatic disease. Twenty-eight patients received nivolumab 1 mg/kg plus ipilimumab 3 mg/kg (intravenously [IV] every three weeks for four cycles) and 104 patients treated nivolumab 3 mg/kg plus ipilimumab 1 mg/kg (IV every three weeks for four cycles), with all receiving maintenance with nivolumab 3 mg/kg IV every two weeks. The primary endpoint was investigator-assessed confirmed ORR.

Median age was greater in patients in the nivolumab 1-mg/ipilimumab 3-mg group (50.0% versus 45.2% were 65 years of age or older). Both groups had approximately 60% of patients treated with two or more prior regimens. Programmed death ligand-1 expression was higher than 1% in more patients in the nivolumab 1-mg/ipilimumab 3-mg group (38.5% versus 28.8%).

More patients are continuing treatment in the nivolumab 1-mg/ipilimumab 3-mg group (46.2% versus 14.4%). Also in that group, discontinuation for disease progression was lower (38.5% versus 64.4%). Elevation of alanine aminotransferase and aspartate aminotransferase levels was greater with the higher nivolumab dose (17.3%/11.5% versus 0%/0%, respectively). Treatment discontinuation rates were 7.7% for nivolumab 1 mg/ipilimumab 3 mg and 13.5% for nivolumab 3 mg/ipilimumab 1 mg.

Dr. Sharma said, “Grade 3–4 adverse event rates were around 30% and very similar for both groups.”

“It’s very important to note the overall response rate compared to the 19% with nivolumab monotherapy reported in Lancet Oncology and the 15% rate previously reported for atezolizumab,” Dr. Sharma said, stating that confirmed ORR was 38.5% in the nivolumab 1-mg/ipilimumab 3-mg group (95% confidence interval [CI], 20.2–59.4) and 26.0% in the nivolumab 3-mg/ipilimumab 1-mg group (95% CI, 17.9–35.5). Historical controls, she added, were 10% or less.

Complete response (3.8% versus 2.9%) and partial response rates (34.6% versus 23.1%) were higher with the higher ipilimumab dose regimen. The progressive disease rate, however, was higher with the lower ipilimumab dose regimen (26.9% versus 41.3%). Median tumor change from baseline in the target lesion was ~27.8% in the nivolumab 1-mg/ipilimumab 3-mg group and 0% in the nivolumab 3-mg/ipilimumab 1-mg group. While median time to response was similar for both groups (1.4 months), ongoing response rates were higher for the higher ipilimumab dose group (80% versus 70%), as were the median progression-free survival (4.3 months versus 2.6 months) and median OS rates (10.2 versus 7.3 months).

“Efficacy with nivolumab 3 mg plus ipilimumab 1 mg did not appear to differentiate from that with nivolumab monotherapy,” Dr. Sharma observed. Nivolumab monotherapy findings had been reported previously.

While the cohort size is small, she said the findings are “very promising.” Dr. Sharma noted that the nivolumab 1-mg/ipilimumab 3-mg cohort is being expanded to 92 patients.

Commenting on a question raised after her presentation regarding the possibility of using ipilimumab at 10 mg/kg, Dr. Sharma responded, “With ipilimumab 3 mg/kg you get the same T-cell activation as with ipilimumab 10 mg/kg. Our monitoring showed, however, that ipilimumab 1 mg/kg does not give you the same level of T-cell activation as with 3 mg/kg—which would not give you the same level of antitumor response.”

**American Heart Association (AHA)**

This year’s AHA meeting, held November 12–16 in New Orleans, attracted approximately 18,000 medical professionals from nearly 100 countries. We review below key sessions focusing on anticoagulation for peripheral artery disease and for stroke protection in atrial fibrillation, cholesterol-lowering strategies, COX-2 inhibitors, and cognitive decline.

**Effects of Ticagrelor Compared With Clopidogrel In Patients With Peripheral Artery Disease**

- Manesh R. Patel, MD, Associate Professor of Medicine, Duke University Medical Center, Durham, North Carolina

EUCLID, a trial designed to test whether long-term monotherapy for symptomatic peripheral artery disease (PAD) with ticagrelor (Brilinta, AstraZeneca) is superior to clopidogrel in preventing cardiovascular death, myocardial infarction, or ischemic stroke, found identical combined event rates for both agents. PAD is associated with both cardiovascular and limb morbidity and mortality, Dr. Patel noted in an AHA press briefing. He also said that composite cardiovascular death, myocardial infarction, or ischemic stroke with clopidogrel in the CAPRIE trial (1996) was reduced by 8.7% (P = 0.043) versus aspirin. In further research among patients with acute coronary syndromes (ACS), chronic therapy with the antiplatelet agent ticagrelor demonstrated superiority over clopidogrel for the same composite endpoint.

EUCLID investigators enrolled 13,885 symptomatic PAD patients (811 sites, 28 countries) double-blind to ticagrelor 90 mg twice daily or clopidogrel 75 mg once daily. Median age was 66 years, and approximately 28% of the patients were women. Eight percent of the patients had prior stroke, approximately 29% had coronary artery disease, and about 18% had a prior myocardial infarction. Claudication was mild or moderate in approximately 53% of patients.

Reporting the combined primary endpoint, Dr. Patel said that 36-month cardiovascular death, myocardial infarction, or ischemic stroke occurred at an identical rate of 12.5% with both ticagrelor and clopidogrel. While individual components of the endpoint were generally similar between groups, ischemic stroke was more common among patients receiving clopidogrel compared with ticagrelor (2.4% versus 1.9%; P = 0.03). The rate for major bleeding (measured with the Thrombolysis in
Inhibition of PCSK9 Synthesis via 
RNA Interference: 90-Day Data From 
Orion-1—A Multicenter, Phase 2, 
Randomized, Controlled Trial

• Kausik K. Ray, MD, Imperial College, London, United Kingdom

“LDL-C [low-density lipoprotein-cholesterol] reduction is a proven strategy to prevent atherosclerotic cardiovascular disease,” Dr. Ray stated at an AHA press conference. While monoclonal antibodies that block proprotein convertase subtilisin/kexin type 9 (PCSK9) have demonstrated significant LDL-C lowering with or without statins, the needed 12 to 24 subcutaneous (SC) injections per year remain logistically and economically difficult. RNA interference, Dr. Ray said, is a highly efficient approach to inhibiting PCSK9 synthesis in the liver, and in a phase 1 trial of 300 mg of SC inclisiran in 69 patients, LDL-C was reduced by about 50% for four to six months. Inclisiran is a synthetic double-strand 21–23mer oligonucleotide.

The ORION-1 trial included 501 patients (mean age, approximately 63 years) with atherosclerotic cardiovascular disease or high atherosclerotic cardiovascular disease risk with LDL-C greater than 70 mg/dL or 100 mg/dL, respectively, despite maximally tolerated statin therapy. About 69% of patients had atherosclerotic cardiovascular disease, and 24% had diabetes. Thirteen percent were being treated for primary prevention, and the rest had familial hypercholesterolemia (5%). At baseline, 81% of patients were on statins, and 31.7% were on the cholesterol-lowering drug ezetimibe (Zetia, Merck).

ORION investigators compared six different SC dosing regimens of inclisiran to SC placebo. The primary endpoint was percent change in LDL-C levels from baseline at day 180. A single dose of inclisiran produced durable PCSK9 and LDL-C lowering (P < 0.0001 versus placebo for all inclisiran doses) at 90 days. A second inclisiran dose at 90 days sustained these reductions to day 180. The mean absolute change in LDL-C from baseline in the placebo group was –3.1%; for inclisiran, it was 64.9% (two doses). Looking at the 300-mg dose, Dr. Ray said that a single dose achieved a mean LDL-C reduction of 51%, while two 300-mg doses achieved a 57% LDL-C reduction.

Treatment-emergent adverse events at day 90 were reported at similar levels for placebo (54%) and pooled inclisiran doses (54%; 100 mg [62%], 200 mg [52%], 300 mg [56%], 500 mg [43%]). Severe adverse event rates were 4% for placebo and 3% for inclisiran. Myalgia was reported in 4.7% and 5.7% of placebo and inclisiran patients, respectively. Injection site adverse event (erythema, pruritus, rash, or reaction) rates were 0% for placebo and 3.2% for the pooled inclisiran groups.

The findings, Dr. Ray commented, affirm potential for biannual or triannual dosing and warrant continued evaluation of inclisiran in a phase 3 trial. RNA interference with inclisiran would be less expensive and has potential for sustained suppression of hepatic PCSK9 production with fewer injections. “The efficacy, safety, and dosing profile of inclisiran are likely to ensure significant and durable reductions in LDL-C and, thus, potentially impact cardiovascular outcomes.”

Cardiovascular Outcomes With Celecoxib Versus Ibuprofen or Naproxen: The PRECISION Trial

• Steven E. Nissen, MD, Cleveland Clinic, Cleveland, Ohio

Nonsteroidal anti-inflammatory drugs (NSAIDs) and celecoxib (Celebrex, Pfizer), a cyclooxygenase type-2 (COX-2) selective inhibitor, reduce pain and inflammation through the inhibition of prostaglandins in osteoarthritis and rheumatoid arthritis patients. When rofecoxib, another COX-2 selective inhibitor, was withdrawn from the market in 2004 because of increased risks of heart attack and stroke associated with its long-term, high-dosage use, the Food and Drug Administration required a post-marketing cardiovascular safety trial comparing the only remaining COX-2 selective inhibitor, celecoxib, with traditional nonselective NSAIDs.

To meet that requirement and to address doubts about the cardiovascular safety of COX-2 inhibitors, the PRECISION trial was designed to evaluate the effects of celecoxib (100–200 mg twice daily) and ibuprofen (600–800 mg three times daily) compared with naproxen (375–500 mg twice daily) on the first occurrence of an Antiplatelet Trialists Collaboration (APTC) composite cardiovascular endpoint (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke). PRECISION included 24,081 patients at 924 sites in 13 countries with osteoarthritis or rheumatoid arthritis and with or at high risk for concomitant cardiovascular disease. Administration of aspirin 75–100 mg daily was allowed according to local guidelines. Patients were provided with daily esomeprazole for gastrointestinal protection.

Meeting Highlights: American Heart Association

Myocardial Infarction score) was also identical for the ticagrelor and clopidogrel groups at 1.6% (P = 0.49).

The findings demonstrated that the active comparator in EUCLID, clopidogrel, is an “effective antiplatelet therapy in PAD. Ticagrelor was not superior to clopidogrel for the reduction of cardiovascular events,” Dr. Patel said. A further message from EUCLID, he added, “is that caution needs to be exercised in extrapolating evidence from coronary artery disease patients to peripheral artery disease.”

A possible explanation for the discrepancy between CAPRIE and EUCLID results, commented AHA discussant Carl Pepine, MD, from the University of Florida, could be that clopidogrel is a prodrug that needs to be metabolized to exert its antiplatelet action. EUCLID excluded patients who were poor metabolizers of clopidogrel, perhaps accounting for the equivalent effectiveness with ticagrelor. The signal for reduced stroke with ticagrelor may also be explained by concomitant blood pressure reduction, as was demonstrated for ticagrelor versus clopidogrel in the DISPERSE-2 trial, Dr. Pepine said.

“Clearly many knowledge gaps remain relative to PAD,” he said, noting that PAD, which occurs in 10% of Americans older than 60 years of age, is associated with higher risk for adverse outcomes, ostensibly through large atherosclerosis risk factor burden, more diffuse atherosclerosis, enhanced platelet activation, and inflammation.

Nonsteroidal anti-inflammatory drugs (NSAIDs) and celecoxib (Celebrex, Pfizer), a cyclooxygenase type-2 (COX-2) selective inhibitor, reduce pain and inflammation through the inhibition of prostaglandins in osteoarthritis and rheumatoid arthritis patients. When rofecoxib, another COX-2 selective inhibitor, was withdrawn from the market in 2004 because of increased risks of heart attack and stroke associated with its long-term, high-dosage use, the Food and Drug Administration required a post-marketing cardiovascular safety trial comparing the only remaining COX-2 selective inhibitor, celecoxib, with traditional nonselective NSAIDs.

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No Cognitive Decline Benefit for Cholesterol or Blood Pressure Lowering Among the Elderly in HOPE-3

- Jackie Bosch, PhD, McMaster University, Hamilton, Ontario, Canada

"Dementia, vascular cognitive impairment, vascular dementia, and cognitive aging are some of the biggest concerns of our elderly and aging populations. Unfortunately, we don’t have any treatments or approaches that actually alter that risk," said Ralph Sacco, MD, University of Miami Health System and former AHA President, the AHA-appointed discussant for this trial. Despite many smaller studies showing strong relationships between blood pressure, diabetes, and cholesterol control and decreases in cognitive decline, randomized trials have not shown significant reductions in cognitive decline. “HOPE-3,” he said, “is important because it uses a randomized clinical trial design to address this question.”

HOPE-3 randomized moderate-risk individuals from 228 centers in 21 countries to receive either candesartan/hydrochlorothiazide or placebo and rosvastatin or placebo. Dr. Bosch’s HOPE-3 trial substudy examined the effect of cholesterol and blood pressure lowering on cognitive decline in the subset of 1,626 patients 70 years of age or older. Participants answered questions relative to decline in processing speed (primary outcome measured by the Digit Symbol Substitution Test [DSST]), executive function, psychomotor speed, functional changes, and global activity.

Cognitive and functional decline were observed over the 5.6 years of follow-up. Blood pressure-lowering agents and rosvastatin, however, did not significantly prevent cognitive or functional decline. Study end DSST scores were similar for individuals receiving blood pressure medications or placebo ($P = 0.86$), statin lowering with rosvastatin or placebo ($P = 0.38$), and the combination of blood pressure and cholesterol lowering versus double placebo ($P = 0.63$). A post hoc analysis among 93 patients revealed a positive trend toward reduced cognitive decline in those in the highest tertile of blood pressure and LDL cholesterol (greater than 145 mm Hg and greater than 140 mg/dL, respectively) at baseline. Longer duration of blood pressure lowering was also associated with less cognitive decline. “Both of these findings,” Dr. Bosch emphasized, “require further confirmation.”

While anecdotal and observational studies have raised concerns that statins may adversely affect cognition and have led to black box warnings in statin labeling, she said, in this trial, administration of rosvastatin had no adverse effects on cognitive function.

Effect of Evolocumab on Progression of Coronary Atherosclerosis in Statin-Treated Patients: A Placebo-Controlled Intravascular Ultrasound Trial

- Steven E. Nissen, MD, Cleveland Clinic, Cleveland, Ohio

Statins have been shown to slow progression or induce regression of coronary disease in proportion to the magnitude of low-density lipoprotein-cholesterol (LDL-C) reduction in intravascular ultrasound (IVUS) trials. The lowest LDL-C in these trials has been about 60 mg/dL. Dr. Nissen said in an AHA press conference. He further noted that proprotein convertase subtilisin/kexin type 9 (PCSK9) targets LDL receptors for degradation, reducing hepatic removal of LDL-C from blood. PCSK9 inhibitors induce large LDL-C reductions and, when added to statins, allow very low LDL-C levels to be reached. Effects on atheroma burden are unknown, however.

Evolocumab (Repatha, Amgen), a monoclonal antibody, is a PCSK9 inhibitor administered by subcutaneous injection. In the Global Assessment of Plaque Regression With a PCSK9 Antibody as Measured by Intravascular Ultrasound (GLAGOV) trial, 968 statin-treated patients with established coronary heart disease at 226 sites in 32 countries were randomized to evolocumab (420 mg monthly) or placebo for 78 weeks. GLAGOV is the first intravascular outcome trial testing the effects of a PCSK9 inhibitor on the regression or progression of coronary atherosclerosis as measured by intravascular ultrasound. All patients in GLAGOV underwent an IVUS examination of a single coronary artery during a clinically indicated angiogram at baseline and at study end. The primary efficacy endpoint was the nominal change in percent atheroma volume from baseline to the poststudy IVUS.

Mean patient age was 59.8 ± 9.2 years, and 72% of patients were male. Rates of current smoking and diabetes were 24.3% and 20.6%, respectively. Mean LDL-C was 92.6 ± 27.2 mg/dL, mean high-density lipoprotein-cholesterol was 46.0 ± 12.8 mg/dL, and median high sensitivity C-reactive protein was 1.61 mg/L.
Analysis showed steep reductions in LDL-C levels in the PCSK9 inhibitor arm after 78 weeks (from 90 mg/dL to 29 mg/dL; 59.8%). LDL-C levels in the placebo arm increased by 3.9%. The primary endpoint of percent atheroma volume increased by 0.05% in the statin plus placebo arm and decreased by 0.95% in the statin plus evolocumab arm (P < 0.0001). Similarly, total atheroma volume decreased by 0.9 (P = NS) with statin monotherapy and by 5.8 in the statin plus evolocumab arm (P < 0.0001). More patients in the statin plus evolocumab arm had atheroma regression than in the statin plus placebo arm (64% versus 47%; P < 0.0001).

“GLAGOV provides intriguing evidence that clinical benefits may extend to LDL-C levels as low as 20 mg/dL,” Dr. Nissen said, “and no safety issues were identified at the mean LDL-C level of 36.6 mg/dL.” He cautioned, however, that the modest sample size precludes firm safety conclusions, and large outcome trials for PCSK9 inhibitors are awaited. “Benefits of combination therapy in GLAGOV were observed in patients with baseline LDL-C below the lowest levels recommended by global guidelines (less than 70 mg/dL),” Dr. Nissen said.

**Rivaroxaban and Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategies In Patients With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention**

- C. Michael Gibson, MD, Beth Israel Deaconess Medical Center, Boston, Massachusetts

“Coronary artery disease and atrial fibrillation often occur together because of the strong association of both conditions with aging and overlapping risk factors,” Dr. Gibson said at an AHA press briefing. He further noted that among the more than 18,000 atrial fibrillation patients enrolled in the ARISTOTLE trial, 24.9% had undergone prior percutaneous coronary interventions (PCIs). Optimal management of atrial fibrillation and acute coronary syndromes differ, however. While warfarin is more effective for atrial fibrillation, the combination of aspirin and a thienopyridine is more effective in patients who have had coronary stents implanted, Dr. Gibson said.

Rivaroxaban (Xarelto, Janssen) has demonstrated efficacy in both acute coronary syndromes and atrial fibrillation. Rivaroxaban dosing for atrial fibrillation, however, is four times that used in PCI, where triple therapy using an oral anticoagulant plus dual antiplatelet therapy (DAPT) is typically administered. Prior randomized studies have suggested that a dual-pathway therapeutic approach using a factor Xa inhibitor and a single antiplatelet agent may be superior. The potential risk for clinically significant bleeding from combining DAPT with rivaroxaban remains uncertain, and the optimal combination and duration of therapy remain uncertain, Dr. Gibson observed.

The PIONEER AF-PCI trial was an open-label, randomized, controlled, multicenter study exploring two treatment strategies of rivaroxaban and a dose-adjusted oral vitamin K antagonist in patients with atrial fibrillation who underwent PCI. The trial tested whether rivaroxaban plus either a thienopyridine or DAPT would be associated with an increase in bleeding rates compared with standard-of-care triple therapy including a vitamin K antagonist among nonvalvular atrial fibrillation patients who undergo PCI with stent placement. The 12-month fixed-duration trial enrolled 2,124 patients in 26 countries at 426 sites. All had paroxysmal, persistent, or permanent nonvalvular atrial fibrillation and were undergoing PCI with stent placement. They were randomized in a 1:1:1 ratio to rivaroxaban 15 mg every day plus a thienopyridine for 12 months, rivaroxaban 2.5 mg twice daily (with stratification to a prespecified duration of DAPT for one, six, or 12 months), or dose-adjusted warfarin every day (with stratification to a prespecified duration of DAPT for one, six, or 12 months). The primary safety endpoint was clinically significant bleeding (measured by the Thrombolysis in Myocardial Infarction scale [major and minor bleeding] and whether bleeding required medical attention).

Dr. Gibson reported that clinically significant bleeding occurred in 26.7% of patients receiving warfarin plus DAPT. In rivaroxaban plus DAPT patients, the bleeding rate was 18.0% (P < 0.001 versus DAPT plus warfarin). For those receiving rivaroxaban plus a thienopyridine, the rate was 16.8%. The number needed to treat (NNT) to prevent one bleeding event for the latter versus warfarin was 11. Major bleeding rates for rivaroxaban plus a thienopyridine and warfarin plus DAPT were 2.1% and 3.3%, respectively (P = 0.234).

For the secondary endpoint of combined first occurrence of cardiovascular death, myocardial infarction, or stroke, rates were not significantly different among the three treatment arms (6.5% for rivaroxaban plus thienopyridine, 5.6% for rivaroxaban plus DAPT, and 6.0% for warfarin plus DAPT).

The rivaroxaban arms had reduced rates of all-cause death or hospitalization, with low NNTs to prevent one event (rivaroxaban plus thienopyridine, NNT = 15; rivaroxaban plus DAPT, NNT = 10).

“Among stented atrial fibrillation participants, administration of either rivaroxaban 15 mg daily plus a thienopyridine for one year or rivaroxaban 2.5 mg twice daily plus one, six, or 12 months of DAPT reduced the risk of clinically significant bleeding as compared with standard of care warfarin plus one, six, or 12 months of DAPT with comparable efficacy,” Dr. Gibson concluded.